Original Article

Clinicopathological Features and Management of Orbital Cholesterol Granuloma

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Abstract

Purpose: To investigate the clinical features, radiographic features, treatment strategies, pathological features, and prognosis of orbital cholesterol granuloma (CG).

Methods: Twelve patients with orbital CG who were referred to Tianjin Eye Hospital between January 2002 and December 2020 were included in this retrospective case series study. Data collected including patient ophthalmic manifestations, imaging findings, treatment strategies, pathological features, and prognosis were retrospectively reviewed.

Results: The patients comprised 10 males and 2 females. The mean age was 34.5 years (standard deviation [SD] = 8.9, median: 36 and range: 16–45 years). Four patients had a history of orbital trauma. The clinical manifestations at the first visit were proptosis (7/12, 58.3%), periorbital or eyelid swelling (6/12, 50%), limitation of eye movement (4/12, 33.3%), ptosis (2/12, 16.7%), and decreased visual acuity (1/12, 8.3%). Computed tomography (CT) showed a nonenhancing, well-circumscribed lesion in the orbit with extensive erosion of the adjacent frontal bone and temporal bone. Magnetic resonance imaging (MRI) showed a nonenhancing mass with intermediate-to-high signal intensity on T1- and T2-weighted images. Ten patients underwent lateral orbitotomy, and two patients underwent supraorbital orbitotomy. All patients had aggressive bone erosion. Histopathologic evaluation of the cyst contents and wall revealed cholesterol clefts, multinucleated giant cells, histiocytes, foamy macrophages, and altered blood pigments. The mean follow-up time of 79.6 months (SD = 49.8, range: 19–193 months). Three patients were lost to follow-up. No postoperative diminution of vision was noted, and no recurrence was observed.

Conclusions: CGs can present as superotemporal or temporal orbital lesions. The diagnosis can be established based on CT and MRI. Most of the patients can have no history of orbital trauma.

Keywords: Cholesterol granuloma, Immunohistochemistry, Orbit, Orbital surgery, Radiographic feature

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Introduction

Cholesterol granuloma (CG) is an osteolytic lesion with a granulomatous reaction, and these lesions include cholesterol clefts and are frequently surrounded by a fibrous capsule.[1] CG describes a lesion that has an accumulation of organized blood byproducts, including cholesterol clefts, hemosiderin, and hematoidin, that lacks both an epithelial and endothelial lining. These lesions arise in a broad range of anatomical locations, including the petrous apex, lung, and breast.[2] Orbital CG is a rare entity that mostly occurs in middle-aged men and usually affects the frontal bone and zygomatic and petrous temporal bones.[3] The first orbital case was reported by Denig in 1902.[4] Over the years, only 200 cases have been well reported in the English literature.[2,5] The cause of CG is not yet known. It

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was thought that these cases were preceded by trauma. Some authors suggest the presence of an intradiploic abnormality predisposing to hemorrhage.[6] Imaging studies of orbital CG are useful and should be performed for the differential diagnosis of dermoid cysts and aneurysmal bone cysts. The final diagnosis is determined by pathological examination.

Here, we report 12 cases of primary orbital CG admitted to Tianjin Eye Hospital over a 19-year period. In this study, we analyzed clinical features, radiological findings, histopathological variables, and treatment results.

Methods

Twelve patients with orbital CG who were managed at Tianjin Eye Hospital between January 2002 and December 2020 were included in this study. A comprehensive retrospective review was performed to evaluate the characteristics of the orbital CG. Twelve patients were selected from 1248 patients with a pathological diagnosis of orbital lesion at Tianjin Eye Hospital. Information regarding the clinical course, including clinical manifestations and treatment, was collected from the patients' medical records. Complete medical information included age, sex, presenting symptoms, regular ophthalmic examinations, examination of exophthalmos by a Hertel exophthalmometer, examination of eye movements, B-mode ultrasonography, Color Doppler Imaging (CDI), computed tomography (CT), and magnetic resonance imaging (MRI). Outcome information was obtained from follow-up data and phone calls to the patients.

