Ophthalmic Plastic and Reconstructive Surgery
Vol. 21, No. 5, pp 383–404

Brief Reports

Primary Squamous Cell Carcinoma Arising From an Epithelium-Lined Cyst of the Lacrimal Gland

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Abstract: **A 66-year-old man presented with a slowly enlarging, nontender left orbital mass of 2 months' duration. CT and MRI showed a left lacrimal gland mass with enhancement and internal irregularity of cystic structures. Histopathologic analysis of the biopsy specimen revealed a squamous cell carcinoma arising from an epithelium-lined cyst. The patient underwent left orbital exenteration followed by radiation treatment. No evidence of tumor recurrence was observed after a follow-up of 30 months. We believe this primary squamous cell carcinoma may have arisen either from preexisting lacrimal duct cyst (dacryops) with areas of squamous metaplasia or, less likely, from a choristomatous epithelium-lined cyst of the lacrimal gland. Although rare, this entity should be included in the differential diagnosis of cystic lesions of the lacrimal gland.**

Squamous cell carcinoma (SCC) is a rare neoplasm of the lacrimal gland, accounting for less than 2% of primary malignant epithelial tumors.[1] In most reported cases, it arises from the malignant transformation of a pleomorphic adenoma (benign mixed tumor).[2–7] Well-documented cases demonstrating features of pure SCC arising from the lacrimal gland are rare.[8] We describe the clinical, radiologic, and histopathologic findings of a primary SCC arising from an epithelium-lined cyst within the lacrimal gland.

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Accepted for publication March 21, 2005.

Supported in part by grants from the Retina Research Foundation, Houston, Texas, and Research to Prevent Blindness, Inc., New York, New York. Dr. Font is the recipient of the Senior Investigator Award from Research to Prevent Blindness, Inc., New York, New York.

Presented at the 35th Annual American Society of Ophthalmic Plastic and Reconstructive Surgery 2004 Symposium, New Orleans, Louisiana, October 22 to 23, 2004.

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DOI: 10.1097/01.iop.0000176263.07921.22

CASE REPORT

A 66-year-old man complained of double vision of 9 months' duration after cataract surgery of the left eye. He also noted a slowly enlarging mass of 2 months' duration in the upper lateral aspect of his left orbit. The patient reported a sense of orbital pressure but had no pain. Ocular history was significant for uncomplicated cataract surgery in both eyes. There was no history of penetrating ocular trauma, infection, or radiation treatment. The medical history was significant for excision of several cutaneous basal cell and squamous cell carcinomas of his extremities. There was no clinical evidence of basal cell nevus/Gorlin syndrome or Bazex syndrome and no family history of cancer.

Best-corrected visual acuity was 20/20 OU. There was a 1-cm, nontender, soft tissue mass in the left upper eyelid and lateral orbit (Fig. 1). Exophthalmometry readings were 14 mm OD and 17 mm OS. Extraocular movements showed marked limitation of elevation and abduction OS. No palpable lymphadenopathy was present. The remainder of his ocular examination, including slit-lamp and dilated ophthalmoscopic examination, was normal.

CT revealed a left lateral orbital mass without involvement of bone. MRI demonstrated a mass lesion centered in the region of the left lacrimal gland measuring 2.5 × 2.5 × 1.5 cm in greatest dimensions (Fig. 2). On T_1-weighted imaging, the lesion showed low signal intensity and was isointense to muscle or gland parenchyma. On T_2-weighted imaging, the lesion was heterogenous, with areas of hyperintense signal. Gadolinium contrast imaging showed enhancement of the lesion with tiny areas of nonenhancement, consistent with either cystic changes or necrosis. The margins of the lesion were ill-defined, with local infiltration of the extraconal fat. The mass molded itself along the temporal margin of the globe, which was slightly displaced medially. The lesion merged with the insertion of the lateral rectus muscle. No extension in the temporalis muscle was noted. The bone structures appeared intact. MRI of the brain was normal. Metastatic workup, including bone scans and CT of the head, neck, chest, abdomen, and pelvis, were unremarkable.

The patient underwent excisional biopsy of the left lacrimal gland, and the frozen sections revealed an epithelial lacrimal gland tumor. The lacrimal gland was excised, but residual tumor was present at the posterior orbital margin and was not resectable due to its posterior location. The initial anatomic pathology was an infiltrating moderately well-differentiated SCC of the lacrimal gland. Due to the diagnosis and residual tumor, which

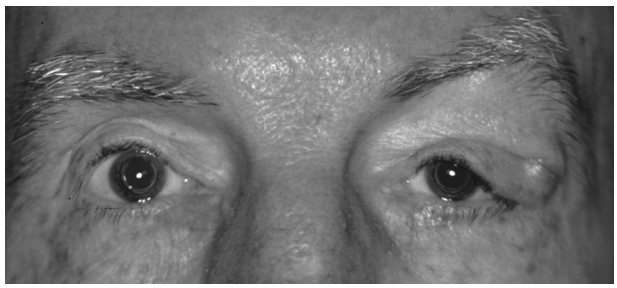

FIG. 1. Mass involving the left lacrimal gland region causes an S-shaped deformity of the left upper eyelid.

was not resectable with clear margins, a subsequent orbital exenteration was performed. The bone from the superior orbital rim lateral to the superior orbital neurovascular complex and extending to the lateral canthus was resected. The entire orbit was exenterated en bloc. The final pathology margins were free of tumor. The patient subsequently underwent radiation treatment and was reported to be alive and well without evidence of recurrence 30 months after initial surgery.

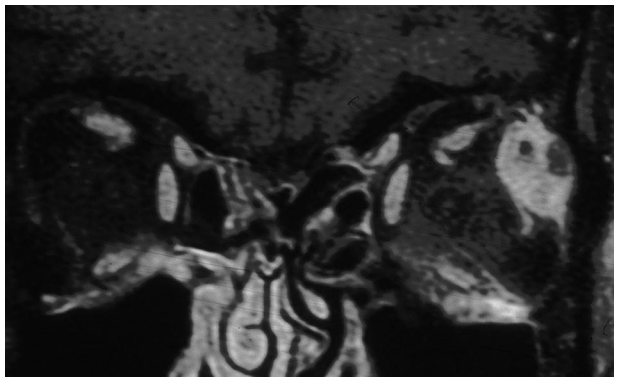

FIG. 2. Coronal MRI shows a mass with several cystic areas involving the lacrimal gland.

Pathologic Findings

Histopathologic examination revealed a chronic sclerosing dacryoadenitis and areas of lymphoid hyperplasia associated with infiltrating islands of moderately well-differentiated SCC arising from an epithelium-lined, multiloculated cyst (Fig. 3). Immunohistochemical markers for pankeratin demonstrated that the tumor cells were moderately immunoreactive. Islands of invasive squamous cell carcinoma were located adjacent to the inflamed lacrimal gland (Fig. 4). In some areas, the tumor was well keratinized and formed masses of keratin pearls. No evidence of a preexisting benign mixed tumor of the lacrimal gland was present. On the basis of the exenteration specimen, all surgical margins were tumor-free.

DISCUSSION

Squamous cell carcinoma is a rare neoplasm of the lacrimal gland and may be either primary or secondary in origin. Primary SCC may arise from squamous transformation in a pleomorphic adenoma (benign mixed tumor). In addition, primary SCC may develop from the malignant degeneration of epithelium-lined cysts, including lacrimal duct cysts (dacryops) and choristomatous cysts. SCC may also occur secondarily from postsurgical or posttraumatic implantation cysts and metastatic spread to the lacrimal gland.

In our case, we believe the SCC probably resulted from the malignant transformation of either preexisting lacrimal duct cyst (dacryops) or, less likely, from a choristomatous epithelium-lined cyst. The cyst may have developed in association with chronic nongranulomatous dacryoadenitis, where the inflammatory process led to ductal ectasia and squamous metaplasia of the ductal elements. Invasive SCC developed from the malignant degeneration of the squamous-lined cyst. Alternatively, the SCC may have resulted from the malignant transformation of a choristomatous epithelium-lined cyst. Al-

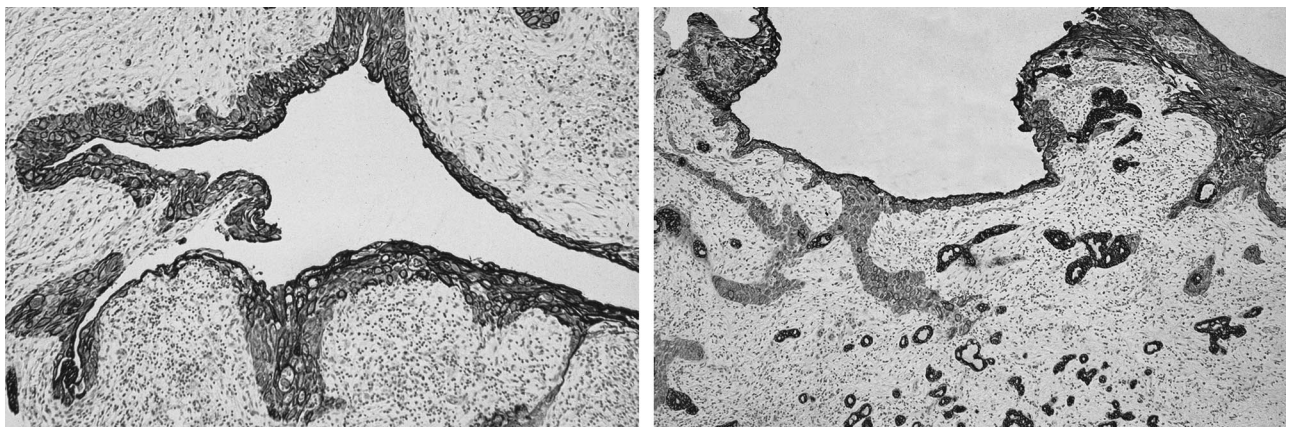

FIG. 3. Left, Epithelial cyst lined by stratified squamous epithelium (pankeratin, magnification 26). Right, Another epithelium-lined cyst with infiltrating cords of squamous cell carcinoma originating from cyst walls (pankeratin, magnification 16).

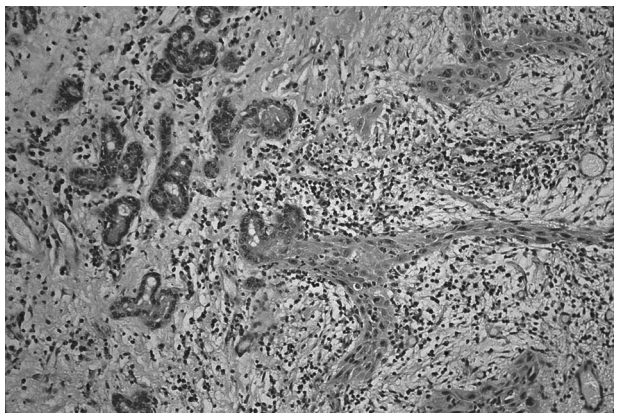

FIG. 4. Chronic dacryoadenitis with remnants of an inflamed lacrimal gland (on left) merging with infiltrating epithelial lobules of a moderately well-differentiated squamous cell carcinoma (hematoxylin and eosin stain, magnification 40×).

though uncommon, several well-documented cases of invasive SCC arising from choristomatous cysts of the orbit have been reported.[9]

Given the history of cutaneous squamous cell skin carcinoma, direct or metastatic extension may have occurred. However, there were no histopathologic or radiographic data to support this process. An extensive metastatic workup was also negative. The patient had no history of penetrating trauma or orbital surgery to suggest the possibility of epithelial implantation. Furthermore, no evidence of a pleomorphic adenoma (benign mixed tumor) of the lacrimal gland was found on histopathologic examination.

Primary epithelial tumors of the lacrimal gland exhibiting only malignant squamous elements are exceedingly rare, with only one other well-documented case reported. Fenton et al.[8] described an 80-year-old woman who presented with an 8-month history of painless progressive proptosis of the left eye. CT revealed a left-sided lacrimal gland mass without bony erosion. Surgical excision of the tumor revealed a poorly differentiated invasive SCC of the lacrimal gland, arising from a cyst lined by dysplastic squamous epithelium. No evidence of a pleomorphic adenoma (benign mixed tumor) or metastatic process was present. Given the incomplete excision, the patient subsequently received postoperative radiation treatment. In this case,[8] follow-up of 20 months showed no evidence of recurrence.

