18

Lacrimal Gland Tumors

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Lacrimal gland tumors typically present with upper eyelid fullness, alteration of the upper eyelid contour, and downward and nasal displacement of the globe. Lacrimal fossa masses consist of inflammatory, neoplastic, and structural disorders. In managing lacrimal tumors appropriately, it is imperative to differentiate benign mixed tumors of the lacrimal gland with diagnostic accuracy so that the initial management is complete extirpation without preceding incisional biopsy.

Traditionally it has been said that about 50% of lacrimal masses are epithelial and 50% are nonepithelial.[1] More recent data indicate that inflammatory lesions and lymphoid tumors of the lacrimal gland are two to three times more common than epithelial tumors.[2,3] In reported series on epithelial tumors of larger size, the relative frequency is approximately 50% benign mixed tumors and 50% carcinomas. About half of the malignancies are adenoid cystic carcinoma (Table 18.1).[4–8] The incidence of epithelial tumors of the lacrimal gland ranges from 5 to 8% of orbital neoplasia.[1,6,9]

In managing lacrimal fossa mass lesions, preoperative characterization of a particular lesion is highly desirable. This recommendation is based on the duration of symptoms, the presence of pain, and radiologic findings.[10,11] Acute onset of swelling, periorbital pain, chemosis, or an erythematous indurated lid indicate an inflammatory process of either idiopathic or of bacterial or viral etiology (Figure 18.1). A computed tomography (CT) scan will reveal a diffuse lacrimal enlargement with irregular margins, frequently demonstrating contrast enhancement and no bony change. Most cases of bacterial dacryoadenitis resolves rapidly with appropriate systemic antibiotics. Idiopathic acute inflammation can be treated with a short course of corticosteroids (Figure 18.2). Failure to resolve over a few weeks should lead to incisional biopsy, since acute inflammatory episodes may be related to an underlying carcinoma.[10]

Orbital lymphoproliferative lesions are another common cause of lacrimal gland swelling (see Chapter 13). They are characterized by insidious and painless onset in a slightly older population and can often be bilateral. CT scans show that all lymphoid tumors mold themselves around the existing orbital structures, such as the globe and the bony orbit, without eroding bone or enlarging the orbit (Figure 18.3).[12]

When painless swelling in the upper lid without inflammatory symptoms and signs presents for more than 12 months, benign mixed tumor (pleomorphic adenoma) should be suspected. On CT scans pleomorphic adenomas usually show round to oval, well-circumscribed mass and enlargement of the lacrimal fossa without invasion of overlying bone. Such a tumor should be excised intact through a lateral orbitotomy.[10,13] When biopsy is done before excision, the 5-year recurrence rate is estimated to be 32%, and many of these recurrences undergo malignant transformation.[4] Biopsy of pleomorphic adenoma should be avoided. It is advisable to completely remove all encapsulated or well-circumscribed masses without incisional biopsy.

Most patients with malignant epithelial tumors present with painful swelling in the upper eyelid that developed within one year.[14] High-resolution CT reveals more elongated mass extending along the lateral orbital wall with expansion of the lacrimal fossa with bone invasion. Calcifications are more commonly seen in malignant tumors. A biopsy through a transseptal incision should be performed without delay in all these patients.

Dermoid cysts are not true lacrimal gland tumors; rather, they originate from epithelial rests located in the orbit, particularly in the superolateral quadrant. Deep dermoids in the lacrimal fossa most often present as painless proptosis in a younger age group. Bony change in the superolateral wall is common. When a tumor extends through the suture line, it may appear on both sides of the bone (the "dumbbell" dermoid). Rarely, these patients present inflammatory reaction when the cyst ruptures. Dermoid cysts can be diagnosed easily by typical findings on CT or magnetic resonance (MR) images of a lesion of fatty density with no or only faint enhancement and smoothly outlined osseous changes. It appears as an image of low intensity on T1-weighted and high intensity on T2-weighted MR images (Figure 18.4).[15]

TABLE 18.1. Incidence of Primary Epithelial Neoplasms of the Lacrimal Gland.

Authors	*Number of cases*	*Benign mixed*	*Malignant mixed*	*Adenoid Cystic*	*Other carcinoma*
Font and Gamel[4]	265	136 (51%)	34 (13%)	70 (27%)	25 (9%)
Ni et al.[5]	160	90 (56%)	10 (6%)	46 (29%)	14 (9%)
Henderson[6]	66	25 (38%)	10 (15%)	22 (34%)	9 (13%)
Wright[7]	54	30 (56%)	3 (6%)	11 (20%)	10 (18%)
Ashton[8]	54	30 (55%)	2 (4%)	13 (24%)	9 (17%)
Total	599	311 (52%)	59 (10%)	162 (27%)	67 (11%)

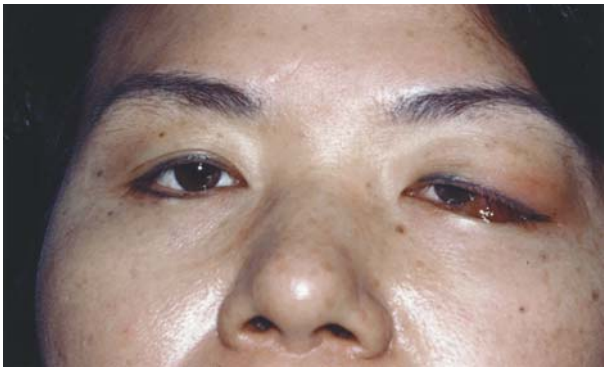

FIGURE 18.1. Acute dacryoadenitis in a 39-year-old woman with a 1-week history of pain and swelling over the left lacrimal gland with marked chemosis.

DACRYOPS (LACRIMAL DUCTAL CYSTS)

The ducts of the lacrimal gland may become obstructed, leading to a cystic mass in the lacrimal region. The palpebral lobe is affected far more commonly than the orbital lobe. The typical findings of dacryops are bluish transilluminating cystic swellings visible through the conjunctiva (Figure 18.5A). Imaging usually reveals a cyst without any bone changes (Figure 18.5B). On histopathologic examination they are typically composed of two layers: an inner cuboidal or columnar layer and an outer flattened myoepithelial layer (Figure 18.5C).[16] The treatment is

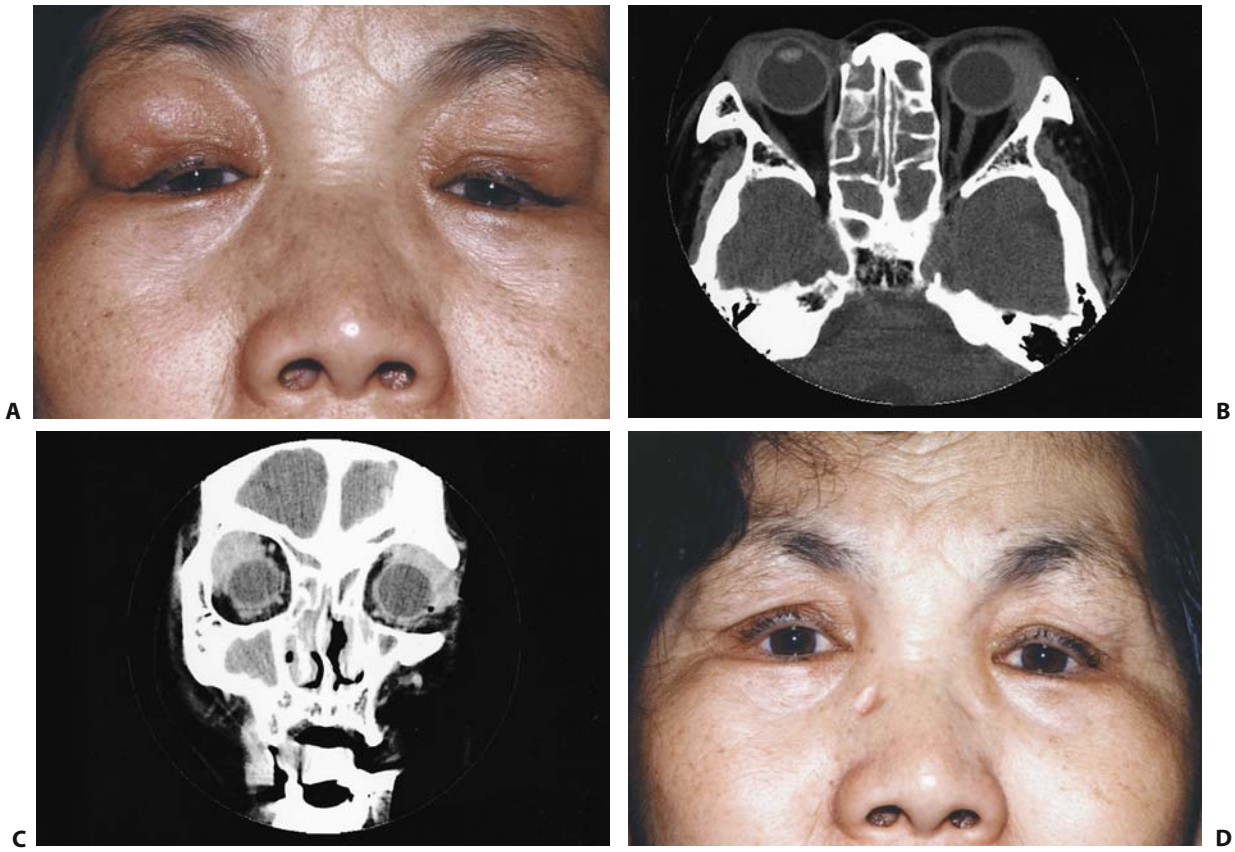

FIGURE 18.2. Idiopathic inflammatory pseudotumor in a 63-year-old woman with bilateral, nontender masses in the lacrimal gland region for 3 months (A). The S-shaped eyelid is typical for lacrimal gland enlargement. (B) Axial and (C) coronal CT images demonstrate bilateral enlargement of the lacrimal glands. (D) The patient 2 months after systemic steroid therapy.