The present study was approved by the Tianjin Eye Hospital Foundation Institutional Review Board and adhered to the HIPAA regulations as well as the principles of the Declaration of Helsinki. Written informed consent for the publication of case details was obtained from all patients in our study.

Twelve patients were treated with excision of the lesion through supraorbital orbitotomy or lateral orbitotomy. Pathological examinations were available in all 12 cases. Hematoxylin- and eosin-stained slides were available in all 12 cases. The diagnoses of orbital CG were confirmed by the review of these data by experienced pathologists at Tianjin Eye Hospital.

Results

From January 2002 to December 2020, 12 patients with orbital CG were referred for evaluation and treatment. There were 10 (83.3%) males and 2 (16.7%) females. The mean age at presentation was 34.5 years (standard deviation [SD] = 8.9, median: 36 and range: 16–45 years). The mean duration of symptoms was 3.8 months (SD = 2.4, range: 1–8 months). Past medical history at presentation revealed that 4/12 (33.3%) of the patients had trauma. The lesion was located in the right orbit in three cases and in the left orbit in nine cases. There were nine lesions located in the superotemporal orbit, two in the superior orbit, and one in the temporal orbit. The clinical manifestations at the first visit were proptosis (7/12, 58.3%), periorbital or eyelid swelling (6/12, 50%), limitation of eye movement (4/12, 33.3%), ptosis (2/12, 16.7%), and decreased visual acuity (1/12, 8.3%). Five patients had a best-corrected decimal visual acuity of 20/20. Seven patients were observed to have different degrees of unilateral exophthalmos. Five patients were misdiagnosed with dermoid cysts, and two patients with aneurysmal bone cysts.

All patients underwent B-mode ultrasonography, CDI, and CT, and 66.7% of patients underwent MRI. B-mode ultrasonography showed a well-delimitated lesion, medium echogenicity, and heterogeneity [Figure 1a]. CDI showed no blood flow signal [Figure 1b]. CT showed a nonenhancing, well-circumscribed lesion in the orbit with extensive erosion of the adjacent frontal bone and temporal bone [Figure 1c-e]. For further characterization of the orbital CG, MRI was performed, which showed a nonenhancing mass with intermediate-to-high signal intensity on T1- and T2-weighted images [Figure 1f-h]. B-mode ultrasonography, CDI, CT, and MRI images of the patients are shown in Figure 1.

Ten patients underwent lateral orbitotomy, and two patients underwent supraorbital orbitotomy. All patients had aggressive bone erosion. Intraoperatively, the presence of a thin-walled mass along the orbital wall with cheesy yellowish content was found [Figure 1i]. There were altered blood pigments included in the lesions. Histopathologic evaluation of the cyst contents and wall revealed cholesterol clefts (arrow), multinucleated giant cells, histiocytes, foamy macrophages, and altered blood pigments [Figure 2a and b].

The mean period of follow-up following surgical treatment was 79.6 months (SD = 49.8, range: 19–193 months) in the series of the present study. Three patients were lost to follow-up. No postoperative diminution of vision was noted, and no recurrence was observed.

Discussion

An osteolytic lesion with a granulomatous reaction due to the presence of cholesterol clefts is defined as CG.[7] The cholesterol clefts may be derived from disintegrated erythrocyte cell membranes, plasma lipids, or fatty degeneration of connective tissue in a cyst blocked by inflammation.[8] CGs are expansile cystic lesions with the potential for osseous erosion. CGs within the head-and-neck location have been mostly reported in association with bony structures such as the mastoid antrum and air cells of the temporal bone.[9] CG is rarely found in the orbit region, and little is known about its etiology or clinical manifestations. Trauma with hemorrhage has been proposed as the initiating event in CG of the orbit. The predilection of frontal bone and the male preponderance further support the trauma theory.[10] Nine males made up the majority of our patients, and four patients had a history of trauma. The current literature supports two mechanisms for CG. One of the theories postulated for the cause of CG is restricted airflow in pneumatized temporal bone cells that results in negative pressure, followed by inflammation, angiogenesis, and blood vessel breach with hemoglobin deposition. Subsequent dissolution of hemoglobin

