

Orbital cholesterol granuloma: a retrospective case series

Yun Zhao

Tianjin Eye Hospital

Jingwen Hui

Tianjin Eye Hospital

Shasha Yu

Tianjin Eye Hospital

Jinyong Lin

Tianjin Eye Hospital

Hong Zhao (✉ zhaohongeye@163.com)

Tianjin Eye Hospital

Research Article

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Abstract

Background

To review the clinical features, radiographic features, therapy, 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 included 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 ± 8.9 years (range 16 to 45 years). Four patients had a history of orbital trauma. The clinical manifestations at first visit were proptosis (7/12, 58.3%), periorbital or eyelids swelling (6/12, 50%), limitation of eye displacement (4/12, 33.3%), ptosis (2/12, 16.7%), decreased visual acuity (1/12, 8.3%). CT showed a non-enhancing, well-circumscribed lesion in the orbit with extensive erosion of the adjacent frontal bone and temporal bone. MRI showed a non-enhancing mass with intermediate to high signal intensity on T1- and T2-weighted imaging. 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 median recurrence time was 79.6 ± 49.8 months (range 19 months to 193 months). Three patients were lost to follow-up. No postoperative diminution of vision was noted, and no recurrence was observed.

Conclusions

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

Background

Cholesterol granuloma (CG) is an osteolytic lesion with a granulomatous reaction including cholesterol crystals, frequently surrounded by a fibrous capsule [1]. CG describes 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, mostly occurring in middle-age men and usually effect the frontal bone, zygomatic and petrous temporal bones[3].The first orbital case was reported by Denig in 1902[4].Over the years,only few cases being well reported in the English literature[5]. The cause of the CG was not yet known. Typically, this is 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 with dermoid cyst and aneurysmal bone cyst.The final diagnosis was determined by the pathological examination.

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

Materials And Methods

Twelve patients with orbital CG that were managed at Tianjin Eye Hospital, China,between January 2002 and December 2020 were included in this study. A comprehensive retrospective review was performed to evaluate the characteristics of orbital CG. The twelve patients were selected from 1248 cases 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 including age, gender, presenting symptoms, regular ophthalmic examinations, examination of the exophthalmos by a Hertel exphthalmometer, examination of eye movement, B-mode ultrasonography, color doppler ultrasound 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 HIPAA regulations as well as principles of the Declaration of Helsinki. Written informed consent for the publication of case details was obtained from all patients in our study.

The twelve patients were treated with excision of the lesion through superior lid crease approach or lateral orbitotomy. Intraoperatively, presence of a thinwalled mass along the orbital roof or lateral wall with cheesy yellowish content was found. Pathological examination were available in all twelve cases. Haematoxylin and eosin stained slides were available in all twelve cases. The diagnosis 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 83.3 % (n=10/12) males and 16.7 % (n=2/12) females. The mean age at presentation was 34.5 ± 8.9 years (median 36 and range 16 to 45 years). The mean duration of symptom was 3.8 ± 2.4 (range 1 to 8 month). Past medical histories at presentation revealed that 33.3 % (n= 4/12)

had trauma. The lesion was located in the right orbit in 3 cases and the left orbit in 10 cases. There were 9 lesions located in the superiotemporal orbit, two in the superior orbit, and one in the temporal orbit. The clinical manifestations at first visit were proptosis (7/12, 58.3%), periorbital or eyelids swelling (6/12, 50%), limitation of eye displacement (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 as having dermoid cyst, two patients were aneurysmal bone cyst.

All patients underwent B-mode ultrasonography, CDI, CT and 66.7% patients underwent MRI. B-mode ultrasonography showed a well-delimited lesion, medium echogenicity and heterogeneity. CDI showed no signal of blood flow. CT showed a non-enhancing, well-circumscribed lesion in the orbit with extensive erosion of the adjacent frontal bone and temporal bone. For further characterization of orbital CG, MRI was performed, which showed a non-enhancing mass with intermediate to high signal intensity on T1- and T2-weighted imaging. 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, presence of a thin-walled mass along the orbital wall with cheesy yellowish content was found. There were altered blood pigments included in the lesions. Histopathologic evaluation of the cyst contents and wall revealed cholesterol clefts, multinucleated giant cells, histiocytes, foamy macrophages, and altered blood pigments (Figure 2).

The median period of follow-up following surgical treatment was 79.6 ± 49.8 months (range 19 months to 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. The clinical features of these patients are listed in Table 1.