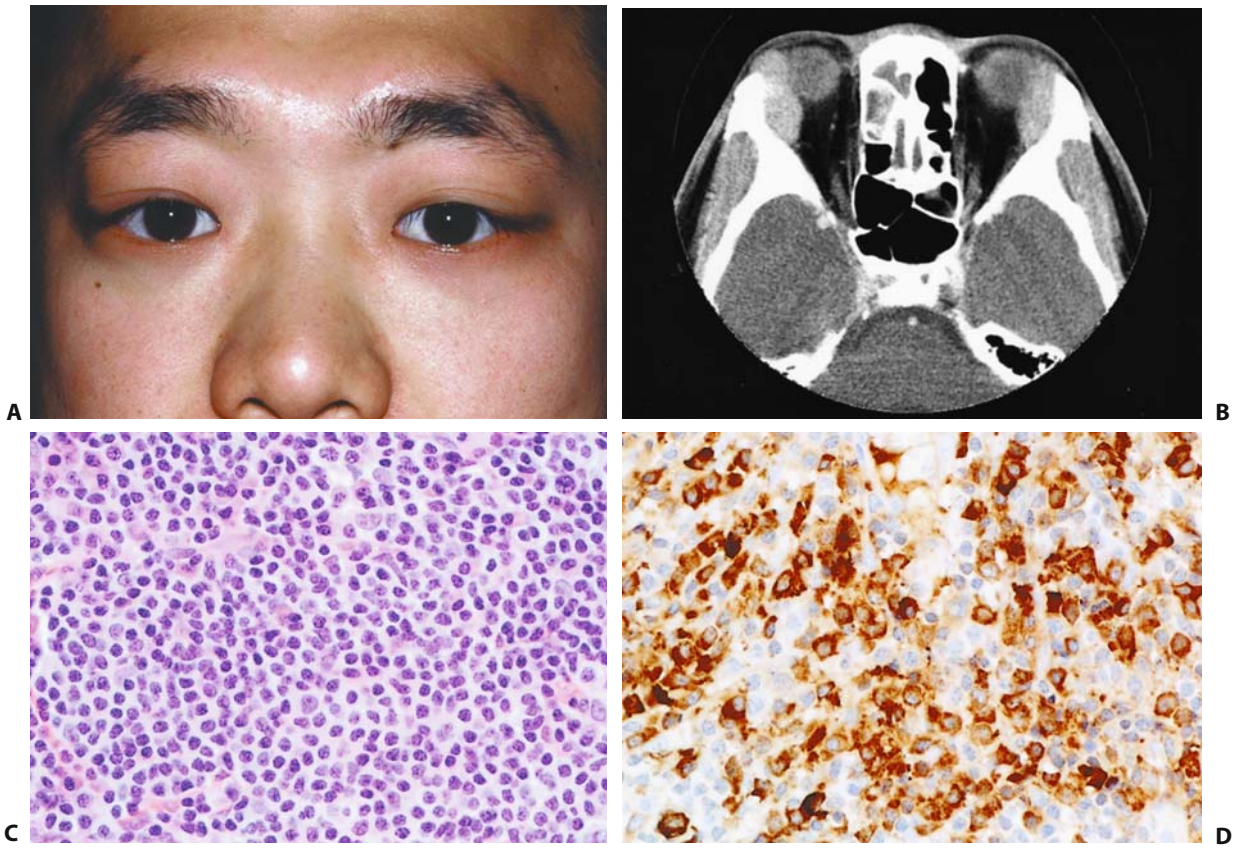

FIGURE 18.3. Lymphoma in a 26-year-old man with bilateral, nontender enlargement of the lacrimal glands. (A) Facial photograph. (B) Axial CT image shows diffuse enlargement of the lacrimal glands that is smooth in outline, of homogeneous density, and molds around the eyeball. (C) Low-grade, marginal zone B-cell lymphoma is composed of small lymphocytes [H&E, original magnification ×400]. (D) Immunohistochemical stain shows monoclonality of tumor cells for kappa light chain (original magnification ×400).

meticulous and complete removal of the intact cyst. An approach through the superior cul-de-sac with lateral cantholysis is adequate (Figure 18.5D).

PLEOMORPHIC ADENOMA (BENIGN MIXED TUMOR)

The most common benign neoplasm of the lacrimal gland is the pleomorphic adenoma. The term "benign mixed tumor" came from an earlier hypothesis, which remains popular, that these tumors derive from a mixture of epithelial and mesodermal elements. In fact, these tumors are epithelial in origin. Ductal epithelium develops into the epithelial component, and cells in the stroma and myoepithelium develop into cells in the stroma.[17] The World Health Organization proposed the name *pleomorphic adenoma*, which more accurately describes the nature of the neoplasm.

Clinical Features

Pleomorphic adenomas usually occur in the fourth and fifth decade of life, and incidence is equal for both genders.[13] However the age range is wide, and the tumor has been reported in children as young as 6 years old.[18]

Pleomorphic adenomas commonly present with symptoms of painless, unilateral progressive proptosis and downward and inward displacement of the globe (Figures 18.6A and 18.7A). These symptoms are usually present for over 12 months with no inflammatory signs. Other presenting symptoms or signs include diplopia or an ocular motility disturbance, a change in refractive error, orbital discomfort, lacrimation, ptosis, and choroidal folds. A palpable mass in the superotemporal orbital quadrant is present in most patients and is not tender.[13]

Although pleomorphic adenomas commonly involve the orbital lobe of the lacrimal gland, they can involve the palpebral lobe in about 10% of cases.[13] The palpebral lobe tumors are freely movable, nontender, and present for a shorter duration. They do not produce proptosis or bony changes.[19,20] Pleomorphic adenomas arising in the palpebral lobe are excised with some normal lacrimal gland tissue through a lid crease incision.[19]

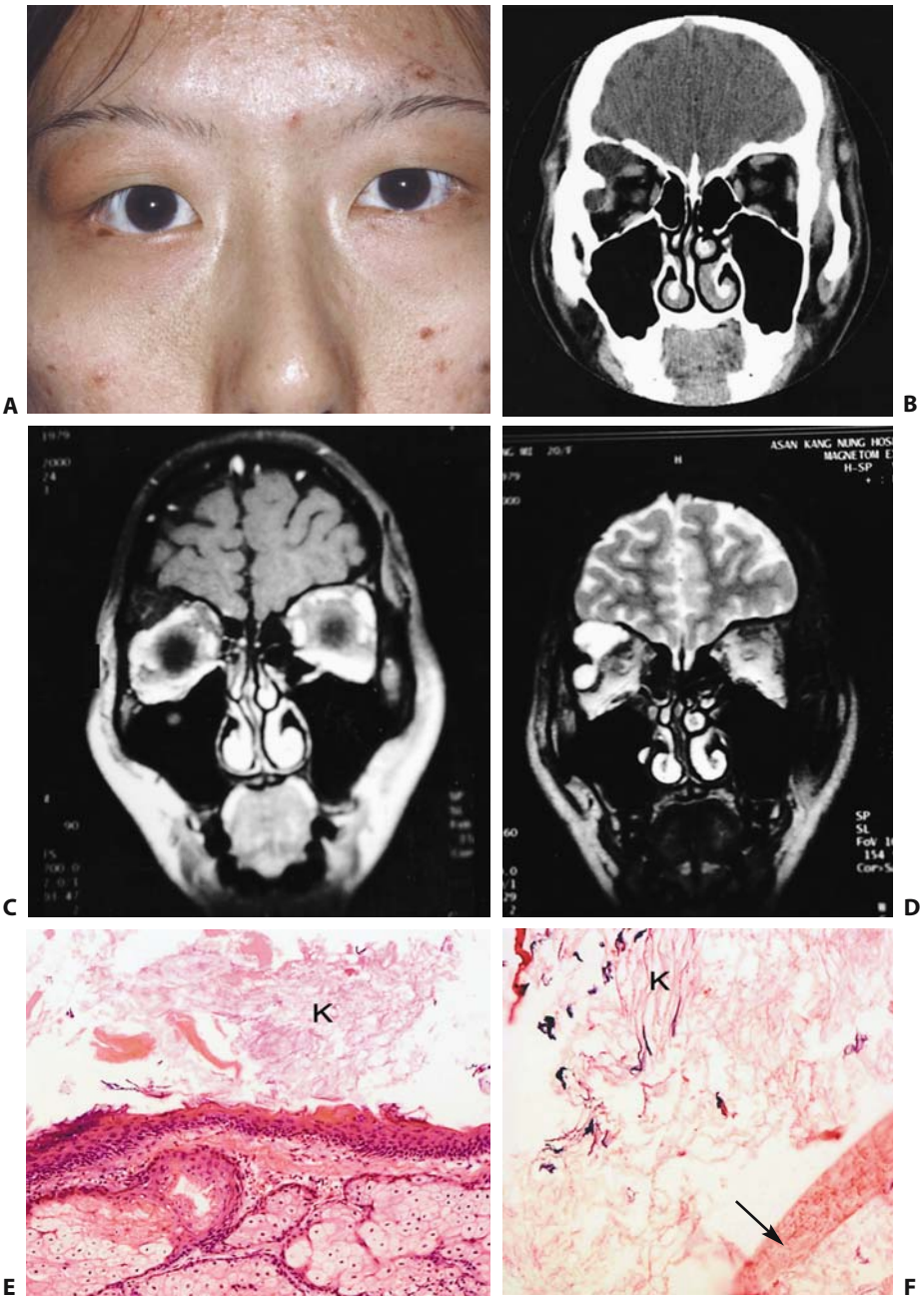

FIGURE 18.4. (A) Dermoid cyst in a 21-year-old woman who had experienced slowly progressive proptosis of the right eye for several years. (A) Facial photograph. (B) Coronal CT image shows a large cystic mass that erodes the superior and lateral walls of the orbit. (C) T1-weighted MR image shows a low-intensity mass with no enhancement. (D) The mass shows high intensity on a T2-weighted MR image. (E) The cyst wall is lined by well-differentiated epidermal and dermal tissues containing all the skin appendages (H&E, original magnification ×100). (F) The cystic lumen is filled with keratin materials (K), sebum and hairs (arrow) (H&E, original magnification ×200).