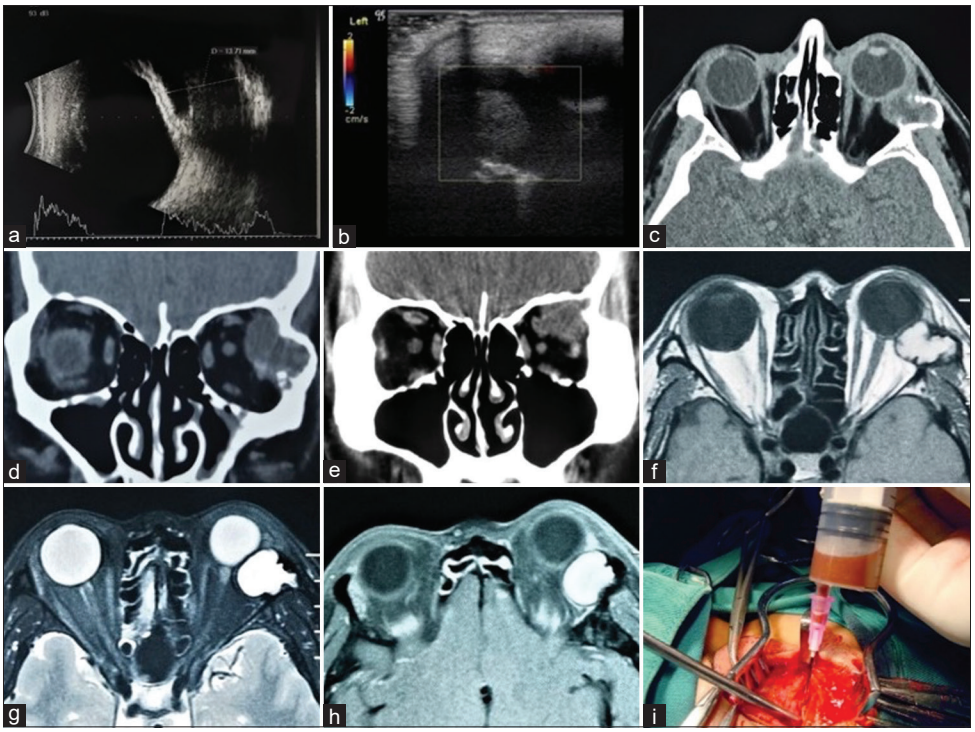

Figure 1: (a) B-mode ultrasonography of case 2 showing a well-delimitated lesion, medium echogenicity, and heterogeneity. (b) Color Doppler ultrasound imaging of case 6 showing no signal of blood flow. (c) Axial computed tomography (CT) of case 1 showing a cystic lesion in superotemporal aspect, with erosion of the lateral wall of orbit. (d) Coronal CT of case 1 showing an osteolytic mass lesion arising in the left temporal bone with extension into the orbit. (e) Corneal CT of case 10 showing irregular bony erosion of the left orbital roof. (f and g) T1- and T2-weighted axial magnetic resonance imaging (MRI) of case 1 showing mass with intermediate-to-high signal intensity on T1- and T2-weighted images. (h) Gadolinium-enhanced MRI of case 1 showing no central enhancement although peripheral enhancement may be difficult to see due to intrinsic high T1 signal of lesion. (i) Altered blood pigments drained from the cyst during surgery

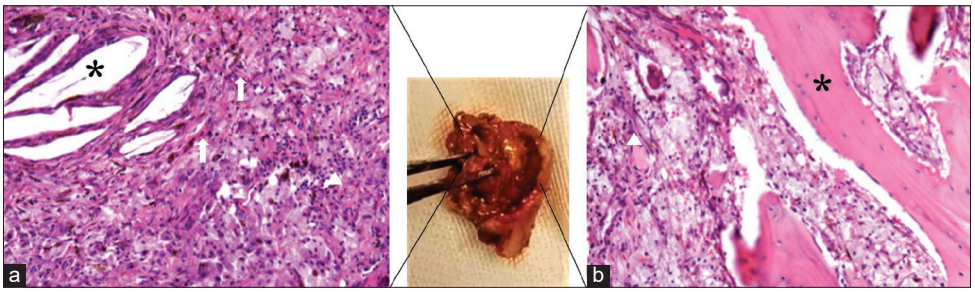

Figure 2: (a) Hematoxylin and eosin (H and E) staining of orbital cholesterol granuloma (CG) showing cholesterol clefts (asterisks) surrounded by foreign body giant cells (arrowheads), packed macrophages, lymphocytes, and extravasated red blood cells (arrows) (H and E, ×200). (b) H and E staining of orbital CG adjacent to the bone cortex showing amounts of histiocytes, hemosiderin-laden macrophages (arrowheads), fibrosis, and calcification (asterisks)