Although rare, malignant degeneration of epithelial cysts should be considered in the differential diagnosis of cystic lesions of the lacrimal gland. Primary SCC arising from the malignant degeneration of epithelial cysts may not exhibit the characteristic signs of malignant epithelial tumors of the lacrimal gland, such as pain and bony erosion. Surgical excision followed by radiation therapy may play an important role in the treatment of primary SCC of the lacrimal gland.

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Orbital Peripheral T-Cell Lymphoma in a Child

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Abstract: **A 6-year-old boy with known peripheral T-cell lymphoma had progressive left periorbital swelling and CT findings consistent with abscess or necrosis. Biopsy revealed peripheral T-cell lymphoma and associated necrosis involving the lacrimal gland and surrounding orbital tissue. Immunohistochemical and T-cell receptor gene rearrangement studies confirmed the diagnosis. The patient responded to local radiation and systemic chemotherapy. This is the first pathologically confirmed case of orbital peripheral T-cell lymphoma with subpanniculitic features.**

Peripheral T-cell lymphomas (PTCL) are characterized by infiltrates of malignant cells whose immunophenotypes mimic mature T cells.[1] These lymphomas comprise a wide variety of entities distinguished from one another by their clinical and pathologic features. Involvement of extranodal sites, including skin, is a common feature of PTCL.[1] Ocular manifestations of PTCL are rare and occur almost exclusively in adults, in whom the eyelid is the most commonly involved.[2,3]

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Accepted for publication March 18, 2005.

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DOI: 10.1097/01.iop.0000176264.30697.02

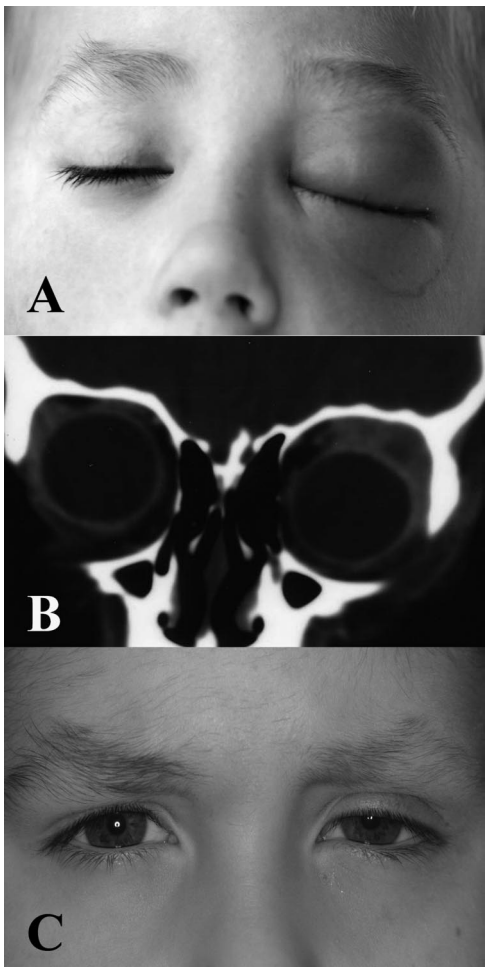

FIG. 1. **A,** Six-year-old boy with acute left periorbital swelling; **B,** coronal CT image with superolateral infiltrate containing central lucency; **C,** reduced left periorbital swelling after radiotherapy and chemotherapy.

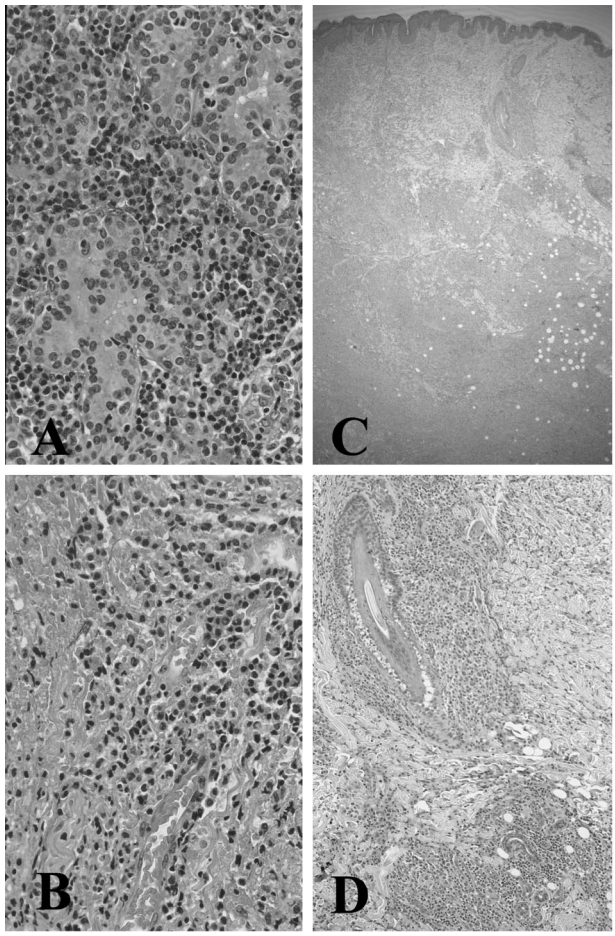

FIG. 2. **A,** Lacrimal gland infiltrated by malignant T-lymphocytes; **B,** orbital tissue with necrosis and malignant lymphocytic infiltrate (hematoxylin and eosin stain; magnification 200×); **C,** skin biopsy demonstrating diffuse dermal and subdermal fat SPTCL infiltrates (hematoxylin and eosin stain; magnification 25×); **D,** subdermal fat and periadnexal infiltrates of SPTCL in skin biopsy (hematoxylin and eosin stain; magnification 100×).

Subcutaneous panniculitis-like T-cell lymphoma (SPTCL) is a type of primary extranodal PTCL that has not been histopathologically documented in the orbit. We report the only documented case of orbital involvement by SPTCL.

CASE REPORT

In August 2002, a 6-year-old boy with known PTCL involving the skin and subcutaneous tissues was referred for evaluation of left periorbital swelling characterized by diffuse redness and pain (Fig. 1). His immunocompromise by weekly vinblastine treatment raised the possibility of orbital cellulitis, even though his involvement resembled his other PTCL lesions. CT revealed preseptal and superolateral orbital infiltrates that involved the lacrimal gland and molded to the eye (Fig. 1). The lucent areas within the infiltrate were consistent with necrosis or abscess. An orbital biopsy was performed.

Histopathology revealed diffuse infiltration of lacrimal gland tissue by neoplastic, large lymphocytes and a polymorphous infiltrate of T -cells, B cells, histiocytes, and plasma cells (Fig. 2A). The periglandular orbital connective tissue revealed extensive necrosis and hemorrhage with an infiltrate consisting almost exclusively of neoplastic lymphocytes, without abscess formation (Fig. 2B). Immunohistochemistry of lacrimal gland tissue demonstrated numerous CD3- and CD43-positive neoplastic T cells and modest numbers of B cells staining with CD20 and CD79a antibodies. The periglandular, partially necrotic orbital tissue also contained numerous neoplastic CD3- and CD43-positive T cells but no CD20- or CD79a-positive B cells. Polymerase chain reaction of the specimen revealed T-cell receptor-γ (TCR-γ) gene rearrangement. There was no immunoreactivity for Epstein-Barr small nuclear RNA (EBER), CD30/Ki-1, or CD56/CD57 nuclear killer cell markers.

To confirm that the orbital lymphoma was a manifes-

tation of PTCL, previous skin biopsies were reviewed. At age 23 months, as the first manifestation of his disease, persistent, painful, red nodules appeared over the course of 2 months. Biopsy specimens of these lesions were used to diagnose PTCL. Histopathology revealed large neoplastic cells with convoluted nuclei and intermingled, numerous benign histiocytes. The neoplastic cells spared the epidermis and were present in large aggregates with massive extension in subdermal fat (Fig. 2C). The neoplastic cells congregated around skin appendages and blood vessels (Fig. 2D). Immunohistochemistry confirmed CD3 and CD43 tumor cell positivity and CD68 positivity of intermingled histiocytes. Rare CD20 or CD79a stained B cells were present. Concurrent chest wall masses were present at the time of initial diagnosis, but no lymph node or bone marrow involvement was ever documented. Vinblastine induced tumor regression, and an autologous peripheral stem cell transplant was performed but failed due to persistent subclinical disease. Subsequent clinically evident tumor recurrence required weekly maintenance vinblastine therapy to control PTCL.

After the diagnosis of orbital SPTCL, radiation therapy (36 Gy) was used to eradicate the lymphoma. Subsequent systemic pentostatin (10 cycles of 5 mg/m^2 given daily, for 3 days, every 3 weeks) treatment, initiated to address his residual systemic disease, resolved his orbital and skin manifestations (Fig. 1). His disease has remained under control for 2.5 years after this regimen. His left eye exhibits mild enophthalmos and a deep superior sulcus.

DISCUSSION

Peripheral T-cell lymphomas account for up to 20% of non-Hodgkin lymphomas in children.[4] This heterogenous group of T-cell lymphomas includes those with chiefly extranodal skin manifestations.[4] Nevertheless, a distinctive subtype of PTCL, SPTCL,[1] is rare in children and has only been reported in the orbit once.[5] In that case, the presumed diagnosis of orbital SPTCL was based on skin biopsy and CT detection of a mass in the lacrimal gland region. To our knowledge, this is the first pathologically confirmed case of orbital SPTCL.

Our pathologic findings of the orbital specimen were characteristic of SPTCL (Fig. 2), including the presence of necrosis, infiltration by large, malignant T cells, and TCR-γ gene rearrangement.[6] Inasmuch as the clinical presentation of the lesion resembled the patient's other SPTCL lesions and the orbital biopsy was beneath the dermis, his periocular involvement was subpanniculitic, meeting the criteria for SPTCL. The skin biopsy specimens also demonstrated SPTCL characteristics reported in children, namely, periappendiceal and perivascular tumor cell aggregates, diffuse involvement of subdermal fat, and permeation of the tumor cell aggregates by numerous CD68$^+$ histiocytes.[6] As in other cases of SPTCL, our case was not immunoreactive for Epstein-Barr small nuclear RNA (EBER), CD30/Ki-1, or CD56/CD57 nuclear killer cell markers.[6]

The clinical and radiologic differential diagnosis in our case included orbital cellulitis/abscess, whose CT findings may mimic the necrosis due to SPTCL. Biopsy of the involved tissue, however, showed only malignant T cells in areas of necrosis, inconsistent with an infectious pathology. It is likely that the necrosis associated with SPTCL was at least partially responsible for the enophthalmos and deep superior sulcus.

The clinical course of SPTCL is varied, ranging from rapidly progressive and fatal to protracted and recurrent.[5] Our patient has survived 6 years since presentation with a chronic, recurring course controlled by systemic chemotherapy and local radiation. However, he failed bone marrow transplantation, which has been advocated.[5]

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Superior Ophthalmic Vein Thrombosis in a Patient With Dacryocystitis-Induced Orbital Cellulitis

Nicholas J. Schmitt, M.D., Randall L. Beatty, M.D., and John S. Kennerdell, M.D.

Abstract: **A 71-year-old-man presented with chronic left-sided epiphora and a 5-day history of progressive left orbital swelling that had started with a "bump"**

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Accepted for publication March 2, 2005.

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DOI: 10.1097/01.iop.0000176269.84949.96

on the left side of his nose. Orbital CT revealed left-sided preseptal and postseptal inflammation, along with marked thickening of the left superior ophthalmic vein. Orbital MRI with gadolinium enhancement and fat suppression revealed a low-intensity signal in the left superior ophthalmic vein, consistent with a superior ophthalmic vein thrombosis. There was no cavernous sinus involvement. A diagnosis was made of left-sided dacryocystitis-induced orbital cellulitis and superior ophthalmic vein thrombosis. Treatment consisted of intravenous vancomycin, followed by early dacryocystorhinostomy and postoperative intravenous dexamethasone. Anticoagulation was not used. Within 1 week after surgery, the orbital congestion had dramatically improved. Though rare, isolated superior ophthalmic vein thrombosis can be a harbinger of cavernous sinus thrombosis; therefore, early detection is the key to avoiding cavernous sinus thrombosis.

Isolated septic superior ophthalmic vein thrombosis (SOVT) is uncommon in the literature.[1–4] To our knowledge, SOVT in the setting of dacryocystitis-induced orbital cellulitis has not been reported. In an estimated 33% to 75% of cases, septic SOVT may lead to cavernous sinus thrombosis,[2] a potentially lethal complication with a mortality rate of approximately 20%.[1] Thus, early detection of SOVT is the key to avoiding cavernous sinus thrombosis.

