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Enclosed:
Glass slide (H&E) – 1
Written protocol

Oncocytoma of the Lacrimal Sac
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History: A 74-year-old male recently diagnosed with primary cutaneous anaplastic large T-cell lymphoma presented for evaluation of possible orbital involvement of lymphoma. On PET scan, intense uptake was present in the left nasolacrimal sac and duct area. He has had tearing from the left eye for over 15 years, which has not changed. He could also feel a mass near his medial canthus which has grown in size over the last year.

PMH: Primary cutaneous anaplastic large T-cell lymphoma diagnosed on biopsy of a left anterolateral chest wall, treated with radiation and concurrent chemotherapy. Bone marrow biopsy was negative for lymphoma.
POH: Choroidal nevus right eye, Pseudophakia both eyes, Epithelial basement membrane dystrophy both eyes
Medications: Tamsulosin, Calcium/vitamin D and vitamin C supplements, Melatonin, Saw palmetto
Family history: Father with colon cancer and prostate cancer, Brother with cutaneous malignant melanoma, Mother with glaucoma
Social history: Non-smoker, Occasional alcohol

Clinical examination: Uncorrected visual acuity was 20/20-2 in the right eye and 20/20 in the left eye. Pupil exam was normal without relative afferent pupillary defect. Extraocular motility and confrontation visual fields were full bilaterally. Intraocular pressure was also within normal limits. On external exam, a firm subcutaneous mass without overlying skin changes was palpable at the left medial canthus. It measured approximately 4 mm in greatest dimension. There was also mild left punctal ectropion and edema of the caruncle. Irrigation and probing of the nasolacrimal drainage system revealed a patent system on the right and obstruction of the upper canaliculus, lower canaliculus, and nasolacrimal duct on the left.

Clinical management: The patient underwent biopsy of the left lacrimal sac for acquired left nasolacrimal drainage system obstruction secondary to mass.

Pathology:
Grossly, the specimens were multiple pink-tan soft tissue fragments measuring 4 mm to 7 mm in greatest dimension. Fresh tissue was sent for flow cytometry and the remainder placed in formalin and submitted for processing. On microscopic examination, the tissue consisted of a proliferation of cells with mildly pleomorphic nuclei and granular eosinophilic cytoplasm forming glandular structures. No mitotic figures were identified.

Diagnosis: Oncocytoma of the lacrimal sac.

Further evaluation and management: Nasal endoscopy in otolaryngology clinic revealed a visible mass extending from the left inferior meatus under the inferior turbinate bulging into the sinonasal cavity. The mass was covered by mucosa. On maxillofacial CT scan, an expansile lesion was present in the left

lacrimal sac and filling the osseous canal of the nasolacrimal duct without bony erosion. He then underwent open left dacryocystectomy, endoscopic resection of the left lacrimal duct and sinonasal tumor, and placement of Jones tube. Pathology of the complete resection confirmed oncocytoma involving the nasolacrimal sac and duct.

Discussion:

The term oncocyte is derived from the Greek word *onkousthai* which means "to swell." It was first used in 1931 by Hamperl to describe an epithelial cell with a characteristic phenotype including large size and finely granular eosinophilic cytoplasm[1,2]. Jaffe was the first to introduce the term to the American pathology literature in 1932. He described a salivary gland tumor that consisted of oncocytic cells[3]. The lesion he originally reported is now referred to as adenolymphoma or Warthin tumor. The modern oncocytoma is similar to that of adenolymphoma of the salivary glands except for a lack of lymphoid tissue. An abundance of mitochondria was identified as underlying the oncocytic cellular appearance after the introduction of electron microscopy. Ultrastructurally, the cells demonstrated an increase in mitochondria with a variety of morphological changes[4]. Oncocytosis represents a special degenerative metaplasia that does not prevent the cells from dividing. It occurs in glandular and secretory epithelial cells with high metabolic activity. This is felt to be an age-related change. Oncocytomas have not been reported in children or adolescents, and the incidence increases dramatically with increasing age[7]. There have been occasional cases reported in patients in their 30s and 40s, and some authors have suggested chronic inflammation as a factor in oncocytic transformation[12].

The spectrum of oncocytic lesions includes oncocytic hyperplasia, oncocytoma (oxyphil cell adenoma), and oncocytic adenocarcinoma. Oncocytoma is diagnosed when the tumor is composed predominantly of oncocytes in an adenomatous pattern, forming nests, cords, and tubules surrounding cystic spaces filled with mucinous material. Oncocytic carcinomas are distinguished from oncocytomas by the presence of frequent mitoses, cellular pleomorphism, local invasion or infiltration as well as perineural, intravascular, or lymphatic invasion. These features were initially described for lesions of the major salivary glands, but have been applied to other locations[17].

Oncocytomas occur throughout the body including minor and major salivary glands (most commonly the parotid gland), kidneys, thyroid, parathyroid, pituitary glands, adrenal glands, testes, gastrointestinal tract, upper respiratory tract, and other organs. The first description of an oncocytic lesion of the ocular adnexa was by Radnot who reported oncocytic adenomatous hyperplasia of the lacrimal sac[5]. Since then, various oncocytic lesions have been reported involving the caruncle, conjunctiva, lacrimal gland, lacrimal sac, and eyelid[4-15]. Biggs and Font postulated that the ocular adnexal lesions develop from oncocytic metaplasia of ducts and acinar cells of lacrimal gland tissue located in the ocular adnexa[7]. Although Rodgers et al note that oncocytic lesions typically arise from the ductular rather than acinar cells[9]. Pe'er and colleagues found that lacrimal gland tissue and mixed glands with serous and mucous cells exist in normal lacrimal sac and nasolacrimal duct. They are the likely source for lacrimal sac glandular tumors, including oncocytoma[16].

Caruncular oncocytic lesions are typically benign oncocytomas. Oncocytic lesions of the lacrimal gland are very rare and tend to be malignant[7]. However, oncocytic lesions of the lacrimal sac are a more heterogeneous group including oncocytoma, oncocytic metaplasia or hyperplasia, and oncocytic adenocarcinoma. Hornblass et al reported oncocytic hyperplasia to be the most common lacrimal sac oncocytic lesion while a review by Chen found majority oncocytoma[12,18]. Oncocytic tumors of the lacrimal drainage system and sinonasal tract are more likely to be malignant compared to those of the major salivary glands[17].

The diagnosis and treatment of lacrimal sac oncocytic lesions requires a multi-disciplinary approach, especially if the tumor involves the orbit or the skull base. Lacrimal sac tumors present with epiphora or recurrent dacryocystitis and medial canthal mass. The diagnosis can be confirmed by CT or MR imaging of the orbit or dacryocystogram. Surgical biopsy and histopathology are then necessary for a tissue diagnosis. Surgical excision is the mainstay of treatment. Wide local excision is usually curative for benign oncocytic lesions of the lacrimal sac, but if malignancy is suspected, the lesion should be resected en bloc resection. Recurrence suggests the possibility of malignancy, and malignant transformation has been reported. Peretz et al describe a case where the tumor appeared histopathologically as

oncocytoma, but the patient had repeated recurrences suggesting local infiltration[19]. Perlman et al present another case initially diagnosed as lacrimal sac oncocytoma, but multiple recurrences with paranasal sinus and orbital extension occurred despite surgery and radiotherapy. Additional specimens showed increased atypia progressing to oncocytic adenocarcinoma[11]. These cases support the argument that oncocytomas may not remain benign over time, and they emphasize the importance of complete excision and continued long-term follow-up of these lesions.

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