byproducts results in continual inflammation and aggregation of cholesterol clefts. The second proposed mechanism is what has been called the "exposed marrow hypothesis." The pathogenesis of CGs remains unclear, and more histologic studies are necessary to improve our knowledge about its origin.[11]

The clinical features are similar to any orbital mass, namely, progressive proptosis, periorbital pain, ptosis, reduced visual acuity, extraocular motility restriction, and diplopia.[12] In our patients, the most common clinical presentation was month-long progressive proptosis with or without pain. As previous studies have demonstrated, the imaging features of these lesions can be pathognomonic. In contrast to other vascular and hemorrhagic lesions, no signals of blood flow are seen on CDI of orbital CG. The diagnosis can be established based on CT and MRI. On CT scan, it is a noncalcifying mass lesion that is iso- to hypodense with the brain. Postcontrast images show no enhancement of CG, which is a key difference from orbital neoplasms.[13] The MRI characteristics are unique and include hyperintense signals on T1- and T2-weighted images with the absence of enhancement. The medical history and imaging examinations must be analyzed synthetically to make a proper preoperative diagnosis.

Cholesterol clefts and a surrounding granulomatous reaction are the most characteristic histological findings of CG.[14] The main differential diagnoses of orbital CG are dermoid cysts and aneurysmal bone cysts. Orbital dermoid cysts classically occur as firm, fixed subcutaneous lesions near the orbital rim superotemporally in young children. The superior temporal quadrant at the frontozygomatic suture is the most common location of orbital dermoid cysts, followed by the nasoglabellar region at the frontoethmoidal suture.[15] The majority of aneurysmal bone cysts that present in the second decade of the patient's life have a female preponderance of 5:3. The characteristic histological features of aneurysmal bone cysts include cavernous blood-filled spaces that lack endothelial lining, pericytes, or smooth muscle, and cholesterol clefts are absent.[3] CT is useful in the evaluation of aneurysmal bone cysts. This technique shows an expansile interdiploic lesion that may be multiloculated and harbors areas with different densities.[16]

The definitive management of CG is complete resection of the mass with curettage of the residual material adherent to the bone. Due to the absence of epithelial elements, CG of the orbit rarely recurs.[12] Consequently, some authors have argued that complete extirpation of the adjacent bone is not necessary.[17] Recurrence has been reported to be related to the absence of enough bone drilling.[13] To our knowledge, there have been very few cases of recurrent orbital CG after an initial complete resection.[18] Ong and McNab reported a case of recurrent orbital CG. They conjectured that the abnormal tissue was incompletely removed at the first operation, or alternatively, hemorrhage recurred in the space where the lesion was excised, leading to a recurrence of the CG.[19] Hughes *et al*.[2] retrospectively analyzed the clinical data of 172 patients with orbitofrontal CG reported in the literature, seven patients demonstrated recurrence after surgery,and the median time to recurrence was 36 months. They suggested that the recurrence was associated with incomplete resection and an orbital approach. Thus, as in our study, meticulous curettage of the bone may prevent recurrence. When the lesion is localized in the upper orbital margin, it is important to exercise caution while removing the lesion to prevent inadvertent breach of the dura mater and subsequent cerebrospinal fluid leakage.

In conclusion, orbital CGs are rare lesions that are predominantly found in the superotemporal orbit. We found that orbital CG occurs more frequently in men than in women. Most patients do not have a history of trauma. Bony erosion is common in this lesion, and the most common differential diagnosis is a dermoid cyst or aneurysmal bone cyst.

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Conflicts of interest

There are no conflicts of interest.

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