Radiologic Features

CT images show round to oval, well-defined lesions that are smooth in outline, displacing and deforming the globe (Figure 18.6B,C). The contrast enhancement is moderate to marked. Some long-standing large tumors show lobulations and radiolucent areas of cystic degeneration. In the bone window, the lacrimal fossa is prominent owing to pressure erosion. This condition can progress to a defect in the orbital roof with contact of tumor and dura.[21]

On MRI the tumor is of low signal intensity on the T1-weighted image and of high signal intensity on the T2-weighted image, frequently of heterogeneous distribution. The contrast enhancement is intense (Figure 18.7B). Large tumors can show liquefied portions centrally (Figure 18.8). The pseudocapsule may appear

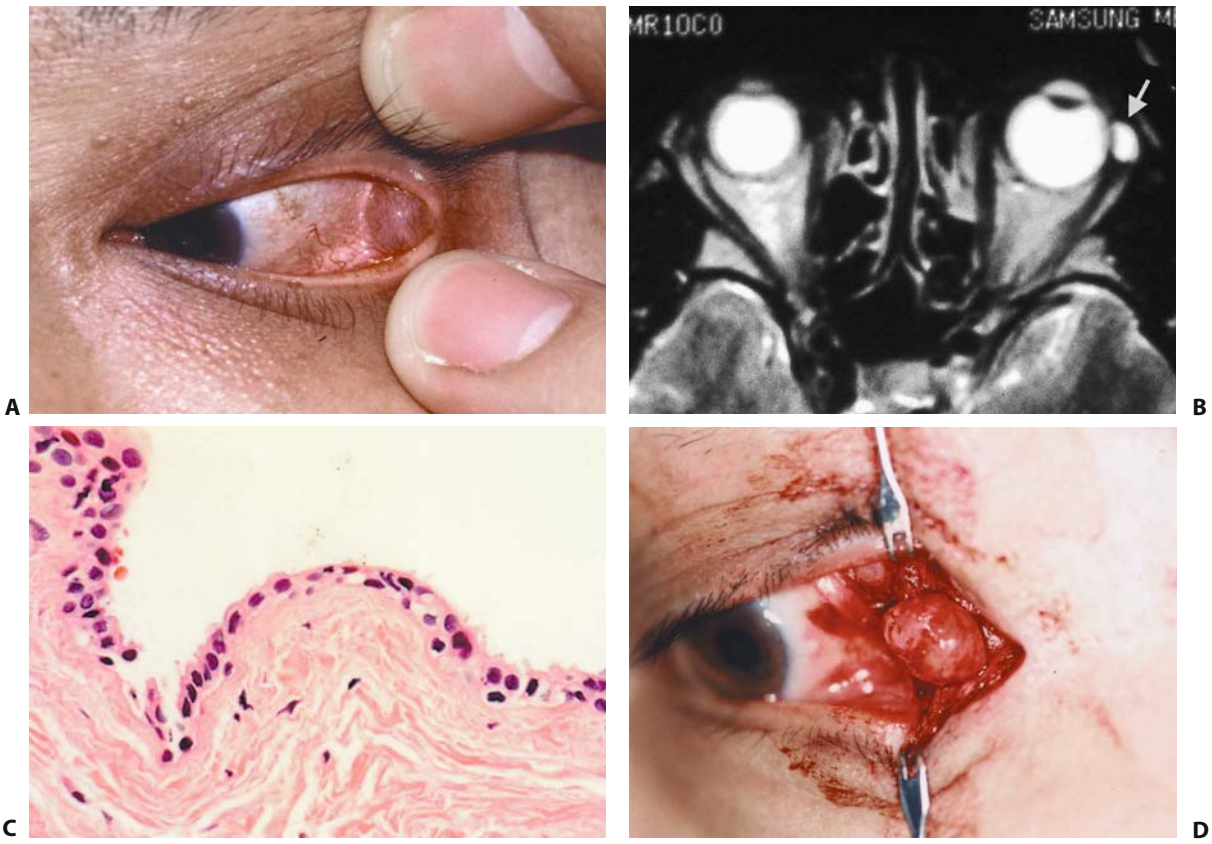

FIGURE 18.5. Dacryops. (A) The transilluminating, cystic mass is visible through the conjunctiva. (B) T2-weighted MR image showing a cystic mass. (C) Histopathologically, the cyst wall is lined by two layers of epithelial cells (H&E, original magnification ×400). (D) The mass is excised by lateral cantholysis.

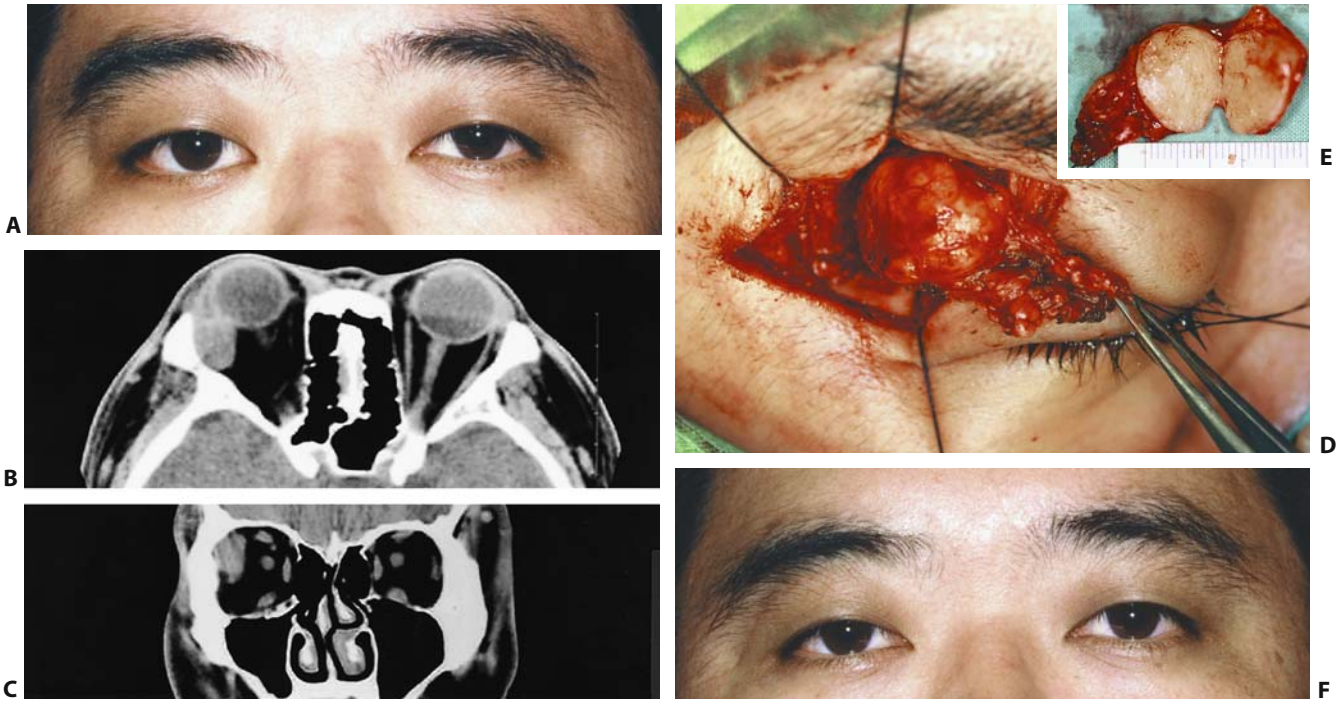

FIGURE 18.6. Pleomorphic adenoma in a 33-year-old man who had experienced progressive proptosis and inferior dystopia of right eye for 1 year. (A) Facial photograph. (B) Axial and (C) coronal CT images show well-defined oval mass with smooth excavation of the adjacent orbital bone. (D) The tumor, inside its pseudocapsule, is removed along with surrounding lacrimal gland. (E) The cut surface shows hyalinized appearance. (F) The patient one year after operation; there had been no recurrences.

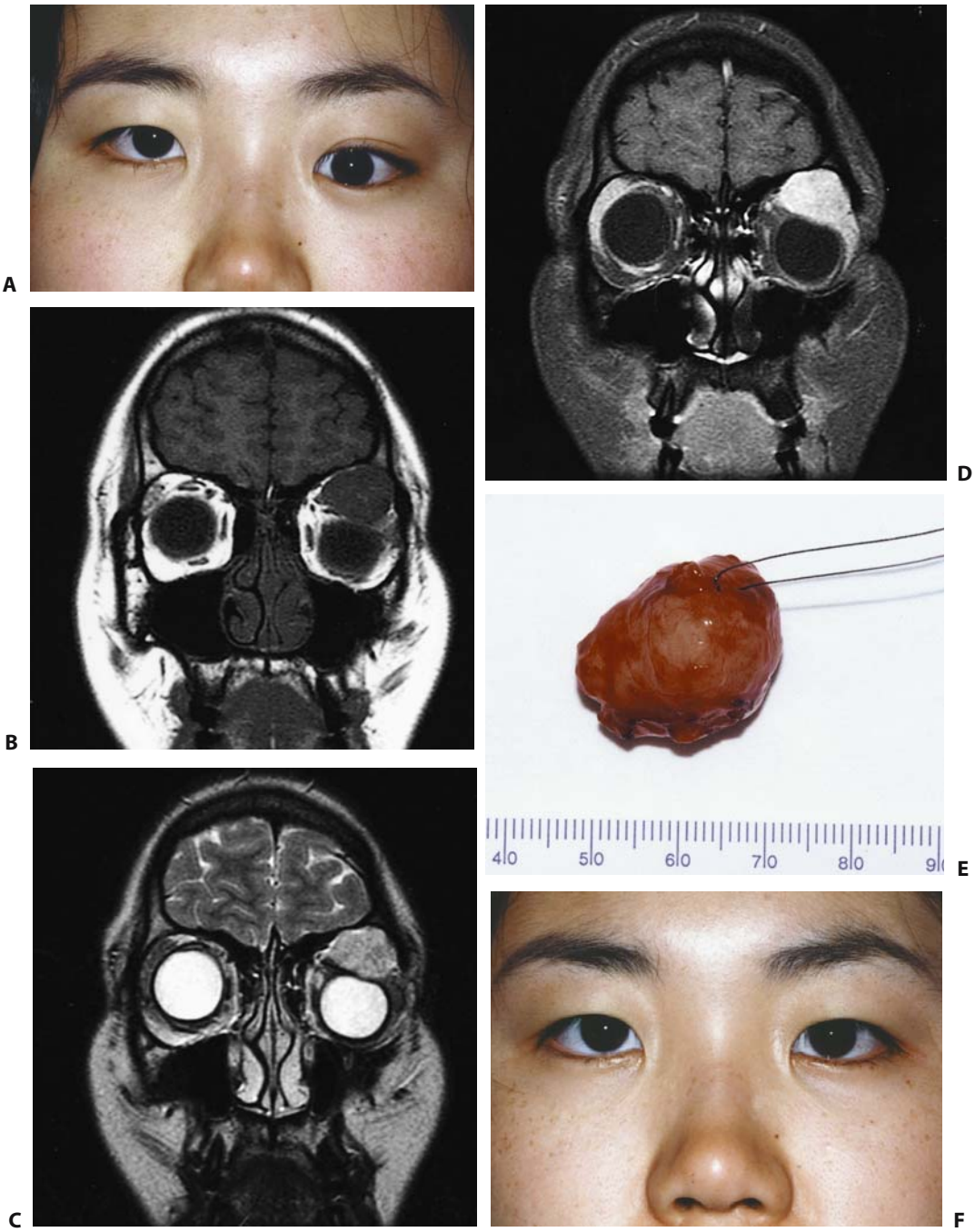

FIGURE 18.7. Pleomorphic adenoma in a 19-year-old woman who presented with slowly progressive proptosis and had experienced downward displacement of the left eye for 3 years. (A) Facial photograph. (B) T1-weighted coronal image shows well-demarcated lacrimal gland mass of low signal intensity with pressure erosion of the superior orbital wall. (C) T2-weighted coronal image shows mass of high signal intensity; the globe is deformed by the mass. (D) After gadolinium DTPA enhancement, visibility of details of the mass is markedly improved. (E) The tumor is excised with its capsule intact. (F) Photograph taken 2 years after the operation demonstrating no tumor recurrence.

as a linear rim of low signal intensity on T1- and T2-weighted images.[21]

Pathology

Grossly, the tumor is grayish white, bosselated, solitary, and well circumscribed by a thin pseudocapsule formed by compressed adjacent tissue and reactive fibrosis. Small tumor cell nests may be seen outside the pseudocapsule; these cause a high incidence of recurrence when a margin of normal tissue is not removed with the tumor. Their cut surfaces show soft mucinous areas alternating with tough fibrous areas.