Clinical differentiation of SOVT from orbital cellulitis is difficult and usually is made only after imaging the orbit. CT typically reveals an enlarged superior ophthalmic vein as a dilated tubular S-shaped image just inferior to the superior rectus and levator complex.[3] MRI is currently the radiologic test of choice for confirming SOVT because it is able to detect all stages of thrombus formation.[2] Magnetic resonance venography and orbital color Doppler imaging with ultrasound offer noninvasive vascular flow information, which may also confirm SOVT.[2,4]

CASE REPORT

An otherwise healthy 71-year-old white man presented to his doctor's office with a history of chronic left-sided epiphora and a 5-day history of progressive left periorbital swelling that had started with a "bump" on the left side of his nose. The patient was admitted to an outlying hospital for left-sided orbital cellulitis and was transferred to our institution the same day for worsening condition.

On initial examination, the patient was hemodynamically stable and afebrile. Best corrected visual acuity was 20/50 OD and counting fingers OS. External examination revealed left-sided periorbital ecchymosis and edema with a painful nodule over the left lacrimal sac; 5 mm of left-sided proptosis, marked resistance to retropulsion, and limited motility were also present. There was no relative afferent pupillary defect. Tonometry by applanation revealed intraocular pressures of 18 mm Hg OD and 55 mm Hg OS. Anterior segment and dilated fundus examinations were normal. CT of the orbits revealed left-sided preseptal and postseptal inflammation, along with marked thickening of the left superior ophthalmic vein (Fig. 1). Orbital MRI with gadolinium enhancement and fat suppression revealed a low-intensity signal in the left superior ophthalmic vein, consistent with a superior ophthalmic vein thrombosis (Fig. 2). There was no cavernous sinus involvement. Blood cultures grew out methicillin-resistant *Staphylococcus aureus*.

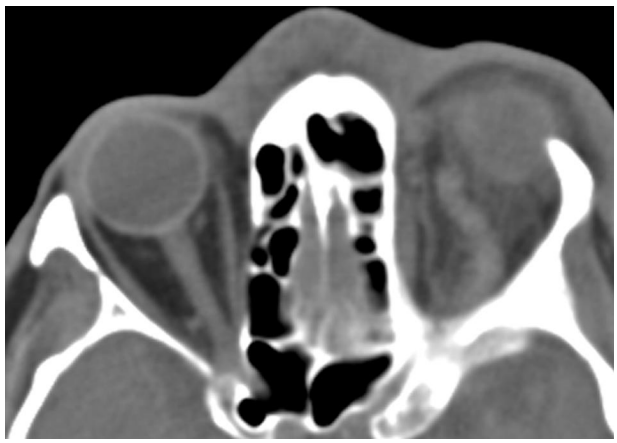

FIG. 1. Orbital CT with left-sided orbital inflammation and dilated superior ophthalmic vein.

Treatment was initiated with intravenous vancomycin on hospital day 1, followed by a left-sided dacryocystorhinostomy on hospital day 3. Postoperative intravenous dexamethasone dramatically reduced the periocular swelling and improved extraocular movements. Anticoagulation was not used. Topical aqueous suppressants and oral acetazolamide adequately controlled the elevated intraocular pressure. The patient was discharged on

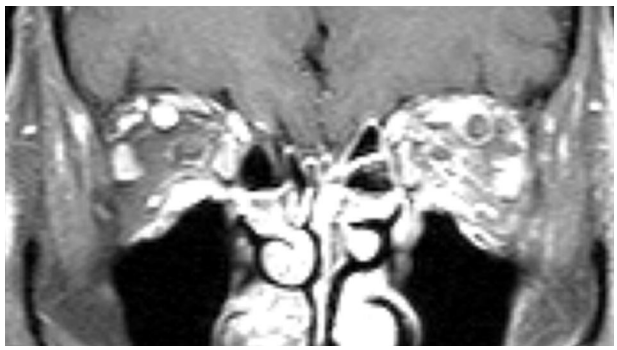

FIG. 2. MRI with gadolinium contrast and fat suppression showing a low-intensity signal within the left superior ophthalmic vein.

hospital day 8 with a peripherally inserted central catheter for home vancomycin therapy. Follow-up at 1 week revealed visual acuity of 20/25 OU, no afferent defect, minimal periocular swelling, near-normal resistance to retropulsion, and full motility.

DISCUSSION

Isolated septic SOVT is rare[1–4] and may be a harbinger of cavernous sinus thrombosis.[1–3] Clinical signs include unilateral chemosis, proptosis, limited ocular motility, and, typically, an unremarkable fundus examination.[3] In this case, an SOVT was suspected after a dilated superior ophthalmic vein was shown on CT. SOVT was confirmed on postcontrast MRI with fat suppression, which revealed a low-intensity signal within the superior ophthalmic vein. There was no cavernous sinus involvement.

The exact pathogenesis of SOVT is unclear. Orbital congestion may incite an inflammatory procoagulant cascade that culminates in thrombophlebitis with thrombus formation; alternatively, it may be due to direct vascular invasion by the pathogen.[2] Offending bacteria may be aerobic or anaerobic, with *S. aureus* and anaerobic streptococci being the most common organisms.[3]

The traditional treatment of septic SOVT consists primarily of aggressive antibiotic therapy.[1] Theoretically, corticosteroids may reduce the inflammatory procoagulant cascade. However, their use is supported only anecdotally[2] or is not recommended.[1] The role of anticoagulation is unclear.[1–3] Although anticoagulants have proved successful in the treatment of septic thrombophlebitis in other body areas,[3] there are no controlled studies of the use of anticoagulants in treating SOVT.[1] Although life-threatening hemorrhage associated with anticoagulant therapy is rare, fatal retroperitoneal hemorrhage associated with heparin treatment of a septic SOVT has been reported.[3]

In this case, an underlying dacryocystitis was thought to be the cause of the orbital cellulitis and SOVT. Therefore, dacryocystorhinostomy was performed early in the hospital course. We postulate that targeted antibiotic therapy, early dacryocystorhinostomy, and postoperative corticosteroids without anticoagulation proved successful in the treatment of an isolated septic SOVT while avoiding a potential septic cavernous sinus thrombosis in this patient.

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Massive Subcutaneous Emphysema Mimicking Necrotizing Fasciitis After Dacryocystorhinostomy

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Abstract: **We present a case of massive subcutaneous emphysema mimicking necrotizing fasciitis after uncomplicated dacryocystorhinostomy surgery. Subcutaneous emphysema progressing down fascial planes of the head and neck after dacryocystorhinostomy has not been reported in the literature. Using the clinical presentation and radiographic imaging, we briefly review the underlying cause of subcutaneous emphysema after dacryocystorhinostomy.**

Subcutaneous air of the eyelids and face is rarely seen in the postoperative setting. Orbital emphysema is seen commonly, especially after trauma to the orbital floor or medial wall.[1] Isolated reports of orbital emphysema have also been noted after dental procedures.[2] We present a case of subcutaneous emphysema after dacryocystorhinostomy (DCR) that involved the eyelids, face, and neck in a manner mimicking necrotizing fasciitis.

CASE REPORT

A 43-year-old woman with a history of diabetes and chronic obstructive pulmonary disease (COPD) was referred to the emergency room by an outside physician with the diagnosis of necrotizing fasciitis. She had severe pain in her right jaw, difficulty chewing, and eyelid swelling. The patient had undergone uncomplicated DCR by the senior author the day before presentation. Several hours after discharge from the hospital, she began to have severe emesis and coughing.

On examination, uncorrected visual acuity was 20/20 OU. The patient was noted to have severe swelling and crepitus of the right side of her face. One hour later, the subcutaneous emphysema had advanced down to the base of her neck. There was no erythema, tissue necrosis, or discoloration of the skin. CT of the head and neck (Figs. 1 and 2) showed significant subcutaneous emphysema extending from the orbit down through the face and in the neck. No focal abscess was noted.

The patient was admitted to the hospital for observation. She was placed on antiemetics and told to avoid blowing her nose. She was also given two doses of clindamycin. After observation for 1 night, the patient was discharged. Over the next 2 weeks, the subcutaneous

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Accepted for publication March 7, 2005.
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DOI: 10.1097/01.iop.0000176267.81599.d8

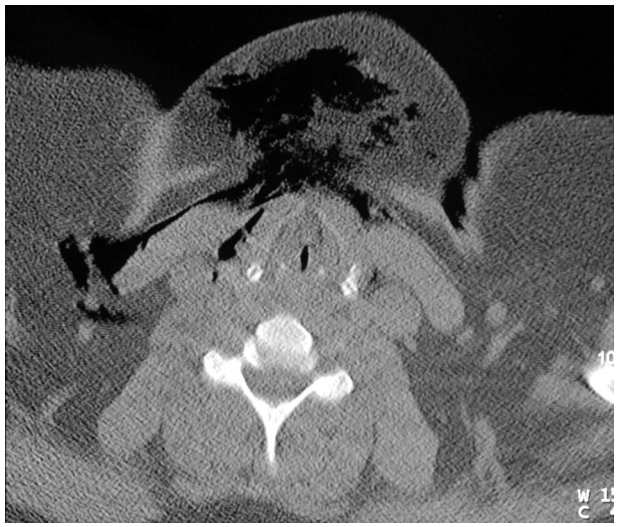

FIG. 1. CT of neck (axial view). Subcutaneous emphysema in neck noted at C6 vertebra.

emphysema resolved completely. The patient has been completely asymptomatic since that time.

DISCUSSION

Orbital emphysema has been described in several settings. Most commonly, it is encountered after orbital blowout and medial wall fractures. Occasionally, orbital emphysema can progress to subcutaneous emphysema. Although trauma is the most common source of subcutaneous emphysema, there are a few postoperative cases described in the literature, including after DCR.[3]

Necrotizing fasciitis is a progressive, rapidly spreading, inflammatory infection located in the deep fascia, with secondary necrosis of the subcutaneous tissues. The presence of gas-forming bacteria results in subcutaneous air, which can be appreciated both clinically and radiographically. The speed of spread is directly proportional to the thickness of the subcutaneous layer. The causative bacteria is typically group A *Streptococcus* but may be aerobic, anaerobic, or mixed flora. These infections can be difficult to recognize in their early stages, but they rapidly progress. They require early aggressive treatment to combat the associated high morbidity and mortality rates.

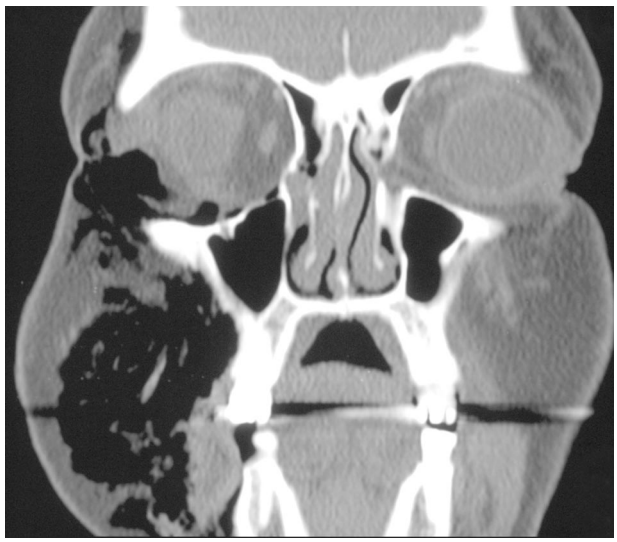

FIG. 2. CT of the head (coronal view). A large area of subcutaneous air can be visualized within the orbit and extending down in face.

Wojno and Walter[3] described a patient who had subcutaneous emphysema and crepitus of the eyelids after DCR. The patient had laryngospasm after surgery and required manual ventilation with a face mask. In this case, the high positive pressure used to overcome the laryngospasm forced air into the nasal cavity and through the DCR ostium, resulting in a high enough pressure to cause subcutaneous emphysema. As in our case, this patient responded well to bed rest and avoidance of nose blowing, sneezing, or strenuous activity. No permanent sequelae were noted by the investigators.

Katz et al.[4] described a series of patients who had postanesthesia orbital emphysema after orbital decompression. They noted that patients with a history of emphysema were most likely to have bouts of coughing and Valsalva maneuvers resulting in acute orbital emphysema. However, none of the patients in this series had long-term visual complications.