Discussion

An osteolytic lesion with a granulomatous reaction to the presence of cholesterol crystals is defined as CG [7]. CG are expansile cystic lesions with the potential for osseous erosion. Within the head and neck location, it has been mostly reported in association with bony structures such as the mastoid antrum and air cells of the temporal bone [8]. CG is rarely found in the orbit region, little is known of its etiology or clinical manifestations. Trauma with hemorrhage has been put forward as the initiating event in the CG of the orbit. The predilection of frontal bone and the male preponderance further support the trauma theory [9]. Males make up the majority of our patients, and four patients have a history of trauma. 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 results in negative pressure, followed by inflammation, angiogenesis, and blood vessel breach with hemoglobin deposition. Subsequent dissolution of hemoglobin byproducts results in continual inflammation and aggregation of cholesterol crystals. The second proposed mechanism is what has been called the "exposed marrow

hypothesis". Pathogenesis of cholesterol granuloma still remains unclear and more histologic studies are necessary to improve our knowledge about its origin[10].

Clinical features are similar to any orbital mass, namely progressive proptosis, periorbital pain, ptosis, reduced visual acuity, extraocular motility restrictions, and diplopia[11]. In our patients, the most common clinical presentation is month-long progressive proptosis with or without pain. As previous studies have demonstrated, imaging features of these lesions can be pathognomonic. Different from other vascular and hemorrhagic lesions, CDI of orbital CG show no signal of blood flow. The diagnosis can be established based on CT and MRI. On CT scan, it is a non-calcifying mass lesion, which is iso- to hypodense with brain. Post-contrast images show no enhancement of CG which is a key difference from orbital neoplasms[12]. MRI characteristics are unique and include hyperintense signal on T1- and T2-weighted imaging with absence of enhancement. Medical history and imaging examinations must be analyzed synthetically in order to make proper preoperative diagnosis.

Cholesterol cleft and surrounding granulomatous reaction are the most characteristic histological findings of CG[13]. The main differential diagnosis of orbital CG are dermoid cyst and aneurysmal bone cyst. Orbital dermoid cyst classically occurs as a firm, fixed subcutaneous lesion near the orbital rim superotemporally in a young child. The superior temporal quadrant at the frontozygomatic suture is the most common location of orbital dermoid cysts, followed by nasoglabellar region at the frontoethmoidal suture[14]. The majority of aneurysmal bone cysts present in the second decade with a female preponderance of 5:3. The characteristic histological feature of aneurysmal bone cyst includes cavernous blood-filled spaces that lack endothelial lining, pericytes, or smooth muscle, and also cholesterol crystals are absent[3]. CT is useful in the evaluation of ABCs. This technique shows an expansile interdiploic lesion that may be multiloculated and harbors areas with different densities[15].

Definitive management of CG is complete resection of the mass with curettage of the residual material adherent to bone. Due to the absence of epithelial elements, CG of the orbit rarely recur[11]. Consequently, some authors have argued that complete extirpation of the adjacent bone is not necessary. Recurrences have been reported to be related to the absence of enough bone drilling[12]. To our knowledge, there were very few cases of recurrent orbital CG after initial complete resection[16]. Lorraine et al reported a case of recurrent orbital CG, they conjectured the abnormal tissue was incompletely removed at the first operation, or alternatively, haemorrhage recurred in the space where the lesion was excised, leading to a recurrence of the CG[17]. Thus, as in our surgery, meticulous curettage of the bone may prevent recurrence. When the lesion was localized in the upper orbital margin, it is important to exercise caution whilst removing the lesion, to prevent inadvertent breach of the dura mater and subsequent cerebrospinal fluid leak.

Conclusions

In summary, 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. Based on the CT and MRI findings,

the diagnosis of orbital CG was established. Bony erosion is common in this lesion, and the most common differential diagnosis is dermoid cyst or aneurysmal bone cyst.

Abbreviations

CG: Cholesterol granuloma; CT: Computed tomography; MRI: Magnetic resonance imaging

CDI: Color doppler ultrasound imaging

Declarations

a

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Authors' Contributions

YZ and JWH contributed equally to the work; YZ and JWH contributed to study design, drafted the manuscript, collected the data and reviewed the literature. SSY interpreted the data, reviewed the literature and helped to draft the manuscript. JYL were involved in the design of the study and coordination. HZ performed surgery, made diagnosis, and critically reviewed the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

All datasets used and/or analysed in the current study are available from the corresponding author upon reasonable request.

Disclosure

Yun Zhao and Jingwen Hui are co-first authors.

Ethics approval and consent to participate

This study was conducted in accordance with the tenets of the Declaration of Helsinki and was approved by Tianjin Eye Hospital Foundation Institutional Review Board (TJYYL-2021-12). All authors had permission to access patients records. We confirmed that all written consent was obtained from the participant.