Histopathologic examination shows the mixture of epithelial and mesenchymal elements that led to the term "benign mixed tumor." As noted earlier, how-

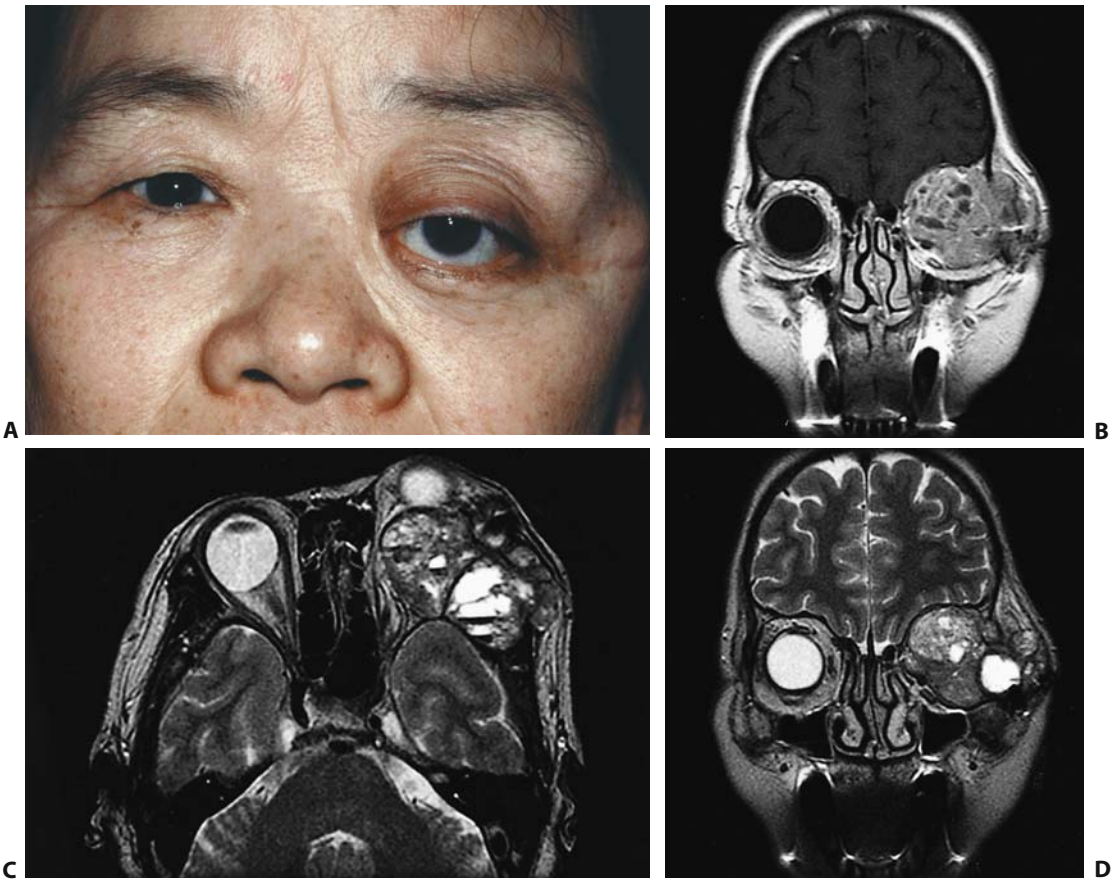

FIGURE 18.8. Pleomorphic adenoma. (A) A 68-year-old woman had had long-standing proptosis and downward displacement of the left eye for 30 years. She had experienced two recurrences after incomplete removal 15 years ago. (B) T1-weighted coronal MR image shows the huge mass of heterogeneous intensity filling the entire orbital cavity and extending into the temporal fossa. The focal area of low-signal intensity in the tumor mass demonstrates the area of cystic degeneration. T2-weighted axial (C) and coronal (D) MR images demonstrate a huge mass with focal areas of high signal intensity and fluid–fluid level of cystic degeneration.

ever, immunohistochemical studies support the hypothesis that this tumor arises from pleomorphism of epithelial components rather than a mixed origin.[17] Thus *pleomorphic adenoma* is the more preferable term. The epithelial components are variably sized ducts containing an inner cuboidal to columnar epithelium and an outer flattened, spindle-shaped myoepithelial layer (Figure 18.9A). The myoepithelial cells

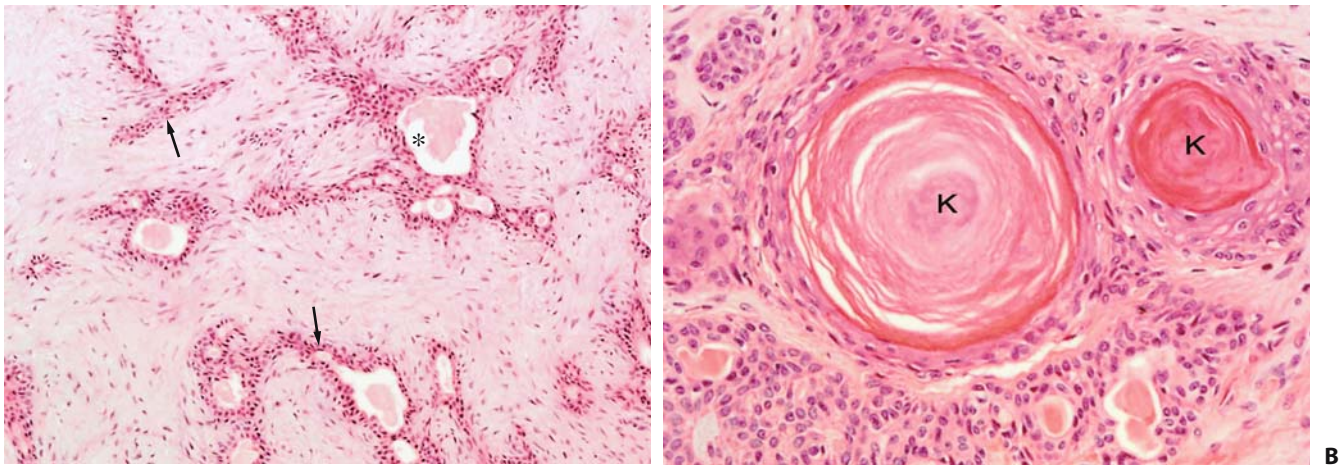

FIGURE 18.9. Pleomorphic adenoma. (A) Histopathologic appearance of the tumor shows the myxomatous matrix and cords of epithelial cells. Duct formation is apparent, with ducts lined with a double layer of cuboidal cells, surrounded by myoepithelial cells (arrows). Secreted eosinophilic material (asterisk) is present in the lumen of the duct (*) (H&E, original magnification ×100). (B) Focal area of squamous metaplasia with keratin formation (K) (H&E, original magnification ×200).

undergo metaplasia to form myxoid tissue, cartilage, and bone. Focal squamous metaplasia and keratin production may be observed (Figure 18.9B).[6,22]

Management and Prognosis

The best management is complete excision of the tumor within its pseudocapsule via a lateral orbitotomy (Figures 18.6D and 18.7E). To minimize any tumor seeding from microscopic extensions through the pseudocapsule, an adequate margin of the surrounding lacrimal gland and the adjacent periorbita should be removed in the extirpation.[6,13] In some cases, small satellite nodules of pleomorphic adenoma may be left behind even after careful in toto excision of the main mass. Therefore, it is good practice to inspect the surgical bed and ensure that no residual tumor nodules remain. When properly handled, the prognosis of pleomorphic adenomas is excellent (Figures 18.6F and 18.7F). Some advocate additional removal of the palpebral lobe of the lacrimal gland with excretory ductules to reduce the recurrence rate.[9] However, preservation of the palpebral lobe greatly reduces the incidence of postoperative dry eye and the need for topical lubricants.[13]

Font and Gamel[4] have emphasized the high recurrence rate following incomplete excision or incisional biopsy. The 5-year recurrence rate was 3% for completely excised lesions and 32% for incompletely excised tumors. Recurrent pleomorphic adenoma can undergo malignant change. Font and Gamel[4] estimated that about 10% of adenomas undergo malignant change by 20 years after first treatment and 20% by 30 years. Because biopsy of pleomorphic adenomas can have disastrous consequences, these tumors should be diagnosed before surgery so that biopsy can be avoided. For patients with pleomorphic adenoma who have had a biopsy, the biopsy track and skin scar are excised in continuity with a total removal of lacrimal gland.[13]

MALIGNANT MIXED TUMOR

The reported incidence of the malignant mixed tumor has ranged from 4 to 15% of the epithelial tumors of the lacrimal gland.[2,4,6,8,23] A malignant mixed tumor represents a pleomorphic adenoma that has undergone malignant degeneration. Patients with malignant mixed tumors tend to be older than those with pleomorphic adenoma. Font and Gamel[4] described different sex ratios for subtypes of these tumors. Men are more often affected by an adenocarcinoma arising from pleomorphic adenoma, whereas women are more often affected by an adenoid cystic carcinoma arising from pleomorphic adenoma.

Clinical Features

Malignant mixed tumors usually present in three clinical ways. First, the patient whose benign mixed tumor was not removed totally may develop a sudden recurrence several years later (Figure 18.10A). Second, the patient with indolent long-standing lacrimal tumor history presents with sudden expansion of the mass, as well as pain and swelling of the upper eyelid. Third, the patient has rapidly developing symptoms of pain and bone destruction, and the tumor is diagnosed as malignant at the first presentation. The third presentation could be considered to be de novo.[6,23,24]

Radiologic Features

On CT, an enlarged lacrimal fossa surrounded by bone destruction means malignant tumors. The bone window shows the osseous changes best. Contrast enhancement helps to reveal involvement of the dura and intracranial extension. It is not possible to differentiate malignant mixed tumor from other carcinomas of the lacrimal gland on CT.[15,21] At times, carcinoma in pleomorphic adenoma may have a smooth contour and no bony changes (Figure 18.10B,C).