The fascial layers of the face are collectively known as the superficial musculoaponeurotic system (SMAS). The SMAS divides the subcutaneous fat into two layers. It contains fibrous septae that extend through the fat and attach to the overlying dermis. The SMAS extends from the malar region superiorly to become continuous with the galea, inferiorly to become part of the platysma, and laterally to invest in the parotid fascia over the parotid gland.[5]

After DCR, patients are instructed to avoid activities such as nose-blowing that create positive pressure in the nasal cavity. In our patient's case, repeated retching due to general anesthesia and poorly controlled emphysema led to high positive pressure through the DCR ostium and in the subcutaneous tissues. The SMAS then provided a pathway for the air to dissect down the face and in the neck. A one-way "valve" was thus created, allowing increasing amounts of air to accumulate in the tissues. The cycle was broken by antiemetics and bed rest and the "valve" was allowed to close spontaneously. Bacteria, like subcutaneous air, can also track along the SMAS. Confusion with necrotizing fasciitis by the referring physician is therefore understandable in this case.

We are not aware of any other published report of subcutaneous emphysema of this magnitude after DCR. Although it is a rare event, ophthalmologists should be aware of the potential for subcutaneous emphysema after

DCR surgery. Equally important, however, is to rule out infection by gas-producing bacteria. Careful monitoring and supportive care of the patient with massive subcutaneous emphysema is usually all that is needed. If an infection is suspected, appropriate treatment with antibiotics is warranted.

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"Pseudo-pseudochalazion": Giant Chalazion Mimicking Eyelid Neoplasm

Lily Koo, M.D., Mark P. Hatton, M.D., and Peter A. D. Rubin, M.D.

Abstract: **A 33-year-old man presented with a solid lesion encompassing the entire left upper eyelid. Multiple biopsies revealed lipogranuloma consistent with chalazion. The induration resolved after multiple triamcinolone injections. This is the only case report to our knowledge of a chalazion that involved the entire upper eyelid.**

CASE REPORT

A 33-year-old man presented to an outside ophthalmologist with a 3-week history of a left upper eyelid lesion that did not improve with warm compress application. He was diagnosed with a "large chalazion" of the left upper eyelid and underwent incision and curettage. After the procedure, he used fluorometholone and erythromycin ointment for 5 days. He returned 2 weeks later with increased swelling and erythema of the left upper eyelid and was prescribed multiple courses of antibiotics including oral cephalexin, amoxicillin/clavulanate, and intravenous gatifloxacin. Despite 3 weeks of antibiotic therapy, the eyelid fullness did not resolve. CT revealed no fluid collection or abscess of the eyelid. He was then referred to our institution.

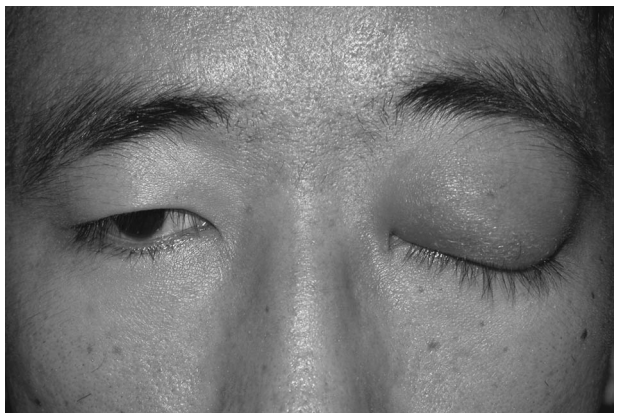

FIG. 1. External photograph at presentation demonstrating ptosis and edema of the left upper eyelid.

Our initial examination revealed normal visual acuities and extraocular motility OU. There was complete ptosis OS with no measurable levator function. External examination revealed fullness of the entire left upper eyelid without overlying skin erythema or edema (Fig. 1). On palpation, there was a firm mass encompassing the entire left upper eyelid. There was no regional lymphadenopathy. There was no evidence of meibomitis, blepharitis, or dermatitis. The remainder of the anterior segment and dilated fundus examinations were unremarkable.

Given the concern of possible malignancy, the patient underwent transconjunctival biopsy of the lesion. At surgery, a dense, solid, nondraining mass was encountered. When frozen-section pathology demonstrated lipogranuloma consistent with chalazion, an additional external biopsy was performed in search of neoplastic tissue (Fig. 2). These biopsies also confirmed the diagnosis of chalazion. Acid-fast bacilli and Giemsa staining were

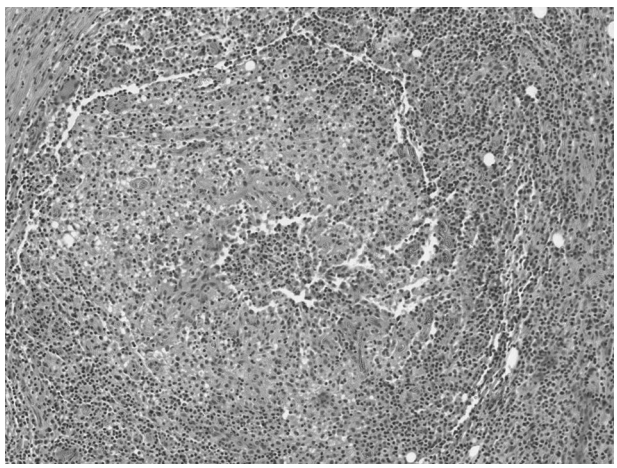

FIG. 2. Histopathology demonstrating lipogranuloma.

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Accepted for publication March 11, 2005.

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DOI: 10.1097/01.iop.0000176266.14388.6b

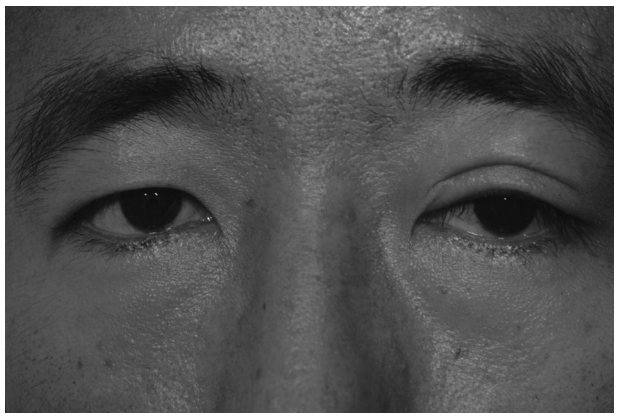

FIG. 3. External photograph 3 months after steroid injections demonstrating improvement of the edema and ptosis.

negative. The patient was started on a course of oral prednisone 1 month after biopsy. Systemic complications (anxiety) limited the dosing to 11 days. There was mild improvement in the left upper eyelid fullness while the patient was taking prednisone. The patient was tried on oral ibuprofen without effect. Two months after presentation, 20 mg triamcinolone acetonide was injected in the left upper eyelid, which resulted in moderate reduction of the fullness of the upper eyelid. He received repeat injections of triamcinolone acetonide (40 mg) across the length of the eyelid 4 months and 14 months after the initial injection, resulting in further improvement. As the swelling resolved, a small, deep nodule was palpable in the eyelid. This was excised 7 months after the last steroid injection, and pathology was consistent with chalazion. There was no further swelling noted at last follow-up, 1 month after surgery (Fig. 3).

DISCUSSION

Given the atypical mass enlargement of the upper eyelid after incision and curettage of what appeared to be an ordinary chalazion, it was obvious to us to pursue histopathologic examination of the eyelid mass to rule out entities that masquerade as chalazia, the most important of these being neoplastic.

Sebaceous carcinoma is most frequently misdiagnosed clinically and histopathologically. It can present as an eyelid mass, recurrent chalazion, or diffuse unilateral blepharoconjunctivitis, and it is important to examine each layer of the eyelid histologically, as was done in this case. One study reported 50% cases misdiagnosed.[1] Although rare, it can be highly malignant, infiltrative, and metastasize and has an associated mortality rate of 22% to 30%.[2]

Other diagnoses documented in the literature that can appear to be chalazia are Merkel cell tumor of eyelid,[3] cutaneous leishmaniasis,[4] tuberculosis,[5] sarcoid,[6] metastases,[7] eosinophilic granuloma,[8] and pilomatrixoma.[9] These diagnoses are rare, and most of these causes can be ruled out by histopathology.

Once the diagnosis of lipogranuloma was confirmed with histopathology, it became an unusual problem to treat, given the size of the lesion and that it had grown in size after incision and curettage. The patient was tried on oral prednisone, and, although improved, could not tolerate the systemic side effects. The lesion was then injected with triamcinolone acetonide. There have been many successful reports with intralesional injection of triamcinolone acetonide of chalazia. Mohan et al.[10] had a success rate of 92.3% in 110 cases. Knowing the enormity of this patient's lesion, surgical management would have resulted in permanent disfigurement of the eyelid; thus, nonsurgical methods were pursued.

Although the histology was consistent with chalazion, the presentation was not. Given the absence of eyelid marginal inflammation, blepharitis, or other signs of inflammation in the eyelids, lack of prior chalazia, and poor response to antibiotic therapy, the leading diagnostic possibilities in this case were neoplastic, but other infectious entities could not be excluded. The excellent response to steroid injections, typical of lipogranuloma and characteristic of chalazia, favor a primary inflammatory lesion. The immense size of this lesion remains an enigma, and we could find no similar cases in the literature.

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Intraconal Grease-Gun Injury: A Therapeutic Dilemma

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Fernando Chahud, M.D.§

Abstract: **The case of a 31-year-old man with an accidental grease-gun injury to his left orbital region is presented. CT and MRI showed a well-delineated intraconal cyst in the superior aspect of the left orbit surrounded by a significant inflammatory response. The patient was followed for 11 months. Diplopia was not reported at any time, and visual acuity, visual fields, and all other examinations remained normal. Uneventful surgical removal was performed at the patient's request. Histopathologic examination demonstrated a typical picture of lipogranulomatous inflammation. In a review of the accessible literature, only four cases of intraorbital grease-gun injuries were detected; all of them submitted to early surgical removal. We conclude, however, that an intraconal oil/grease cyst can be carefully monitored and—in the absence of symptoms—must not necessarily be removed.**

Lubricants include a wide variety of substances such as materials designed to reduce friction between moving surfaces or electric insulation, mold-removing agents, hydraulic fluids, coolants, and so forth. The term grease means a lubricant in gel form containing a base oil lubricant and a gelling agent. Grease-guns are habitually used in heavy duty industry for lubrication of rotating parts. High-pressure injuries from grease-guns have been reported in various parts of the body including hands, genitals, and, in rare instances, in the eye and its adnexa.[1–3] Among the wide variety of orbital foreign bodies, oil is the least reported. Its tolerance for extended periods of time is unknown. We report a case of an intraconal grease-gun injury that was followed for 11 months without visual loss or other symptoms. Surgical removal was performed at the patient's request.

CASE REPORT

A 31-year-old worker was referred to our hospital after an accidental occupational injury from a grease-gun to his left orbital region 3 days earlier. On presentation, he complained of pain and reduced visual acuity OS. Marked edema of the upper and lower eyelids was noted. A laceration on the upper eyelid appeared to be clean and to have been adequately closed with sutures.

Biomicroscopy revealed cells in the anterior chamber. Fundus examination disclosed peripheral vitreous hemorrhage and retinal edema in the inferior temporal quadrant. Ocular motility was norma, and no diplopia was reported. Visual acuity was 20/40 OS and 20/20 OD. Intraocular pressure could not be measured. All other examinations were normal. The working diagnosis was eyelid laceration with blunt trauma of the globe. The patient was treated with steroid and antibiotic eye drops. Intraocular symptoms improved quickly, with full visual acuity being reached after 6 weeks and clearing of the vitreous hemorrhage after 11 weeks.

Orbital CT 1 month after the accident showed a large cyst located in the anterior portion of the intraconal space between the superior rectus muscle and the optic nerve, surrounded by an inflammatory response involving the superior complex. Follow-up CT and MRI (Fig. 1) after 8 months showed that the cyst's size had not changed but the inflammatory response was reduced. Clinical examination including visual acuity and visual fields, optic nerve head, and motility remained completely normal during follow-up, with the exception of persistent palpebral edema.

At the patient's request, uneventful surgical removal of the cyst's contents and its wall was performed 11 months after the accident, using an eyelid crease approach. The palpebral wound was thoroughly cleaned. Histologic examinations of the biopsy specimens showed many foci of granulomatous inflammation surrounding clear spaces in the eyelid. The cyst's wall was formed by thick layers of collagen fibers with lymphoid aggregates (Fig. 2).