Consent for publication

Written informed consent for publication was obtained from all participants.

Competing interests

The authors report no conflicts of interest. The authors alone are responsible for the content and the writing of the article.

Author details

¹Tianjin eye Hospital,Tianjin Eye Institute,NO.4 Gansu Road,Heping District,Tianjin 300020,China. ²Tianjin Key Lab of Ophthalmology and Visual Science,Tianjin,China. ³Clinical College of Ophthalmology Tianjin Medical University,Tianjin,China. ⁴Nankai University Eye Hospital,Tianjin,China.

References

1. Hidenori Yokoi,Hidetaka Yamanaka,Yuma Matsumoto,et al. Modified Lothrop (Draf III) procedure for the treatment of a recurrent orbitofrontal cholesterol granuloma: A case report.SAGE Open Med Case Rep.2020,8: 2050313X20907809.
2. Lucke-Wold B,Fleseriu C,Calcagno H,et al.Endoscopic transsphenoidal drainage of a petrous apex cholesterol granuloma using a frontal sinus nasal stent: a case report with long term follow up.Br J Neurosurg.2021,35(2):139–144.
3. Syed A R Rizvi,Mahboob Hasan,Mohammad S Alam.Cholesterol granuloma of the orbit:an atypical presentation.Indian J Ophthalmol,2014,62(3):344–346.
4. Denig R.Subperiosteal blood cyst of the orbit: report of a case.Ophthalmic Record.1902;11:187.
5. Rong AJ,Erickson BP,Blessing NW,et al.Orbital cholesterol granuloma: A report and discussion of orbital findings.Am J Ophthalmol Case Rep.2019,15:100468.
6. Shrirao N,Mukherjee B,Krishnakumar S,et al.Cholesterol granuloma:a case series& review of literature.Graefes Arch Clin Exp Ophthalmol,2016,254(1):185–188.
7. Tabet P, Saydy N,Saliba I. Cholesterol Granulomas: A Comparative Meta-Analysis of Endonasal Endoscopic versus Open Approaches to the Petrous Apex.J Int Adv Otol,2019,15(2):193–199.
8. Reeve N,Kahane J,Ng M.A case of a nonpetrous cholesterol granuloma presenting as a temporal mass.Case Rep Otolaryngol.2020,2020:8872270.
9. Imre A,Pinar E,Paker I,et al.Psteoplastic flap approach versus orbitotomy in case of orbitofrontal cholesterol granuloma.J Craniofac Surg.2015,26(1):e36-e37.
10. Leticia Román-Romero, Raúl González-García.Cholesterol granuloma of the orbit.Report of cases and analysis of controversial treatment.J Maxillofac Oral Surg.2011,10(2):166–169.
11. Adel H Alsuhaibani,Khalid Al-Rubaie,Hattan Al-Khiary,et al.Different patterns of orbital roof involvement by cholesterol granuloma.Middle East Afr J Ophthalmol,2011,18(4):333–335.

12. Loeffler KU, Kommerell G. Cholesterol granuloma of the orbit-pathogenesis and surgical management. *Int Ophthalmol*. 1997; 21:93–98.
13. Kim YS, Ju HJ, Park CJ, et al. A case of cholesterol granuloma presenting as a cutaneous nodule. *Ann Dermatol*, 2017, 29(3):3838–384.
14. Kumar R, Vyas K, Jaiswal G, et al. Deep orbital dermoid cyst bulging into the superior orbital fissure: clinical presentation and management. *J Ophthalmic Vis Res*, 2017, 12(1):110–112.
15. Wang JC, Zhang M, Zhao XX. Aneurysmal bone cyst of the orbit. *Chin Med J(Engl)*. 2015, 128(4):562–563.
16. Kim YJ, Sa HS. Recurrent cholesterol granuloma of the orbit. *Ophthalmic Plast Reconstr Surg*, 2014, 30(5):e109–e110.
17. Lorraine Y Ong, Alan A McNab. Recurrent orbital cholesterol granuloma. *Orbit*, 2008, 27(2):119–12

Tables

Due to technical limitations, Table 1 is only available as a download in the Supplemental Files section.