Pathology

Malignant mixed tumors have the histologic features of a benign mixed tumor with areas of malignant change. In most cases the malignant elements are poorly differentiated adenocarcinoma (Figure 18.10D, E). The other malignant elements are adenoid cystic carcinoma, squamous cell carcinoma, and, rarely, spindle cell sarcoma.[4,23,24]

Management and Prognosis

When preoperative evaluation indicates a malignant tumor, the recommended therapy is transseptal biopsy followed by complete removal of the tumor. Henderson and Neault[25] proposed a one-stage procedure for the surgical removal of the tumor and adjacent adnexa: an en bloc resection of the neoplasm, its periorbital base, and surrounding bone. A radical orbitectomy with regional and cervical lymph node dissection has been advised because an adenocarcinoma arising in a benign mixed tumor may disseminate early via lymphatics. Postoperative radiotherapy may also be recommended.[22,26] If metastases have occurred, treatment is often limited to surgical debulking followed by postoperative radiotherapy.

Even with extensive surgery, patient mortality remains high. Font and Gamel[4] reported that 30% of their patients had died of a tumor at 5 years, 45% at 11 years, and 50% by 12 years. Henderson[6] described 8 of the 9 patients who died during the mean follow-

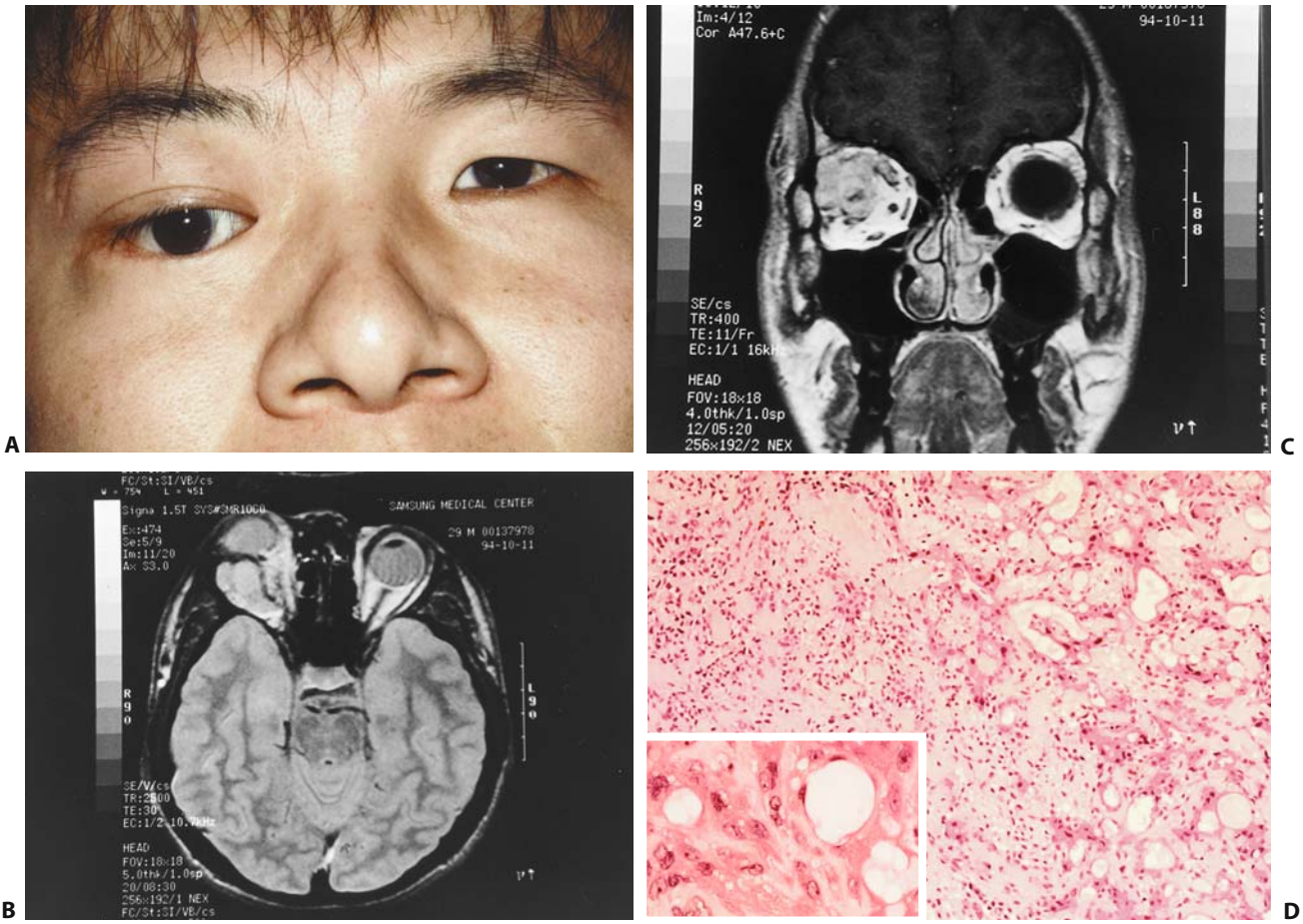

FIGURE 18.10. Malignant mixed tumor. (A) A 28-year-old male presented with a 12-year history of proptosis and downward displacement of the right eye. He experienced multiple recurrences of incompletely excised pleomorphic adenomas for 10 years. The globe was 11 mm proptosed and became frozen in all directions over a 6-month period. (B) Proton-density axial MR image shows a large, lobulated soft tissue mass extends backward along the lateral wall of the right orbit. (C) Coronal enhanced T1-weighted image demonstrates homogeneous enhancement of the lobulated mass. Note erosion of the superolateral bony wall. (D) Histopathologic examination of the tumor shows adjacent area of a benign mixed tumor on the left with solid epithelial tubules on the right indicating malignant transformation (H&E, original magnification ×100). *Inset*: The epithelial component showing the features of the adenocarcinoma (H&E, original magnification ×400).

up period of 14.1 years. The longest survival was 30 years in a patient whose original tumor was benign. Henderson introduced the concept that patients whose original tumor was benign will live longer (mean 19.2 years) than patients with tumors of the de novo type (mean 7.7 years). The cause of death is intracranial extension of the tumor and distant metastases to lung, chest wall, or bone.

ADENOID CYSTIC CARCINOMA

Adenoid cystic carcinoma is the second most common epithelial tumor of the lacrimal gland and the most common malignant epithelial tumor of the lacrimal gland. It accounts for about 1.6% of all orbital tumors and 3.8% of all primary orbital tumors.[6] It occurs in both sexes. Patients are about 40 years of age at presentation, with a range of 6.5 to 79 years.[14,27] Wright and associates suggested a bimodal peak in the fourth and sixth decades.[14] Because this tumor may present at an earlier age, a high clinical suspicion is indicated for any unilateral mass in the upper temporal quadrant, even in teenagers and children, where these tumors might be mistaken for dermoids.[27–29]

Clinical Features

A patient with adenoid cystic carcinoma presents mass effect with a more rapid temporal sequence usually under 1 year (Figures 18.11A, 18.12A, and 18.13A). The presenting symptoms are pain, globe displacement, mass or swelling, numbness, diplopia, visual change, lacrimation, and ptosis. Because this tumor invades perineurally and into adjacent bone, there may be pain and, more rarely, numbness. The reported in-

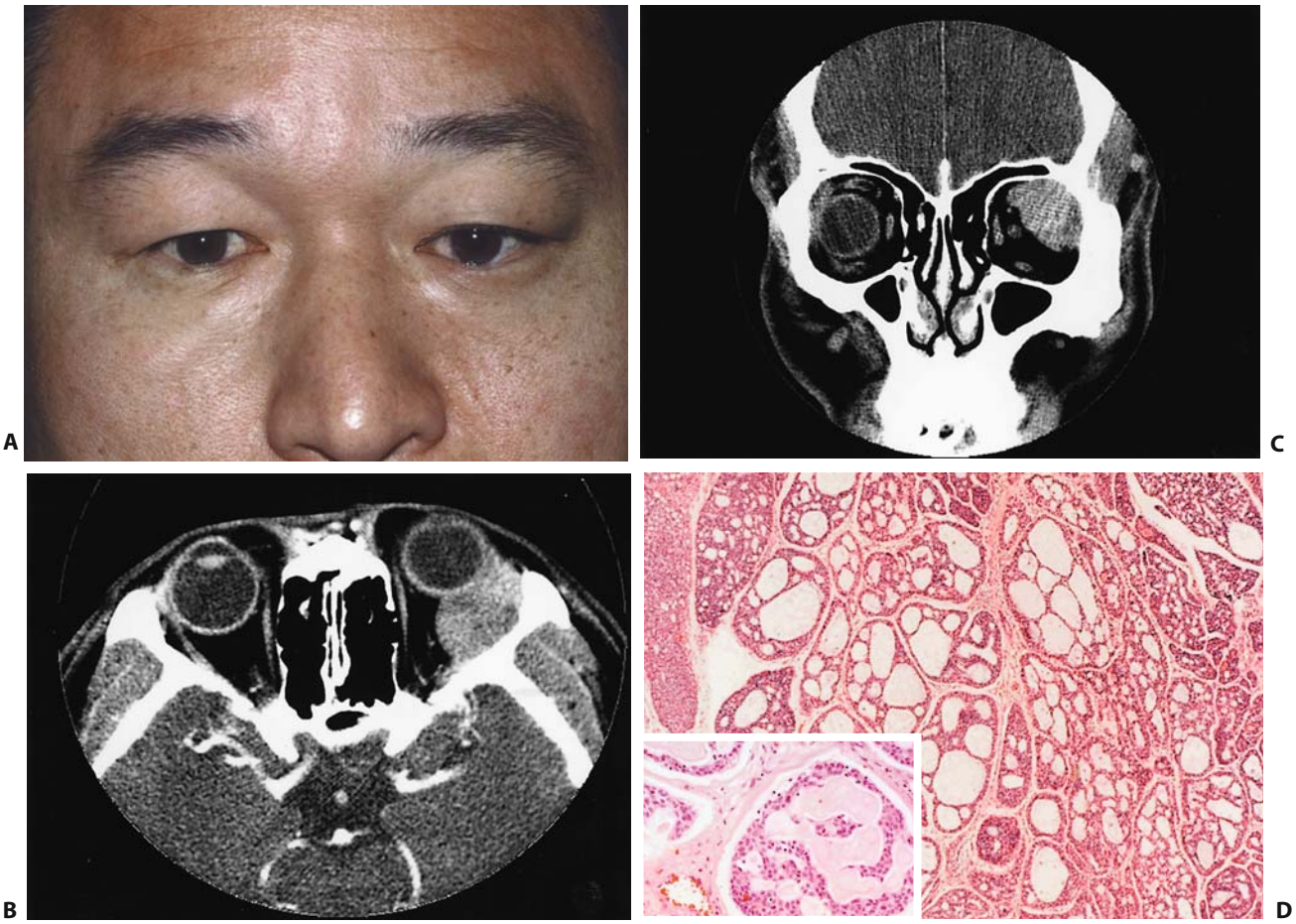

FIGURE 18.11. Adenoid cystic carcinoma. (A) A 40-year-old man presenting proptosis of the left eye for 5 months. (B) Axial and (C) coronal CT images show well-defined oval mass with pressure erosion of the adjacent orbital bone. (D) Histopathologically, the tumor proved to be an adenoid cystic carcinoma with a typical cribriform (Swiss cheese) pattern (H&E, original magnification ×40). *Inset*: Glandlike spaces (pseudocysts) are filled with eosinophilic basal lamina materials (H&E, original magnification ×200).