Follow-up was unremarkable, and the patient's condition is stable, with persistent but markedly reduced swelling of the left upper eyelid.

DISCUSSION

Orbital foreign bodies can cause primary mechanical injury to the eye, extraocular muscles, optic nerve, and bony orbit. They can also cause secondary harm due to compression of orbital contents, mechanical restriction of ocular motility, migration, infection, and toxicity. The composition of a foreign body is a significant determining factor for its tolerance. Some orbital foreign bodies such as most metals and steel are inert and can be well tolerated and must not necessarily be removed. Other materials such as wood or copper can lead to chronic inflammation, extensive scarring, and fistula formation.[4]

Experience with intraorbital oil is limited and in the accessible literature, only four cases of grease-gun injuries

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Accepted for publication February 7, 2005.

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DOI: 10.1097/01.iop.0000175017.30029.f2

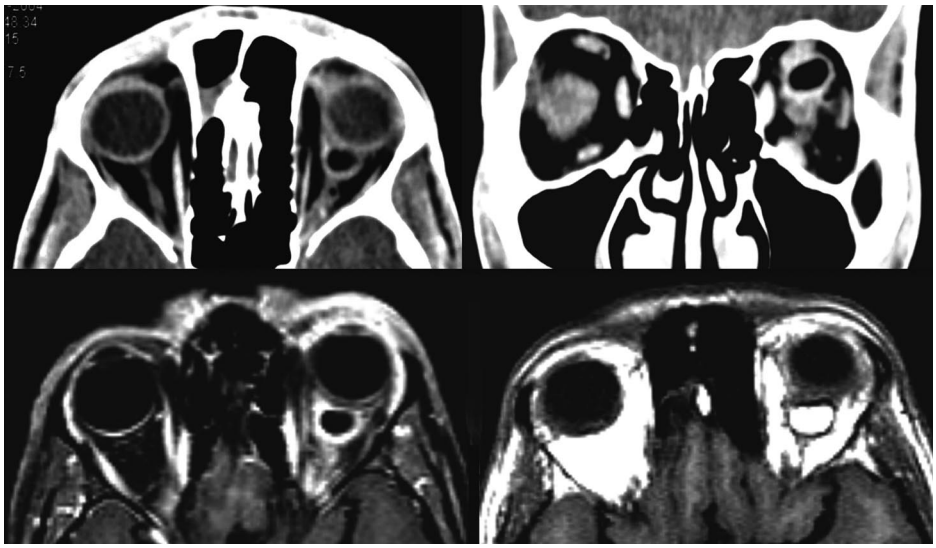

FIG. 1. Top: Axial (left) and coronal (right) CT scans 8 months after the accident showing an intraconal cyst in the left orbit with a residual inflammatory response surrounding the cyst. Bottom: (left) T_1-weighted MRI without contrast: low saturation of the cyst's contents. With fat saturation and administration of gadolinium (right) the contents of the cyst show high saturation.

to the orbit have been reported.[1–3] The management of intraconal deposition of any lubricant agent (oil or grease) is open to debate. The composition of greases and oils is highly variable and may contain many different classes of additives including polymers, alcohols, ethers, phenols, acids, esters, amines, amides, sulphur, selenium, tellurium, silicon, molybdenum, phosphorus, and so forth.

Tissue reaction to the presence of any oily substance is probably more influenced by the vehicle (the oil) than by its additives. In fact, the same histopathologic changes, described as a "Swiss cheese appearance," have been reported in response to the presence of different materials such as paraffin, petrolatum, lanolin, and distinct types of oil. This condition is characterized by cystic spaces in soft tissues surrounded by collagen and inflammatory cells, mainly lymphocytes, epithelioid cells, and multinucleated giant cells (Fig. 2). The cysts may contain clusters of spherical bodies that represent altered red cells. In these cases, the spherules may be confused with fungi.

Different terms have been used in the literature to describe the inflammatory changes caused by oil. The cases reported, occurring in the bulbar conjunctiva, lacrimal system as complications of septorhinoplasty, sinus surgeries, portal vein embolization, cortical block grafting, transconjunctival blepharoplasty, dacryocystorhinostomy, and cosmetic surgeries have been referred to as sclerosing lipogranulomatosis, lipogranuloma, paraffinoma, oil granuloma, myospherulosis, and spherulocystosis.[5]

Most authors favor the surgical removal of the affected tissues as the only possible treatment. However, in cases of intraconal oil deposition, this management is open to debate. It is not clear if these granulomas are harmful to the orbital contents in the absence of mechan-

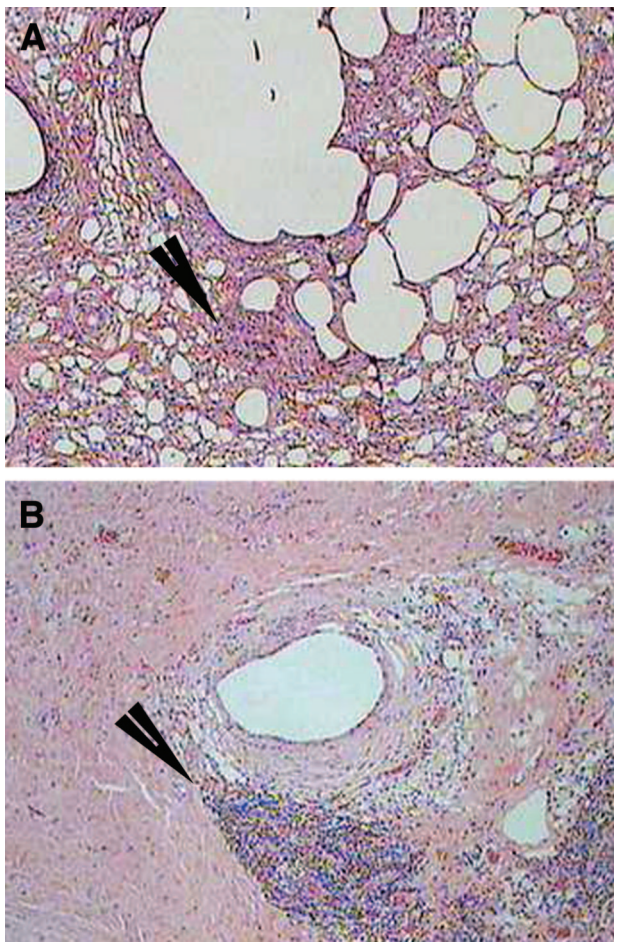

FIG. 2. Hematoxylin and eosin staining. A, preseptal tissues (40×) showing well-formed granuloma (arrow head) and many clear spaces filled with grease; B, cyst wall (200×) showing a lymphoid aggregate (arrowhead) composed of mature lymphocytes on a background of dense collagen fibers.

ical problems such as optic nerve damage or diplopia. Our case was followed for 11 months, showing no consequences to optic nerve function. The inflammatory response in the superior complex was markedly reduced, whereas the cyst size and location remained unchanged. Weighing the potential risks of an intraorbital procedure against damage to the orbital contents by the persisting foreign body is a therapeutic dilemma. In our case, we decided to not operate and to carefully monitor the patient for signs of optic nerve damage. Surgery was performed 11 months after the accident because the patient was concerned and he specifically requested it. In conclusion, we think that our case suggests that small amounts of intraconal deposition of oily substances can be carefully observed for extended periods of time and may not necessarily require surgical intervention.

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Granular Cell Tumor of the Orbit: Magnetic Resonance Imaging Characteristics

Michael Ahdoot, M.D., and I. Rand Rodgers, M.D.

Abstract: **A 56-year-old woman presented with choroidal folds and was found to have a large intraconal mass. MRI disclosed the mass to enhance with gadolinium and be hypointense on both T_1- and T_2-weighted images. The tumor proved to be a granular cell tumor. Granular cell tumors are rare neoplasms that may affect the orbit, lacrimal apparatus, conjunctiva, and caruncle. This is the first report describing the MRI characteristics of orbital granular cell tumors.**

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Accepted for publication January 31, 2005.

All authors involved in this report have no financial interest of any type related to the manuscript, including stock or ownership of a business entity connected to a product described in the paper, paid consulting for the company or competing companies, or patent rights to a drug or piece of equipment.

DOI: 10.1097/01.iop.0000173193.56711.e2

CASE REPORT

An asymptomatic 56-year-old white woman was referred by her private ophthalmologist to the oculoplastic service for the evaluation of choroidal striae in her left eye. Her medical history was significant only for osteoporosis. Her ocular history was unremarkable.

Uncorrected Snellen visual acuity was 20/20 OD and 20/200, improving to 20/40 with pinhole, OS. The pupils were equally round and reactive, with no afferent pupillary defect. Motility examination revealed limitation of left supraduction, and Hertel exophthalmometry was significant for 2 mm of left globe prominence. Intraocular pressures by Goldman applanation tonometry were 18 mm Hg bilaterally. Both optic nerves were flat with distinct margins, and left choroidal striae were again noted.

Imaging of the orbits (Figs. 1 through 3) disclosed a sharply circumscribed, ovoid 20 × 20 × 15-mm left intraconal mass abutting the superior and lateral rectus muscles. The lesion was hypointense on T_1 weighting and homogeneously enhanced after gadolinium. On T_2 weighting, the lesion remained hypointense. Sagittal sections showed the mass to be inseparable from the posterior margin of the globe and immediately adjacent to the optic nerve.

The patient underwent an excision of the lesion via a lateral orbitotomy. During surgery, a firm, gray-colored mass appeared well defined albeit adherent to the surrounding orbital structures, including the superior and lateral rectus muscles. The mass was noted to encroach the optic nerve. The lesion was removed with careful dissection.

On gross inspection, the specimen appeared gray-tan in color and well encapsulated. On histologic examination, the tumor cells were arranged in clusters between strands of collagenous tissue and skeletal muscle cells. The tumor cells were round to oval-shaped with small basophilic, centrally located nuclei that lacked mitotic activity amidst an abundant granular eosinophilic cytoplasm (Fig. 4). The cytoplasm stained positive with periodic acid-Schiff, Sudan black B, Indian red, and Masson trichrome. The cytoplasm also stained positive for the β-subunit of the S-100 protein and was not altered

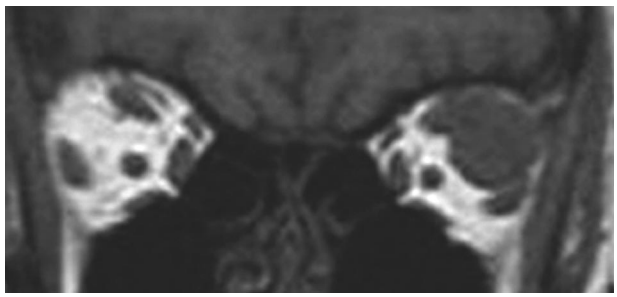

FIG. 1. Gadolinium-enhanced T_1-weighted coronal MRI scan demonstrating a hypointense left intraconal mass abutting the lateral rectus and superior rectus muscles.

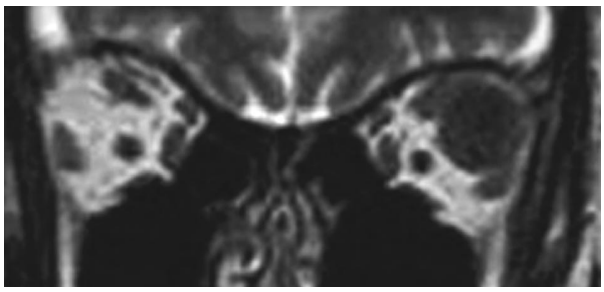

FIG. 2. On T_2-weighted MRI scan, the lesion remains hypointense.

by diastase predigestion. These histologic findings are consistent with granular cell tumor.[2] In addition, the pathologic margins of the tumor were clear, with no evidence of perineural spread.

Fifteen months after excision, the patient remained asymptomatic. Her uncorrected visual acuity had improved to 20/30 OS. There remained a slight albeit improved limitation of supraduction. Postoperative CT revealed only the presence of typical postoperative changes with an intact globe, optic nerve, and extraocular muscles. No evidence of recurrence was noted.