Figures

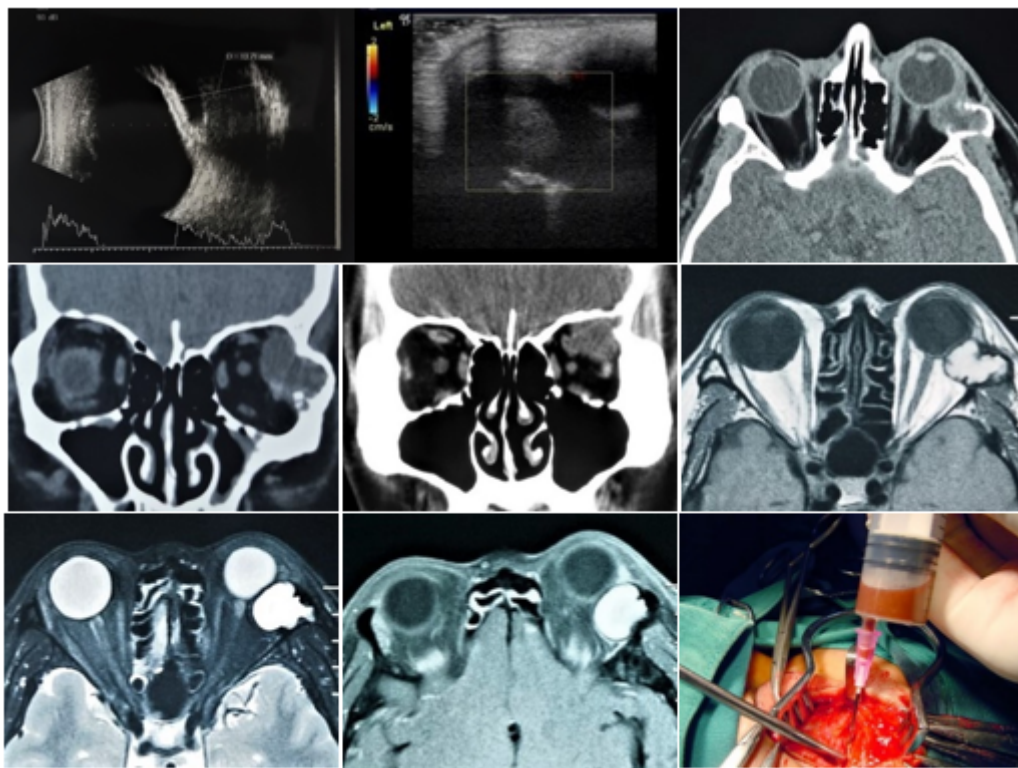


Figure 1

a: B-mode ultrasonography of case 2. showing a well-delimited lesion, medium echogenicity and heterogeneity. b: CDI of case 6. showing no signal of blood flow. c: Axial 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: Coronal CT of case 10.showing irregular bony erosion of the left orbital roof. f,i: Axial T1WI and axial T2WI MRI of case 1. showing mass with intermediate to high signal intensity on T1- and T2-weighted imaging. g :Gadolinium-enhanced MRI of case 1.showing absence of identifiable enhancement. k: Altered blood pigments drained from the cyst during surgery

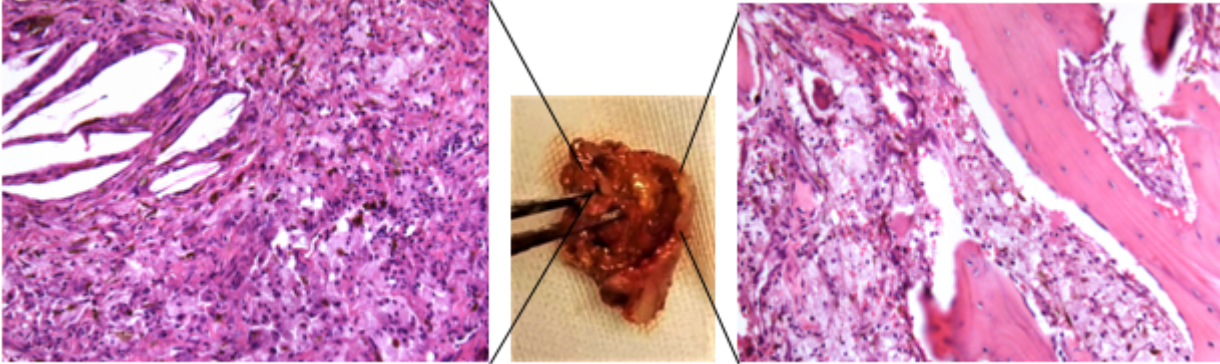


Figure 2

a: H&E staining of orbital CG showing cholesterol crystals surrounded by foreign body giant cells,packed macrophages,lymphocytes and extravasated red blood cells. (hematoxylineosin,original magnification $\times 200$) b: H&E staining of orbital CG adjacent to the bone cortex showing amounts of histiocytes, hemosiderin-laden macrophages ,fibrosis, andcalcification.

Supplementary Files

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- [Table.docx](#)