cidence of pain is variable, between 37.5 and 79%.[6,14,30]

Radiologic Features

High-resolution CT shows more elongated mass extending along the lateral orbital wall, with expansion of the lacrimal fossa with bone invasion.[15,31] This tumor can be globular or round and usually reveals more irregular and serrated borders than those seen in pleomorphic adenoma (Figures 18.11B,C, 18.12B, and 18.13B). In the series of Wright and colleagues', CT abnormalities consisted of bone erosion (75%), bone destruction (34%), and soft tissue calcification (22%).[14] High-resolution CT with bone windows is recommended. Contrast enhancement helps to reveal involvement of the dura and intracranial extension.

MRI with enhancement is best for assessing the invasion of the tumor into the cavernous sinus, brain, and bone marrow (Figures 18.12C and 18.13C). The tumor is hypointense on the T1-weighted image and hyperintense on the T2-weighted image with contrast enhancement.

Pathology

The gross appearance of adenoid cystic carcinoma is grayish-white, firm, nodular, and deceivingly circumscribed. The tumor is more difficult to dissect during surgery than a pleomorphic adenoma.

Microscopically, five histologic patterns have been described: cribriform ("Swiss cheese") (Figure 18.11D), solid (basaloid), sclerosing, comedocarcinomatous, and tubular (ductal), in order of frequency.[32] All or several of these patterns may be present in one tumor, but one pattern usually predominates. In Gamel and Font's series of 54 adenoid cystic carcinomas, patients with a basaloid pattern in their tumor had a 5-year survival rate of 21% and a median survival of 3 years, whereas patients whose tumor contained no trace of a basaloid component had a 5-year survival rate of 71% and a median survival of 8 years.[32] In a study of

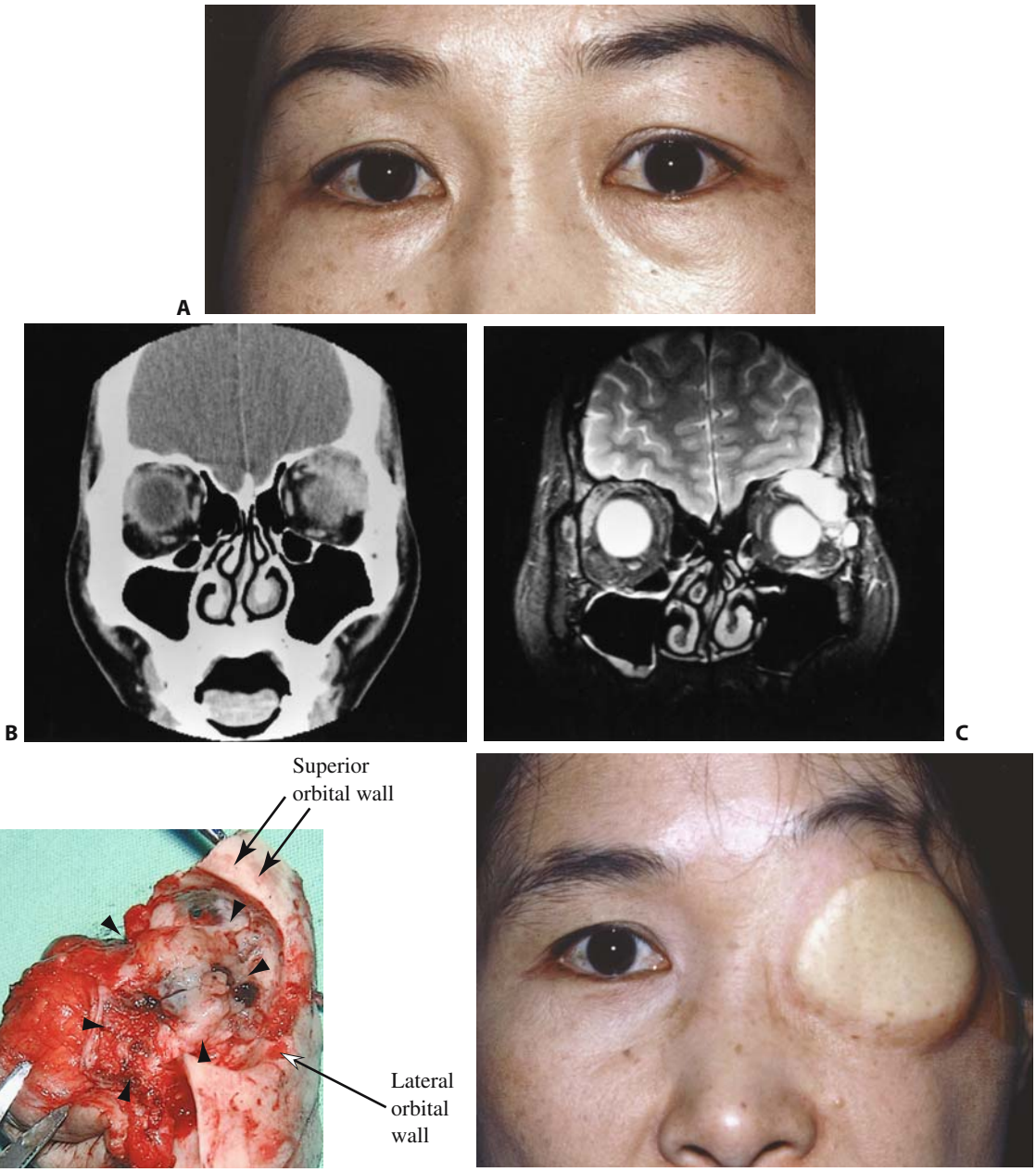

FIGURE 18.12. Adenoid cystic carcinoma. (A) A 39-year-old woman developed painful swelling of left eyelid and headache from several months ago. She had undergone lateral orbitotomy 13 years earlier to remove an unknown benign tumor of the left lacrimal gland. There is 2 mm of proptosis in her left eye. Firm, tender mass is palpable in the left lacrimal gland area. (B) Coronal CT scan of the orbit shows heterogeneously enhancing mass in superolateral portion of the left orbit with excavation of adjacent bone. (C) T2-weighted coronal MR image shows well-defined mass lesion, which, from the superotemporal portion of the left orbit, invades the bony cortex of the superior and lateral wall of the orbit. (D) An orbitozygomatic approach was used to perform radical orbital exenteration with removal of superior and lateral orbital wall. Solid arrows indicate the tumor. (E) The orbital defect was reconstructed with calvarian bone graft and rectus abdominis free flap. This photograph was taken 6 months after the operation.

26 orbital adenoid cystic carcinomas by Lee et al., the "Swiss cheese" pattern was associated with longer survival and the basaloid pattern was not.[30] The basaloid pattern may occur more frequently in patients older than 40 years and is associated with a reduction in estimated disease-free survival.[14]

Perineural invasion is frequently observed in exenteration specimens, accounting for the symptoms of pain and numbness. Tumor cells tend to infiltrate the contiguous bone of the lacrimal fossa to produce the bony changes observed in radiologic studies.

Management and Prognosis

The optimal treatment for patients with adenoid cystic carcinoma has yet to be determined. Tumor removal and postoperative radiotherapy comprise the most common treatment. The surgical techniques of