DISCUSSION

Granular cell tumor (GCT) was originally described by Abrikossoff[1] in 1926. It has been reported throughout the body, with the most frequent sites of involvement being the tongue and subcutaneous tissues. Its occurrence in the orbit and ocular adnexa is rare.[2]

The largest series of ocular GCT was reported by Jaeger et al.[3] in 1987. They presented 6 original patients and reviewed an additional 25 previously reported cases. Ophthalmic sites have included the orbit, periorbital skin and eyelids, extraocular muscles, lacrimal sac, ciliary body, conjunctiva, and caruncle.[3]

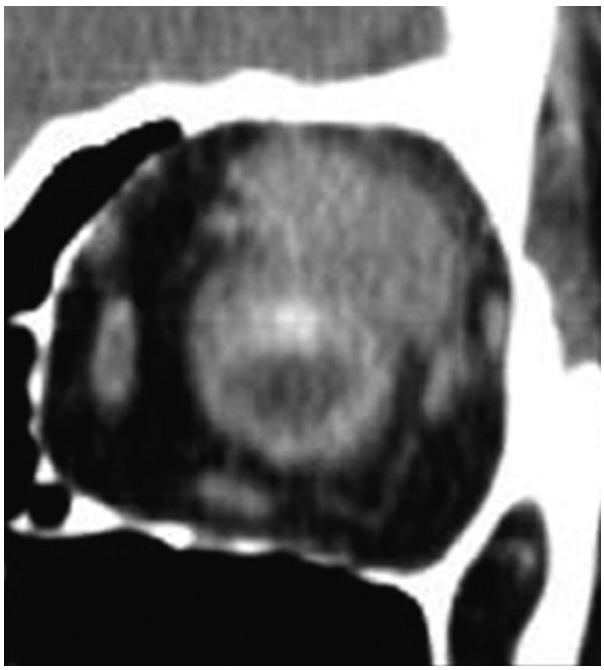

FIG. 3. Noncontrast coronal CT scan of left orbit. The mass is inseparable from the superior and lateral rectus muscles.

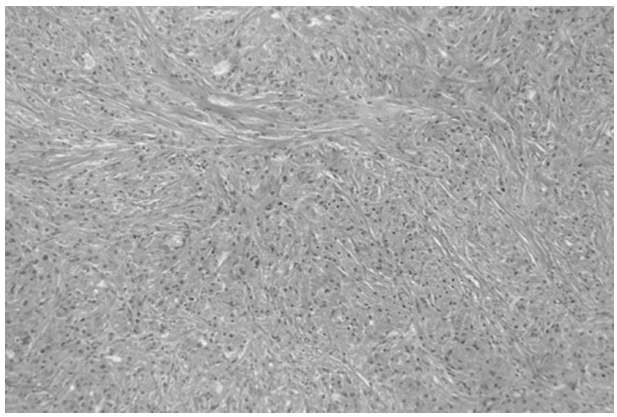

FIG. 4. Oval-shaped tumor cells with small basophilic nuclei arranged in clusters between strands of normal skeletal muscle (hematoxylin and eosin stain, magnification ×100). Abundant granular eosinophilic cytoplasm stained positive for periodic acid Schiff and S-100 protein immunostain.

The histogenesis of GCT is not well understood. Various proposed cell types of origin have included skeletal muscle, smooth muscle, fibroblast, histiocyte, undifferentiated mesenchyme, neural, and Schwann cells.[3] Since 1926, the tumor has been known by various names, mainly derived from the presumed cell of origin.[2] A Schwann cell origin was described in 1962 and has since gained popularity through support with various ultrastructural and immunohistochemical studies.[3] GCT cells and Schwann cells stain positively for the β-subunit of the S-100 protein.[3]

Granular cell tumors of the orbit present commonly with exophthalmos, diplopia, or decreased visual acuity from optic nerve involvement.[3] Although usually benign, invasion of local orbital tissues has been demonstrated, with malignancy occurring in 1% to 3% of cases.[3,4] Perineural spread of GCTs has been reported in other sites[5] but was not seen in this study.

The presentation of orbital GCT is shared by many orbital lesions and thus radiologic characteristics may be helpful in narrowing the differential diagnosis. Our case demonstrates that GCTs are hypointense on T_1-weighted imaging but enhance with gadolinium. On T_2-weighted imaging, unlike cavernous hemangioma, hemangiopericytoma, schwannoma, and fibrous histiocytoma, the lesion remains hypointense. These MRI findings are consistent with GCTs reported in other anatomic sites.[6] Lymphomas, melanomas, and some metastatic lesions may also appear hypointense on T_2 imaging, yet their morphologies may differ.

Granular cell tumors should be considered in all patients presenting with slowly progressing orbital masses.

Our report is the first to describe the MRI characteristics of orbital GCT and may be useful in better defining this uncommon orbital neoplasm.

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Advanced Periocular, Facial, and Oral Amyloidosis

Francesco P. Bernardini, M.D., Susan Schneider, M.D.†, Carlo de Conciliis, M.D.‡, and Martin H. Devoto, M.D.§*

Abstract: **A 57-year-old white man presented with extensive bilateral, symmetric, confluent papules involving the upper and lower eyelids, causing visual impairment and cosmetic deformity. Surgical debulking of the papules was initially performed, but the lesion rapidly recurred and enlarged. Histopathologic examination revealed cutaneous amyloidosis. Six months later, extensive excision of the upper eyelid lesions was required to restore normal visual function.**

Amyloidosis is a disease characterized by the deposition of amyloid, a pathologic proteinaceous intercellular substance in various tissues of the body; amyloidosis can be a primary process or may occur secondary to chronic disease. The primary forms are localized and systemic. Primary localized amyloidosis (a.k.a. tumor-forming amyloidosis) of the ocular adnexa is predominantly unilateral and tends to involve the conjunctiva and spare the eyelid skin. The involvement of the eyelid skin is suggestive of systemic amyloidosis, although even localized amyloidosis may affect the skin in the periocular region.

Primary systemic amyloidosis, when involving the eyelid skin, usually appears as bilateral, symmetric, and confluent papules with waxy appearance and is often accompanied by purpura; the conjunctiva is usually spared. The association of eyelid skin lesions with multiple myeloma is pathognomonic of the AL (immunoglobulin light chain) form of primary systemic amyloidosis. In this entity, peripheral muscles, skin, nerves, and blood vessels are usually involved, and the disease can be rapidly fatal, with a mean survival of less than 2 years from the time of diagnosis. Treatment of periocular amyloidosis remains controversial. In primary localized amyloidosis, simple excision of the conjunctival lesions or debulking of the suborbicularis amyloid deposits with a spooned curette have been advocated,[1,2] whereas more complex excision followed by eyelid reconstruction has been necessary for the treatment of lesions involving the eyelid margin.[3,4] Multiple myeloma–associated amyloidosis is rapidly fatal, and local treatment is therefore not recommended unless the process causes severe cosmetic deformity or interferes with visual function. We report a case of multiple myeloma associated systemic amyloidosis with periocular skin lesions causing mechanical ptosis, visual field restriction, and disfiguration.

CASE REPORT

A 57-year-old man presented with multiple periocular skin lesions infiltrating the medial third of both upper and lower eyelids. The lesions were present for more than 1 year and progressively enlarged over a 1-year period. Medical history was significant for multiple myeloma and an ischemic heart attack 10 years before presentation. Ocular examination revealed the visual acuity, pupillary reaction, and intraocular pressure to be within normal limits. Slit-lamp evaluation of the anterior segment and funduscopic examination of the retina were

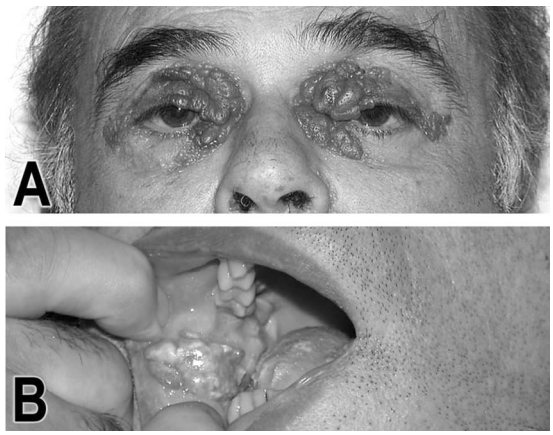

FIG. 1. Preoperative appearance of the amyloid deposits in the periocular region (A) and in the inner surface of the cheek (B).

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Accepted for publication March 21, 2005.

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DOI: 10.1097/01.iop.0000176261.81284.cb

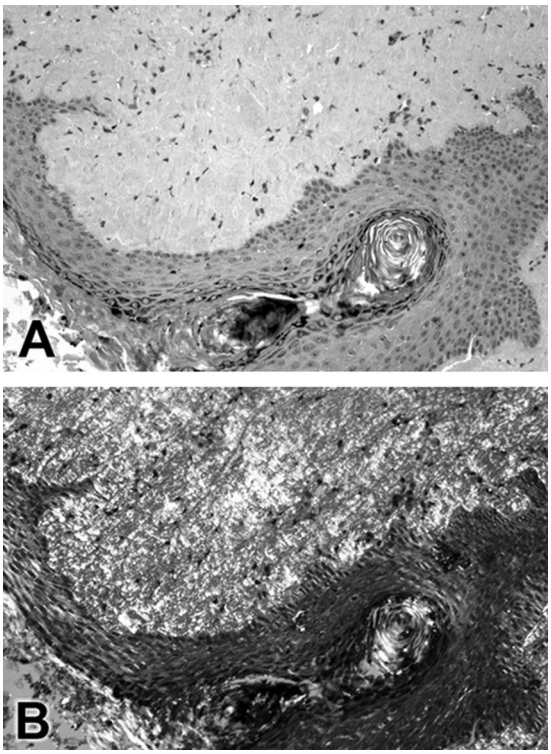

FIG. 2. Histopathologic examination reveals the presence of slightly eosinophilic, amorphous material, consistent with amyloid deposition (A) and confirmed by positive Congo red staining with apple green birefringence (B).

unremarkable. External examination revealed the presence of eyelid skin nodules of various sizes infiltrating both upper and lower eyelids (Fig. 1A). The diagnosis of amyloidosis was suspected, and surgical debulking of the lesions was performed. Histopathologic examination of the resected specimen revealed the presence of slightly eosinophilic, amorphous material, consistent with amyloidosis was confirmed by positive Congo red staining (Fig. 2). After moderate temporary subjective improvement, the lesions recurred and progressed over a period of 8 to 10 months, causing visual field impairment, increased eyelid weight, and difficulty keeping the eyes open throughout the day. The patient noted similar lesions on the skin of the neck and around the nostrils. Examination revealed additional lesions on the inner surface of both cheeks filling the lateral aspect of the mouth and interfering with dental occlusion (Fig. 1B). After the risks, benefits, and alternatives of surgery were discussed with the patient, wide excision of the periocular lesions was performed, proceeding with one eyelid at a time and starting with the left upper eyelid, which was considered the worst. After removal of the affected part of the left upper eyelid skin, the residual defect was reconstructed with two large retroauricular skin grafts harvested from both sides. The grafts were sutured to the residual normal eyelid skin and joined at the upper eyelid crease, which was reformed with deep fixation to the levator aponeurosis. A cotton bolster was sutured in place and removed after 1 week. Follow-up examination 1 year after surgery revealed a viable graft, normal eyelid height with no lagophthalmos, and improved cosmesis of the left upper eyelid. The patient is now receiving chemotherapy to treat his multiple myeloma, and further surgery has been postponed.

DISCUSSION

AL amyloidosis is rapidly progressive and fatal, with a mean survival rate of less than 2 years from diagnosis. Evaluation of the periocular skin lesions can help in establishing the diagnosis. Because the prognosis is not affected by excision, surgery is necessary only if there is severe cosmetic deformity or visual impairment. In this case, we planned a multistep reconstruction to improve cosmesis and visual function and to prevent pupillary axis occlusion by the amyloid deposition in the upper eyelid skin bilaterally.

Periocular skin lesions and macroglossia are well documented features of primary systemic amyloidosis,[5,6] but they usually do not require surgery. To our knowledge, this is the first reported case of amyloidosis of the eyelid skin that required extensive surgery with skin grafting to treat visual field impairment and prevent complete pupillary axis obstruction. The rapid progression of the skin and oral lesions is also a unique characteristic that has not been previously reported with amyloidosis.