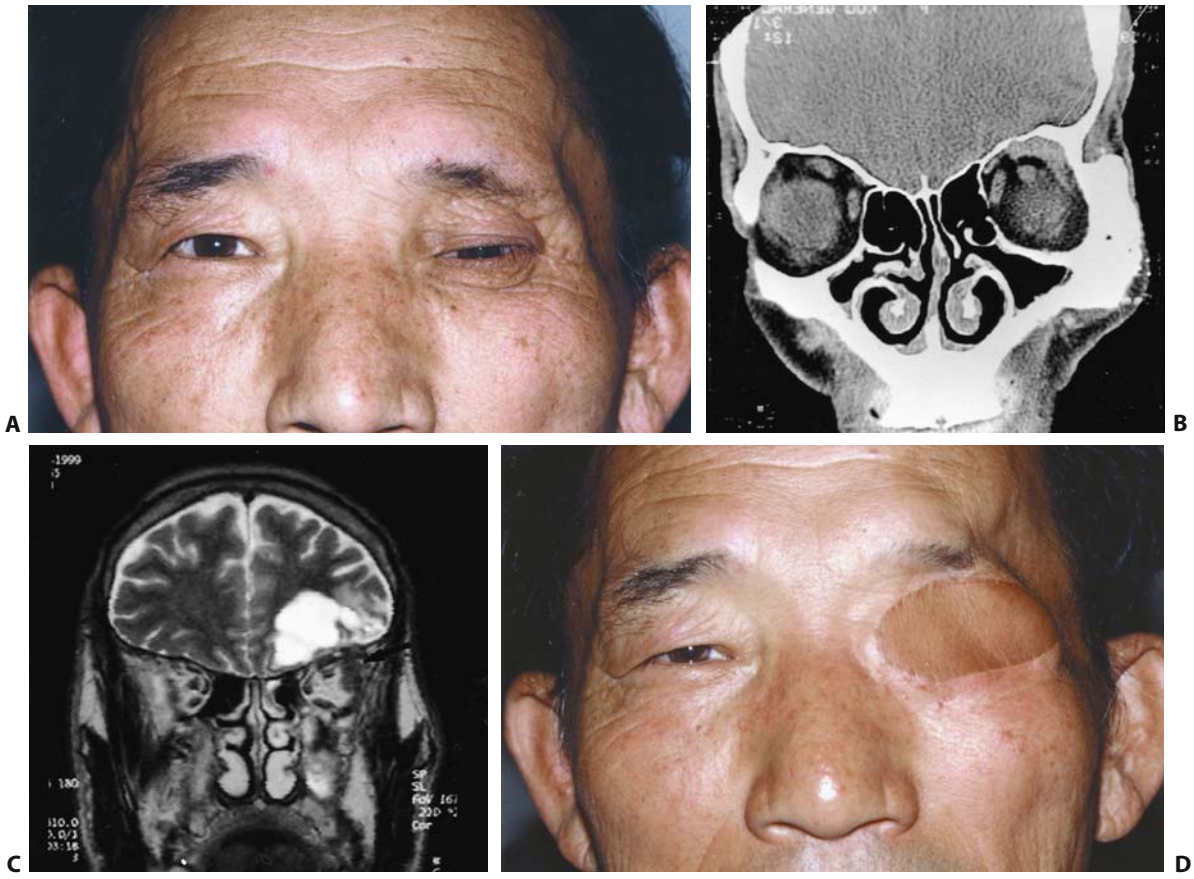

FIGURE 18.13. Adenoid cystic carcinoma. (A) A 57-year-old man had undergone tumor removal by lateral orbitotomy 12 years earlier for adenoid cystic carcinoma of the left lacrimal gland. There were perineural and adjacent bony invasion at that time. He received radiation therapy right after the operation. Upon developing motor aphasia, he visited our clinic. There is 2 mm of proptosis in his left eye. The left upper eyelid is ptotic and hard mass is palpable in the upper lid. The upward movement of the eye is restricted. (B) Coronal CT scan of the orbit shows tubular mass in superolateral portion of the left orbit with excavation of adjacent bone. (C) T2-weighted coronal MR image shows a well-defined 3.5 cm cystic lesion in the left basal frontal lobe from previous radiation necrosis and a tubular mass lesion in superotemporal portion of the left orbit that is isosignal with muscle. (D) Incisional biopsy of the orbital mass revealed recurrence of adenoid cystic carcinoma. Radical orbital exenteration with removal of surrounding orbital wall was performed through orbitozygomatic approach. The intracranial cyst was removed and dura was sutured. The orbital defect was reconstructed with splitted calvarian bone graft and rectus abdominis free flap. There has been no recurrence after 5 years.

tumor removal include local resection, en bloc removal, exenteration, and radical exenteration (radical orbitectomy).[25,33–37] Radical exenteration with removal of the orbital roof, the lateral wall, and the anterior portion of the temporalis muscle where the zygomaticofrontal and zygomaticotemporal nerves extend has been recommended (Figures 18.12D,E and 18.13D). Even with this radical approach, the survival rate has been 20% at 10 years, and the median survival was 5 years.[32] Patients usually die of intracranial spread as a result of perineural invasion and pulmonary metastasis. In one series, cranio-orbital resection did not reduce the incidence of recurrence but might lead to improved survival.[14]

Radiation therapy in the dose of 50 to 60 Gy after local resection of adenoid cystic carcinoma significantly delays the onset of tumor recurrence and prolongs survival. It might be as effective as cranio-orbital resection with radiotherapy.[14] Our experience also shows that good tumor control can be obtained in lesions that have local disease and contiguous spread. We have treated 5 patients with adenoid cystic carcinoma who refused radical exenteration with local resection and adjuvant radiation therapy, and the results were good during a 13- to 17-year follow-up. This is, however, too short a follow-up period to permit us to draw final conclusions. One interesting surviving patient in our series had undergone tumor removal by lateral orbitotomy and radiation therapy for adenoid cystic carcinoma of the left lacrimal gland, 17 years earlier, at which time there were perineural and adjacent bony invasions. Twelve years later motor aphasia from radiation necrosis of the frontal lobe developed. A recurrent tumor was diagnosed by radiologic studies and managed by radical orbital exenteration with removal of surrounding orbital wall. There has been no recurrence or metastasis to date (5-year follow-up, Figure 18.13). This case is noteworthy because the patient was able to avoid destructive surgery for 12 years.

Implanted sources of radiation (brachytherapy) have been tried on 7 patients with adenoid cystic carcinoma and have yielded good results in 6 patients with an average follow-up period of 3.2 years.[38] However the long-term results are unknown.

Intra-arterial chemotherapy has recently been advocated for supplemental management. Intracarotid cisplatin and intravenous doxorubicin were used before and after exenteration and radiation with long-term survival of 9.5 and 7.5 years, respectively.[39,40] The sample size is small, but this modality could be tried for patients with inoperable tumors to shrink them to a more surgically amenable size.

This tumor can grow slowly and exhibit recurrence and metastasis years after the initial treatment. Long-term follow-up of treatment methods has been difficult to obtain. Some patients die early; others may live asymptomatically for years. A long follow-up, perhaps up to 15 years, is needed before meaningful conclusions regarding a cure can be made.

ADENOCARCINOMA

Adenocarcinoma is more common in males and tends to occur in an older population ranging from 18 to 80 years (median age 56 years).[4,6,22,41] This tumor constitutes 7% of epithelial neoplasms of the lacrimal gland.[4,6]

Adenocarcinoma metastasizes earlier and is associated with a shorter patient survival time than adenoid cystic carcinoma. It often manifests as a rapidly growing mass, exceeding the limits of adequate surgical excision at the time of presentation. The most common symptom at presentation is a palpable mass. Other symptoms included proptosis, pain, globe displacement, visual loss, diplopia, and ptosis (Figure 18.14A–C).[14,41]

Histopathologic examination shows pleomorphic cells with many mitotic figures arranged in sheets and cords, and lumen formation with mucin production (Figure 18.14D,E). The mucin content of the adenocarcinoma may be demonstrated with mucicarmine and alcian blue stains. The undifferentiated type does not show mucin production.

Management and Prognosis

In the Mayo Clinic series, adenocarcinoma showed great malignancy. Four of the 5 patients died of the tumor, with a mean survival of only 1.5 years from initial presentation. The shorter survival of the patients with adenocarcinoma probably is related to early lymphatic dissemination to regional lymph nodes and pulmonary metastasis. Henderson recommended a monobloc craniofacial orbitectomy combined with a regional lymph node dissection for longer survival.[6]

In a retrospective study of 13 patients with adenocarcinoma, 4 of 7 patients who received exenteration followed by radiation therapy were alive without recurrence.[41] The authors recommend treatment of primary adenocarcinoma of the lacrimal gland with exenteration and radiation therapy as soon as a diagnosis has been confirmed pathologically.

MUCOEPIDERMOID CARCINOMA

Although it is the most common primary carcinoma of the salivary glands, mucoepidermoid carcinoma is rare in the lacrimal gland. The age range of mucoepidermoid carcinoma patients is 12 to 81 years,[6,42] with an average of 49 years; there is a slight (3:2) preponderance of males over females.[43]

Mucoepidermoid carcinoma usually presents as a painless, slowly enlarging mass of the lacrimal gland fossa that is sometimes mistaken preoperatively for benign mixed tumor.[6,42] Pain, proptosis, diplopia, and globe displacement may occur.

Histologically, these tumors comprise various numbers of mucus-secreting cells interspersed with epidermoid and basal cells. Mucus-secreting cells can assume a signet ring appearance and stain positively with periodic acid–Schiff stain, Alcian blue, and mucicarmine dyes. It is classified as either low or high grade depending on the degree of differentiation and the number of mucin-producing cells. Grade 1(low-grade) tumors have large, well-differentiated cells with abundant cytoplasm, a relative paucity of the epidermoid cells, and no mitotic figures. Grade 3 (high-grade) tumors have smaller cells with hyperchromatism and frequent mitotic figures predominated by epidermoid elements. Grade 2 tumors are intermediate in histologic activity.[43]

Management and Prognosis

The clinical behavior and prognosis parallel the histologic grading. Eviatar and Hornblass[43] reviewed a series of 25 cases of mucoepidermoid carcinoma. Seven of 8 patients with low-grade tumors survived, and 1 of 8 patients with high-grade tumors has remained tumor-free. The authors recommended exenteration, radiation, and resection of involved orbital bone for patients with high-grade tumors. Patients with low-grade tumors can be expected to do well with extirpation with or without adjuvant radiation.

OTHER TUMORS

The following lacrimal gland tumors are rarely encountered even in busy ocular oncology practices.