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Chronic Inflammation From Polycarbonate Motility Peg Inhibits Osteogenesis in a Human Hydroxyapatite Orbital Implant

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Abstract: **The histologic findings of a pegged hydroxyapatite orbital implant removed due to chronic inflammation and pain are described. A 44-year-old woman underwent explantation of a hydroxyapatite sphere and polycarbonate motility peg due to chronic redness, swelling, discharge, and pain. Histology revealed complete fibrovascularization of the implant, with approximately 90% ossification. No bone marrow was identified. Histologic sections revealed fibrous connective tissue at the periphery of a sclerotic bony mass with a granulomatous inflammatory infiltrate at the motility peg aperture. There were no bacterial, mycobacterial, or fungal organisms identified histologically or by culture. Consistent with previous reports, hydroxyapatite orbital implants are amenable to fibrovascular ingrowth and bony transformation. The presence of a granulomatous inflammatory reaction around the polycarbonate motility peg in this case may have prevented complete osseous transformation of the hydroxyapatite implant.**

Over the past decade, porous hydroxyapatite (HA) spheres have been increasingly used in patients requiring orbital implants. This material is amenable to fibrovascular ingrowth, resulting in biointegration with the surrounding host tissues.[1] Theoretical advantages that favor the use of these biointegrated implants include a decreased risk of migration within the orbit and an increased resistance to infection as a result of immunologic surveillance within the implant.[2]

It has also been demonstrated that HA is subject to osteogenesis and conversion in bone with hematopoietic elements.[3] This probably occurs by the process of osteoinduction, whereby osteoblast progenitor cells colonize the implant after vascular ingrowth has taken place. The conversion of HA into the host's bone tissue may also reduce the risks of foreign body reaction and infection and offer increased strength necessary to stabilize motility coupling pegs.

In this report, we show the histologic appearance of a human HA orbital implant removed due to chronic orbital inflammation and pain. We demonstrate a chronic, granulomatous inflammatory reaction around the motility peg site with incomplete ossification of the HA.

CASE REPORT

A 44-year-old woman with left-sided anophthalmia presented to the University of Washington in 2003 with a 10-year history of pain, discharge, and prosthesis intolerance. During childhood, the patient underwent enucleation of the left eye for an "intraocular tumor." Prior medical records and pathology reports were not available. An HA sphere wrapped in sclera was implanted at another institution (patient age, 34 years), and a sleeved polycarbonate motility peg was placed 6 months later. Her symptoms began 2 months after peg placement. Before presentation, there were no cultures performed on the implant. During this time, the patient was empirically treated with multiple courses of systemic antibiotics and topical antibiotic/steroids without improvement.

Examination revealed moderate conjunctival injection, mild mucus discharge, and moderate tenderness to palpation. There was a stable, well-centered polycarbonate motility peg. There was no purulent discharge, implant exposure, papillary reaction, eyelid swelling, or erythema.

Based on the patient's symptoms and possibility of indolent infection, implant removal with dermis-fat reconstruction was performed. Intraoperative cultures of the conjunctiva and implant were obtained, and the implant was submitted for pathologic analysis.

The HA sphere was decalcified and sectioned sagittally. Staining with hematoxylin and eosin, Gomori methamine silver, periodic acid-Schiff, Brown-Brenn, and Ziehl-Nielsen was performed. Bone matrix was present throughout the entire implant except adjacent to the motility peg aperture (Fig. 1, A and B). A fibrous capsule surrounded the periphery of the implant with occasional lymphoid germinal centers adjacent to HA material (Fig. 1, C and D). Surrounding the motility peg aperture was a mixed acute and chronic inflammatory infiltrate with histiocytes and multinucleated cells that may represent giant cells or osteoclasts (Fig. 2, A and B). In the central area of inflammation, there was significantly less bone matrix and more unossified HA compared with the periphery of the implant (Fig. 2A). The collagenous fibers of the bone matrix appeared to be less organized within areas of inflammation (Fig. 2, C and D). Intraoperative cultures and special stains were negative for bacteria and fungi.

DISCUSSION

Evidence suggests that the mechanism of bone formation in porous HA implants is a gradual, multistep process. After implantation, serous fluid fills the porous

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Accepted for publication March 21, 2005.

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DOI: 10.1097/01.iop.0000179375.66916.59

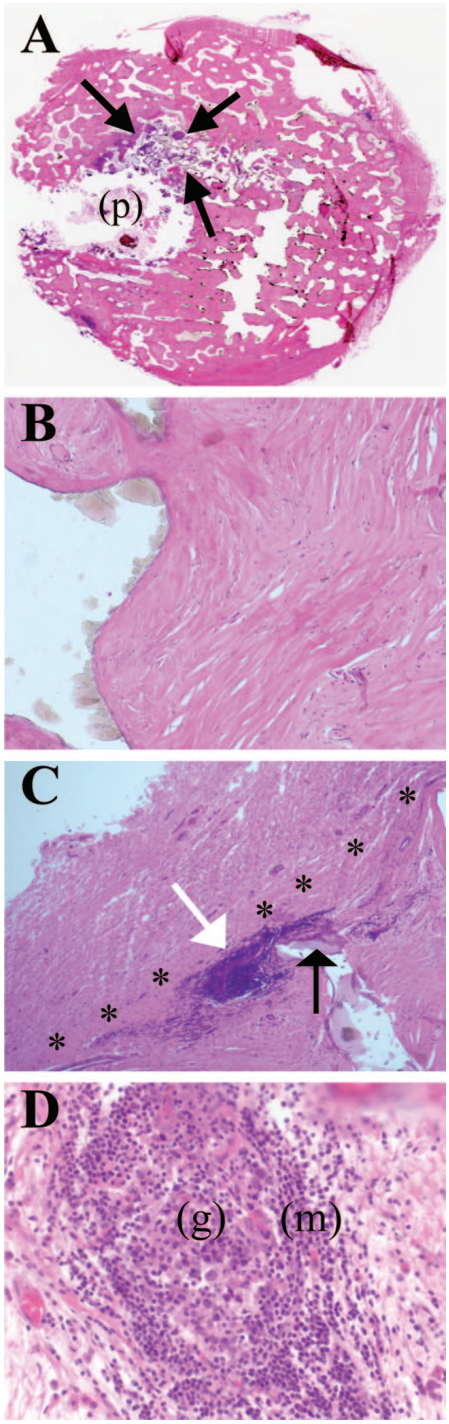

FIG. 1. **A,** Explanted hydroxyapatite sphere showing motility peg aperture (*p*). Bone matrix is present except in the zone adjacent to the peg aperture (*black arrows*) (hematoxylin and eosin stain, magnification 5×). **B,** Higher magnification view demonstrates replacement of hydroxyapatite with bony matrix (hematoxylin and eosin stain, magnification 20×). **C,** Lymphoid follicle (*white arrow*) is present at the junction of the scleral wrap and implant (*delineated by asterisks*). Unossified hydroxyapatite is present adjacent to the follicle (*black arrow*) (hematoxylin and eosin stain, magnification 10×). **D,** Germinal center (*g*) and mantle zone (*m*) of the lymphoid aggregation are discernable at higher magnification (hematoxylin and eosin stain, magnification 40×).

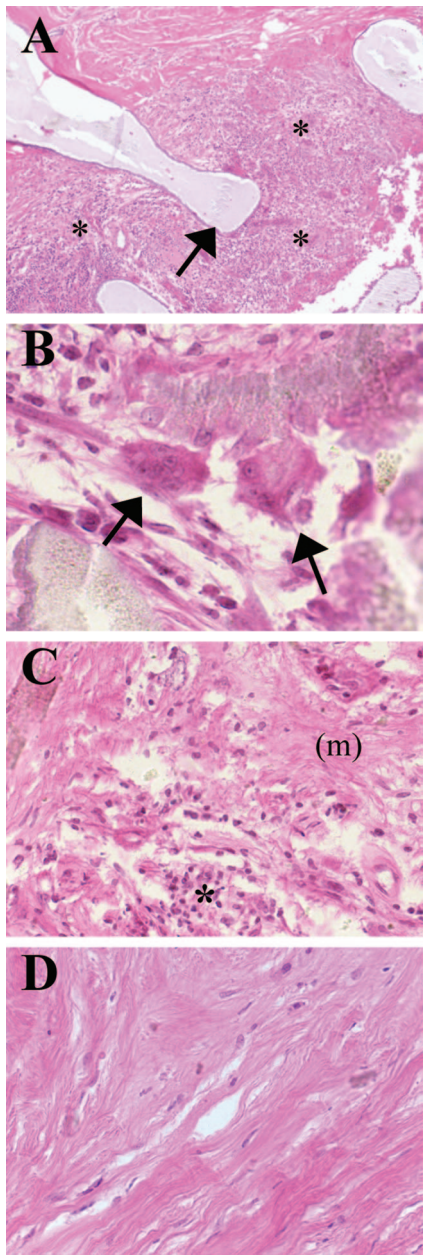

FIG. 2. **A,** Mixed inflammatory infiltrate (*asterisks*) was noted adjacent to the motility peg aperture (hematoxylin and eosin stain, magnification 10×). Ratio of unossified hydroxyapatite (*arrow*) to bone matrix was greatest in this region. **B,** Higher magnification of the inflammatory infiltrate demonstrates the presence of multinucleated cells, indicative of giant cells or osteoclasts (*arrows*) (hematoxylin and eosin stain, magnification 40×). **C,** Appearance of bony matrix (*m*) adjacent to the zone of granulomatous inflammation (*asterisk*) near the motility peg aperture (hematoxylin and eosin stain, magnification 25×). Collagen lamellae of the bony matrix (*m*) in this region appear to be more disorganized (characteristic of immature bone) when compared with uninflamed areas of the implant **(D)** (hematoxylin and eosin stain, magnification 25×).

cavities of the HA.[4] Fibrovascular ingrowth begins in about 2 weeks and is complete by 3 to 6 months; the precise time period dependent on the nature of the wrap

material and whether holes are drilled before implantation.[5] Circulating osteoblast progenitor cells may subsequently gain access to and colonize the HA structure of the implant through this blood supply. By signaling mechanisms related to calcium phosphate and other surface proteins on the implant, these progenitor cells may be stimulated to differentiate in osteoblasts that initiate bone formation.[6]

Animal studies show that bone formation in HA implants can occur as early as 6 weeks.[7] In humans, there are reported cases of HA spheres demonstrating incomplete bone formation as early as 5 and 7 months after implantation.[5] Another report of an explanted human HA sphere without a motility peg demonstrated that ossification of the implant is virtually complete (with bone marrow) after 5.5 years.[3]

Of importance is the granulomatous inflammatory response around the motility peg site. The absence of infectious organisms, presence of histiocytes, and chronic nature of the inflammation suggest that this may be due to a foreign body reaction against the polycarbonate peg. Inflammatory cytokines, such as interleukin-1 and tumor necrosis factor, have been shown in animal models to inhibit osteoblasts and promote osteoclast differentiation and activity.[8] This may in part explain the paucity, disorganization, and lack of ossification of the bone matrix surrounding the motility peg site. Chronic exposure to inflammatory cytokines may also have similarly inhibited differentiation of hematopoietic progenitor cells, resulting in the absence of bone marrow in this implant. If this type of inflammatory/foreign body reaction is common, our findings may in part explain the high rate of complications (i.e., discharge, peg instability, infection) associated with these pegs.[9]

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Delayed Inflammatory Reaction to Hyaluronic Acid (Restylane®)

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Abstract: **A 45-year-old man received an injection of Restylane (cross-linked hyaluronic acid) to a midforehead furrow line in an attempt to reduce its prominence. The injection was uncomplicated and successful in reducing the line. Five months after the injection, he returned with an inflammatory reaction in the area of injection that resolved without treatment over a period of 3 weeks.**

A variety of soft tissue fillers have been used to diminish facial folds and wrinkles, including silicone, autologous fat, bovine and human collagen, and others.[1] A new filler popularized in recent years is injectable hyaluronic acid (HA). Hyaluronic acid is a basic building block of the dermis that binds water and creates volume. It exhibits no species or tissue specificity, and the chemical structure of this polysaccharide is uniform throughout nature. HA may be biotechnologically manufactured with bacterial fermentation techniques (Restylane; Q-Med Aesthetics, Stockholm, Sweden) or extracted from rooster combs (Hylaform; Biomatrix Inc., Ridgefield, NJ, U.S.A.). Manufacturers and distributors of these products suggest that there is no need for skin testing because there is little or no potential for immunologic reactions in humans.[1–3] However, this does not mean these products are risk free, as there are potential problems that may occur.[2–9] This article reports a delayed inflammatory reaction occurring 5 months after an injection of Restylane.

CASE REPORT

A 40-year-old, previously well white man had a prominent horizontal forehead furrow line and the vermillion border of his upper lip injected with Restylane from the same syringe (June 1999). Both areas looked fine 1 week after injection. Five months later, he returned with an elevated, lumpy red line in the forehead that developed over a 24-hour period (Figure). The lip, however, appeared uninvolved. There was no pain or tenderness in the involved area. The inflammatory reaction gradually disappeared over the next 3 weeks.

DISCUSSION

Several authors have questioned the purported lack of immunogenicity to HA products, based on inflammatory

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Accepted for publication January 19, 2005.

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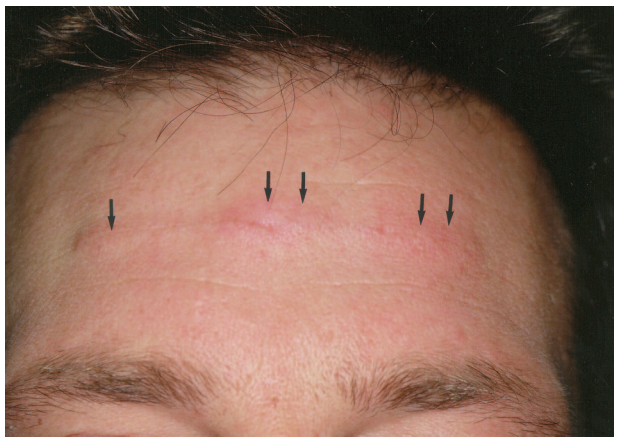
DOI: 10.1097/01.iop.0000173194.18050.b8



An elevated, red, lumpy line is seen in the area of a previous Restylane injection *(arrows)*.

reactions[3–5] and foreign body granuloma development[6,7] that occurred after HA injection.

Lupton and Alster[3] reported a 54-year-old woman who had development of multiple red nodules within the treatment area 2 weeks after a third session of HA injection (June 1999; HA type not disclosed). A potential allergy to an impurity of the bacterial fermentation of the HA gel was the suspected cause. Any impurities present during the manufacturing process could account for a sensitization reaction.[3]

Lowe et al.[4] described delayed inflammatory reactions occurring 6 to 8 weeks after HA injection (Hylaform and Restylane) in 6 patients (1996 to 2000). An allergic reaction to the HA products was implied, but the precise nature of the reactivity was not determined. Furthermore, Klein,[5] through personal communication with Lowe, reports Lowe no longer supports the conclusion of this article as valid.

Micheels[6] reported 8 patients with redness, pruritus, and painful swelling in areas of HA injection that lasted up to 5 months. He suggested these reactions may be secondary to antibodies against the HA products (IgG, IgE), but the evidence to support this was limited.[5] Other articles[7,8] reporting foreign body granuloma formation and suggesting allergic reactions to the HA product similarly provide no supportive evidence that the possible mechanism of the reaction is allergic in nature.[5]

Friedman et al.[9] performed a retrospective review of the worldwide data gathered by the manufacturer for Restylane on reported adverse events in 1999 and 2000. In 1999 there was approximately 1 adverse event reported for every 650 (0.15%) patients treated. The most common reaction to injectable HA was a localized hypersensitivity reaction that consisted of swelling, erythema, and induration at the implant site (medium duration, 15 days). There were also rare reports of localized granulomatous reactions, bacterial infection, and acneiform and cystic lesions. In 2000, the total number of adverse events was 1 for every 1,800 (0.06%) patients treated. This decrease was likely due to a reformulation of the HA. In mid-1999, an HA raw material was introduced with trace amounts of protein 6 times lower than the raw material previously used.[9] Hypersensitivity reactions to HA products were probably secondary to impurities of bacterial fermentation.[9]

In the present case, the lip appeared to have no inflammatory reaction, which may be because only a small amount of Restylane was injected along the vermillion border and a delayed inflammatory reaction was not clinically obvious, or because the inflammatory reaction was camouflaged by the natural redness and indistinct outline of the patient's vermillion border.

In summary, it is clear there may be rare inflammatory reactions to HA products occurring 2 to 8, or even 20 weeks after injection, as in the present case.[3,4,6–9] Whether these are a result of allergy to the HA or a reaction to the impurities in the product has been debated.[3–9] An antibody response to HA itself, however, has never been documented, and if there is any immunologic response to these products, it is most likely a response to the protein contaminants rather than the HA.[5] The reformulation of Restylane in 1999 resulted in a 6-fold reduction of protein load in the final product.[5,9] This reduction has resulted in a concomitant reduction in the reported occurrences of suspected hypersensitivity reactions.[5,9]

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Eyelid Involvement in Acanthosis Nigricans: The Importance of Systemic Screening

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Abstract: **A 53-year-old man presented with thickening and hyperpigmentation of the eyelids. After the diagnosis of acanthosis nigricans was made, further investigation of a possible underlying disorder, including biochemical and instrumental examinations, indicated the presence of glucose intolerance, which had been diagnosed 3 years after the clinical appearance of acanthosis nigricans. Eyelid involvement in acanthosis nigricans is rare. Ophthalmologists should be aware of the possibility that acanthosis nigricans can exist in the periocular area and perform a systemic assessment of the patient for the presence of an underlying condition.**

Acanthosis nigricans (AN) is characterized by skin hyperpigmentation and thickening, most commonly involving the intertriginous areas such as the axillae, neck, groin, and external genitalia. Eyelid involvement is atypical for AN. Although AN itself is an innocuous disorder, it is commonly a manifestation of an underlying systemic disease and often precedes its clinical symptoms. AN may occur secondary to obesity, glucose intolerance, insulin resistance, pituitary hypogonadism, Addison disease, hyperthyroidism, hypothyroidism, and use of nicotinic acid, corticosteroids, and insulin, or, it may develop as a paraneoplastic syndrome accompanying various malignancies, particularly gastrointestinal adenocarcinomas. AN may appear before, concomitant with, or after the clinical manifestations of the underlying pathology.[1,2] We aim to emphasize the significance of further investigation after the diagnosis of AN is made by presenting a rare case with AN that is localized in and limited to the periocular area and forehead. To our knowledge, this is the first report of a case with such a confined and rare localization, which revealed glucose intolerance.

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Accepted for publication March 21, 2005.

Presented at the 38th Turkish National Ophthalmology Congress, Antalya, Turkey, 2004.

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DOI: 10.1097/01.iop.0000176262.58350.38

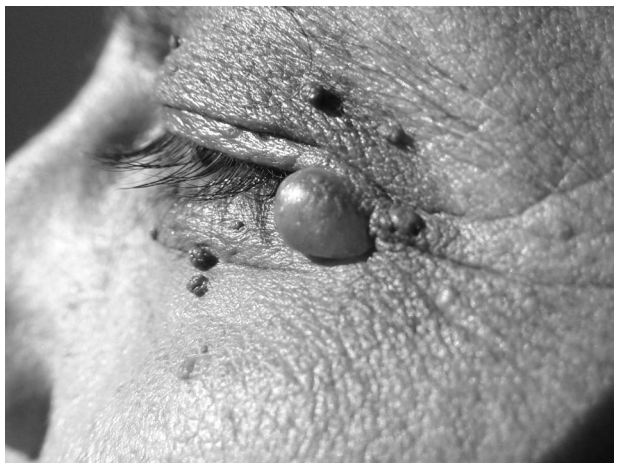

FIG. 1. Photograph demonstrating hyperpigmentation and thickening of the patient's left periocular area and hydrocystoma on the left lateral canthus.

CASE REPORT

Data accumulation was approved by the ethics committee of our university, and the patient gave consent. A 53-year-old white man had a 3-year history of bilateral progressive thickening and hyperpigmentation of the skin of his eyelids and forehead accompanied by papillomatous growths on the eyelids and a 0.5-cm cystic lesion on the left lateral canthus, clinically consistent with AN and hydrocystoma (Fig. 1). A full examination of the entire skin surface was performed by the dermatologists and intertriginous areas such as axillae, neck, and inguinal regions were free from AN. The cutaneous alterations were confined to the periocular region and forehead and did not cause any functional symptoms such as epiphora from occlusion of the canaliculi with papillomatous lesions, but the patient complained of the hydrocystoma for cosmetic reasons. A thorough ophthalmologic examination including pupil reactions, best-corrected visual acuity, intraocular pressure, biomicroscopy, funduscopy, ocular motility, and lacrimal drainage revealed no other pathologic findings except presbyopia. The cystic lesion was excised, and several biopsy specimens adjacent to the lesion were taken. The clinical diagnosis of AN and hydrocystoma was confirmed by the histopathologic study, which demonstrated hyperkeratosis, mild acanthosis, and papillomatosis in the epidermis and a cystic space lined by a double layer of cuboidal cells (Fig. 2). The patient underwent further investigation of a possible occult disorder. The patient's only systemic complaint was an abdominal ache. He had not taken any medication for the past year and had not noted any weight loss. Routine analyses, including full blood count, urine analysis, and thyroid function tests, were within normal ranges. Fecal analysis did not reveal occult blood. Biochemical tests performed twice at a 1-month interval revealed 125 mg/dl and 115 mg/dl fasting

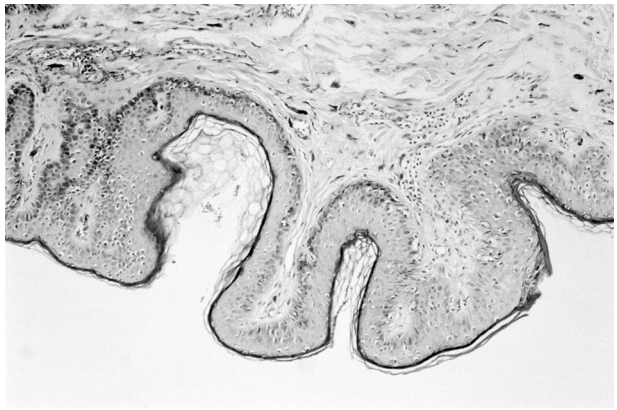

FIG. 2. Histopathology reveals papillomatosis, mild acanthosis, hyperkeratosis, and irregular basal hyperpigmentation (hematoxylin and eosin stain, magnification ×100).

plasma glucose at the first and second tests, respectively (normal range, 70 to 109 mg/dl). The oral glucose tolerance test disclosed a plasma glucose concentration of 163 mg/dl at the second hour. These impaired values of plasma glucose led to the diagnosis of glucose intolerance according to the criteria of the American Diabetes Association. Tumor markers including prostate-specific antigen, free prostate-specific antigen, α-fetoprotein, carcinoembryonic antigen, and CA 19,9 were also within normal limits. Ultrasonography of the abdomen disclosed the presence of gallstones in his gallbladder. Chest radiography, abdominal CT, gastroduodenoscopy, and colonoscopy were otherwise unremarkable.

DISCUSSION

Atypical localizations in AN including hands, feet, lips, buccal mucosa, soft palate, sulcus mentolabialis, eyelids, and submammary region are rarely reported. We report this case to highlight two significant aspects of AN. The first is the rare periocular involvement; the second is the importance of further investigation after the diagnosis of AN has been made.

Bottoni et al.[3] diagnosed AN involving the neck, axillae, mouth, and eyelid conjunctivae and discovered a non–small cell carcinoma of the lung after a series of instrumental and biochemical examinations. Cutaneous alterations had appeared 1 year before the diagnosis of the malignancy and directed the examination that disclosed his lung cancer. In a report by Groos et al.,[4] a case with AN involving the eyes and many other regions of the body was described. AN had developed 1 year before the diagnosis of gastric adenocarcinoma, and the patient had persistent epiphora from occlusion of all four puncta with papillomatous lesions accompanying AN. Other case reports described AN as a paraneoplastic syndrome that led to diagnoses of colon and lung malignancies.[5,6] In our case, all the investigations performed to demonstrate any possible associated disorder indicated the presence of glucose intolerance diagnosed 3 years after the clinical appearance of AN.

In a study by Kapasi et al.,[7] 6 patients who presented to the dermatology clinic with AN were evaluated to rule out endocrine diseases, and glucose intolerance was found to be the associated disorder. Another study concluded that AN could be a reliable cutaneous marker of insulin resistance in obese children. Children with AN showed significantly more glucose intolerance compared with those without AN.[8] However, in these studies, none of the subjects presented with periocular involvement.

AN can often precede the clinical signs of the underlying condition. Therefore, awareness of the possibility that AN can exist in the periocular area may help ophthalmologists suspect an occult endocrine or malignant disorder. It is advisable that thorough systemic assessment of patients presenting with AN be performed after its recognition.

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