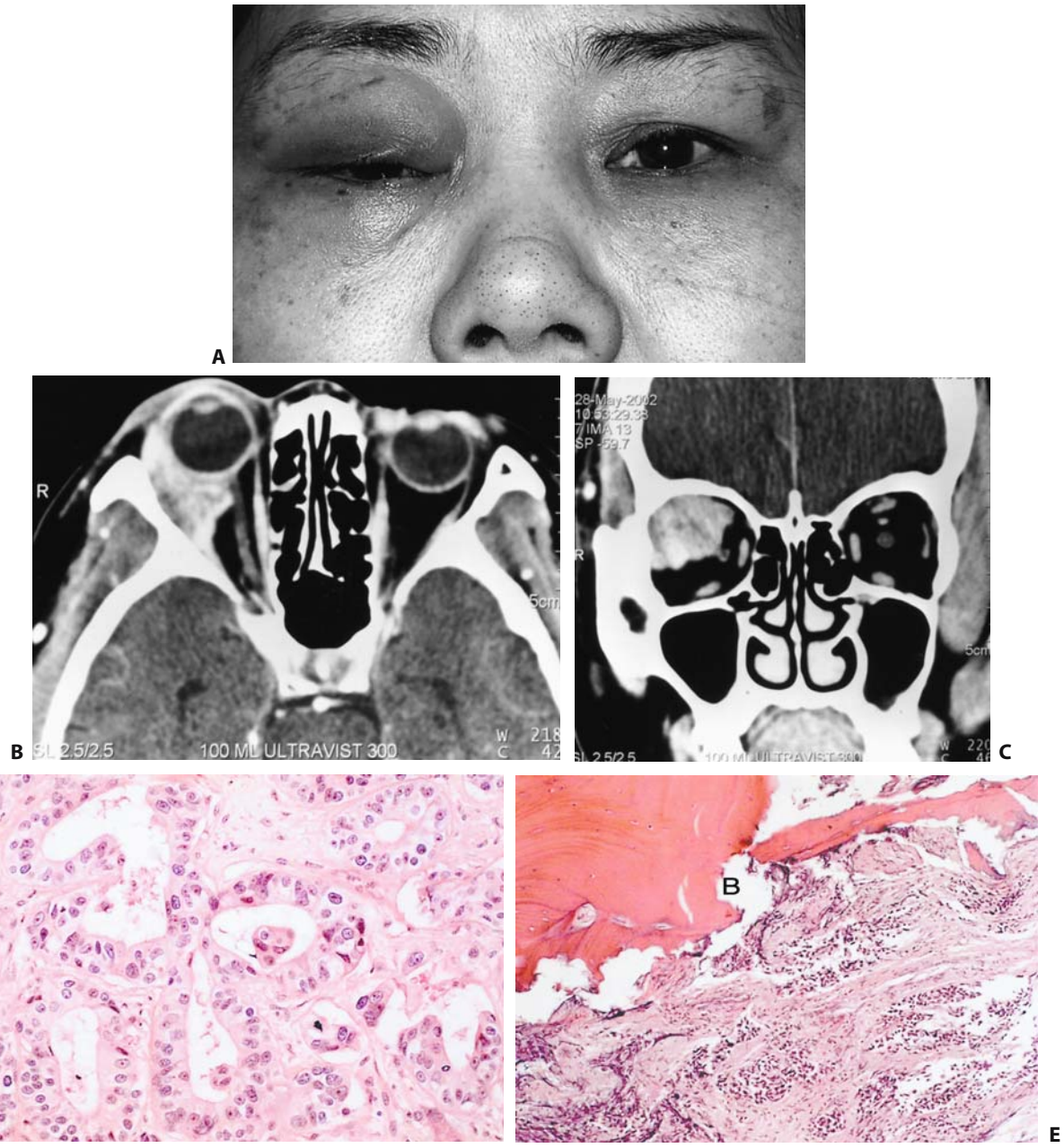

FIGURE 18.14. Adenocarcinoma. (A) A 51-year-old woman was referred with a 3-month history of right upper eyelid swelling and proptosis. She complained of deep orbital pain. Her eyelid was swollen and ptotic; there was limitation of upgaze. (B) Axial CT demonstrating an enhancing mass in the right orbit extending posteriorly in the area of the lacrimal gland. (C) Coronal CT demonstrating an enhancing mass in superolateral portion of the right orbit with excavation of adjacent bone and involvement of superior and lateral rectus muscles. (D) Histopathologic examination shows well-formed glandular or ductal structures composed of malignant epithelial cells with prominent nuclei and dark-staining cytoplasm (H&E, original magnification ×200). (E) The bone (B) is invaded by the tumor (H&E, original magnification ×100).

However, they are briefly reviewed here for the sake of completeness.

Acinic Cell Carcinoma

Acinic cell carcinoma is an uncommon tumor of salivary gland origin that comprises 2 to 4% of primary parotid gland neoplasms. There is a female preponderance and a peak incidence in the sixth decade. Only a few cases in the lacrimal gland were reported in patients from 18 to 56 years of age.[44–46] This cancer manifests as a painless, slow-growing mass but can invade intracranially in a more aggressive manner.

Microscopically, there are four growth patterns: solid, microcystic, papillary cystic, and follicular. The solid and microcystic patterns are considered to be the most common. The reported cases were treated by tumor excision, exenteration, and exenteration with cranial bone resection, with no tumor recurrences during follow-up periods of 2.5 to 4.5 years.[44–46]

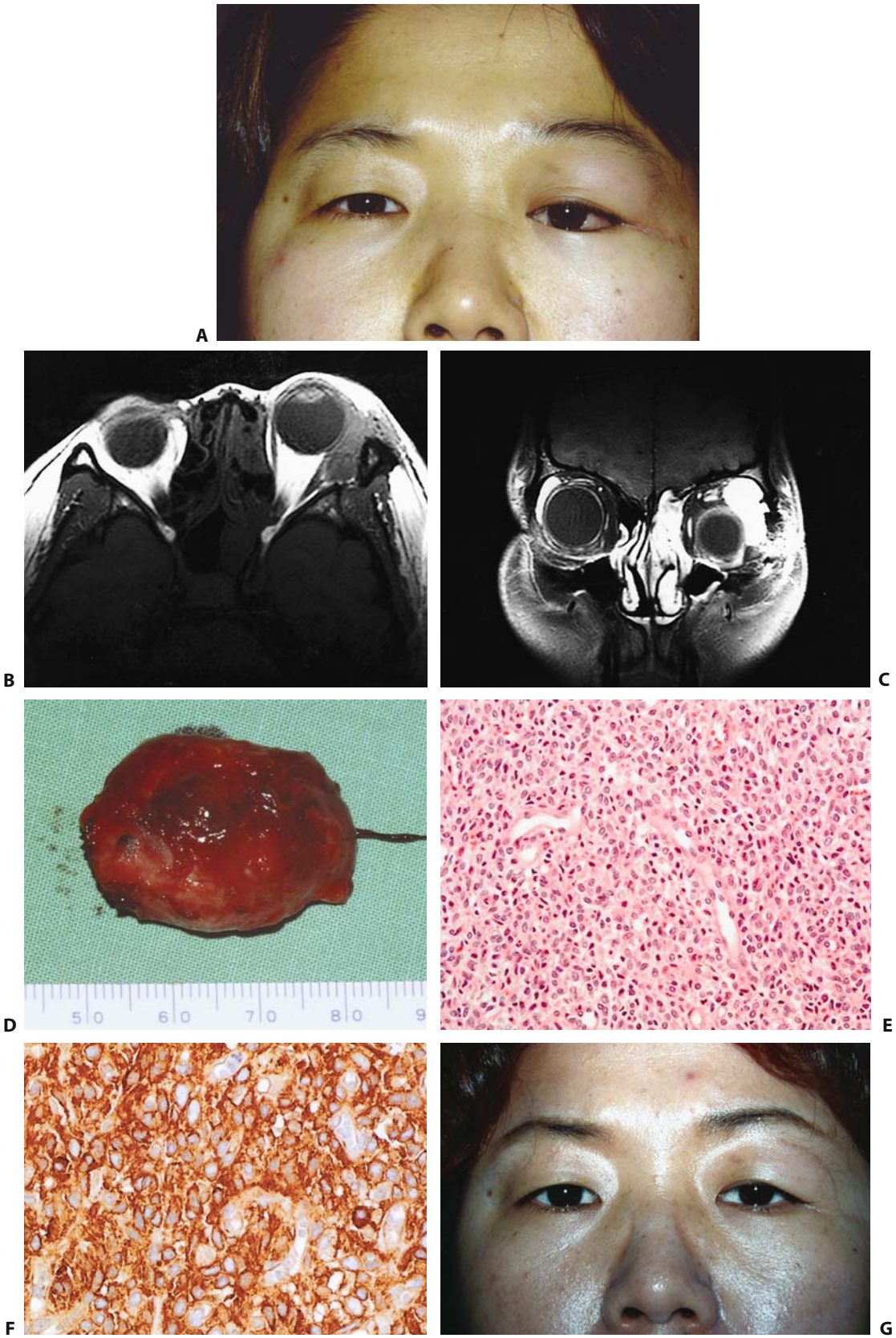

FIGURE 18.15. Solitary fibrous tumor. (A) A 27-year-old woman had had eyelid swelling, chemosis, proptosis, and inferior displacement of left eyeball for 9 months. Three months before referral, she had undergone incomplete tumor removal via lateral orbitotomy. (B) T1-weighted axial image shows well-demarcated oblongated lacrimal gland mass of low signal intensity. Lateral orbital wall is deformed from previous orbitotomy. (C) T1-weighted enhanced coronal image shows marked enhancement of the mass. (D) Complete excision of the tumor was performed via lateral orbitotomy. (E) Histopathologically, the proliferation of mesenchymal spindle cells in a collagenous stroma shows "patternless pattern." The prominent vascularity is noted (H&E original magnification ×100). (F) The tumor cells are strongly stained with antibodies to CD34 (original magnification ×400). (G) Six months after operation, there was no recurrence of tumor.

Oncocytoma (Oxyphil Cell Adenoma)

Because of their eosinophilic cytoplasm, oncocytes are also called *oxyphil cells*. These large cells with acidophilic staining properties may be found in mucous membranes such as the caruncle, conjunctiva, lacrimal sac, and lacrimal glands and seem to increase in number with age. Benign and malignant oncocytomas have been reported in the lacrimal gland. The tumors are usually benign and sometimes cystic. Malignant oncocytoma could show intracranial extension. The tumor tends to occur in older patients and is rare in children.[6,47]

Spindle Cell Myoepithelioma

Myoepithelioma is a monomorphic adenoma with a pure proliferation of myoepithelial cells. Myoepithelioma is defined as a tumor composed of myoepithelial cells with up to 10% ductal elements. The more common pleomorphic adenoma has a proliferation of both epithelial and myoepithelial elements in various combinations.[48–50]

CT scan reveals a well-circumscribed mass in superotemporal orbit. The tumor usually presents as a well-encapsulated mass and should be removed intact through a lateral orbitotomy. Most epitheliomas are benign and exhibit biological behavior similar to that of pleomorphic adenoma.[50]

Sebaceous Carcinoma

Primary sebaceous carcinoma of the lacrimal gland, possibly arising from heterotopic sebaceous tissue, is very rare. It must be differentiated from secondary invasion of the orbit by an eyelid tumor or metastatic spread. The tumor is highly malignant. Orbital exenteration, regional lymph node dissection, and postoperative radiotherapy should be considered in the management.[51,52]

Solitary Fibrous Tumor

Solitary fibrous tumor is a rare spindle cell neoplasm that most frequently develops in the pleura. This tumor usually presents with a painless unilateral proptosis with gradual onset.[53,54] CT scan shows mild remodeling of the bony orbit without calcification. Thus the clinical presentation is similar to that of pleomorphic adenoma. The management is en bloc excision via lateral orbitotomy (Figure 18.15). Generally, the aggressiveness of this tumor is associated with large tumor size, high cellularity, numerous mitoses, pleomorphism, and the presence of necrosis.[54] Solitary fibrous tumors of pleura and mediastinum demonstrated aggressive clinical behavior, such as adjacent tissue invasion, local recurrence, and distant metastases. Careful and continued follow-up is needed for this tumor because there may be recurrence after several years.

Malignant Rhabdoid Tumor

Malignant rhabdoid tumor is a rare and highly aggressive renal tumor of infants. Niffenegger et al.[55] described this tumor in a 50-year-old man. It manifested as a rapidly growing mass in the area of the right lacrimal gland. Because of the highly malignant nature of the tumor, the patient was treated with radical surgery and adjunctive radiotherapy and chemotherapy; he showed no recurrences during a 15-month follow-up period.

Hemangioma

Cavernous hemangioma, hemangioendothelioma, and epithelioid hemangioma have been reported to occur in the lacrimal gland.[56] Simple excision to preserve the lacrimal gland is sufficient treatment if the tumor is limited to the gland.[57]

Warthin Tumor

Warthin tumor frequently occurs in the parotid gland; the extraparotid localization is very rare. Bonavolonta et al.,[58] who described Warthin tumor in a 62-year-old woman, treated the patient with complete excision via lateral orbitotomy.

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