

Total Resection of Unilateral Adult-onset Xanthogranuloma of the Orbit via a Transcranial Orbital Approach

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Adult orbital xanthogranuloma is rare and usually associated with systemic disease. There are several options available to treat this disorder. Periorbital lesions are treated with steroids, chemotherapy, radiotherapy, or local excision; however, there is still no consensus regarding optimal treatment. Here, we report a rare case of orbital xanthogranuloma that was not associated with systemic disease and was treated by transcranial surgery. The patient was a 52-year-old man who presented with a 2-year history of unilateral eye symptoms. A computed tomography scan revealed a well-defined mass in the right orbit. The mass was completely removed via a transcranial orbital approach. The histopathologic diagnosis was xanthogranuloma. No recurrence was observed during 15 months of postoperative follow-up. Complete surgical resection might be an effective treatment option for locally growing sporadic adult xanthogranulomatous disease of the orbit, and allows systemic steroids, chemotherapy, and irradiation to be avoided.

Keywords: xanthogranuloma, orbit, transcranial approach

Introduction

Xanthogranuloma is a rare non-Langerhans histiocytic disorder that is usually associated with systemic disease or blood abnormalities and is particularly uncommon in the orbit.¹⁾ Four forms of adult xanthogranulomatous disease of the orbit (AXDO) can be distinguished depending on clinical characteristics and manifestations, i.e., adult-onset xanthogranuloma (AOX), adult-onset asthma and periocular xanthogranuloma (AAPOX), necrobiotic xanthogranuloma (NBX), and Erdheim–Chester disease (ECD). Histopathology findings are similar for all four of these clinical forms of AXDO.²⁾

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Adult-onset xanthogranuloma is the least common and benign form that is characterized by an isolated lesion without significant systemic involvement.²⁾ The hallmark of AAPOX is the asthma component. Most patients experience adult-onset asthma within a few months to a few years after onset of the periocular lesion.³⁾ Almost all cases of NBX are accompanied by paraproteinemia, which may be associated with monoclonal gammopathy of undetermined significance, multiple myeloma, plasma cell leukemia, macroglobulinemia, or cryoglobulinemia.²⁾ ECD is multisystemic and affects many organs. Most cases involve bone and the central nervous system, descending aorta, retroperitoneum, liver, and lungs.^{2,4)}

The periorbital lesions are treated with systemic corticosteroids, steroid injections, chemotherapy, radiotherapy, or local excision. There is no convincing evidence that any particular treatment yields better results than another. This report describes a patient with orbital xanthogranuloma that was completely resected via a transcranial orbital approach without requiring any systemic treatment.^{2,5)}

Case Report

A 52-year-old man was referred to our office by his primary Ophthalmology Department for further evaluation and treatment of the right orbital tumor. He had a 2-year history of progressively worsening lacrimation. Downward displacement of the right eye and diplopia had been gradually worsening during the previous year. Neurologic examination revealed more deterioration of the right eye visual acuity (20/25) than the left (20/12.5). There was no history of lipoma at any anatomic site. An increased triglyceride level (959 mg/dL) was observed; however, leukemia and asthma were denied on admission. Computed tomography (CT) of the orbits revealed proptosis and inferior displacement of the globe of the right eye by a tumor that was revealed as a 30-mm posterolateral soft tissue density mass. The tumor had destroyed the supra-orbital bar and superior wall of the orbit. Magnetic resonance imaging revealed a well-demarcated mass in the cranial portion of the right orbit that showed mixed intensity on both T₁- and T₂-weighted images without contrast enhancement. A whole-body CT scan revealed no tumor masses in addition to the one in the orbit. Electrocardiography, chest radiography, and pulmonary function tests revealed no abnormalities. There were no signs of punched out regions in the long bones on X-ray examination (Fig. 1).

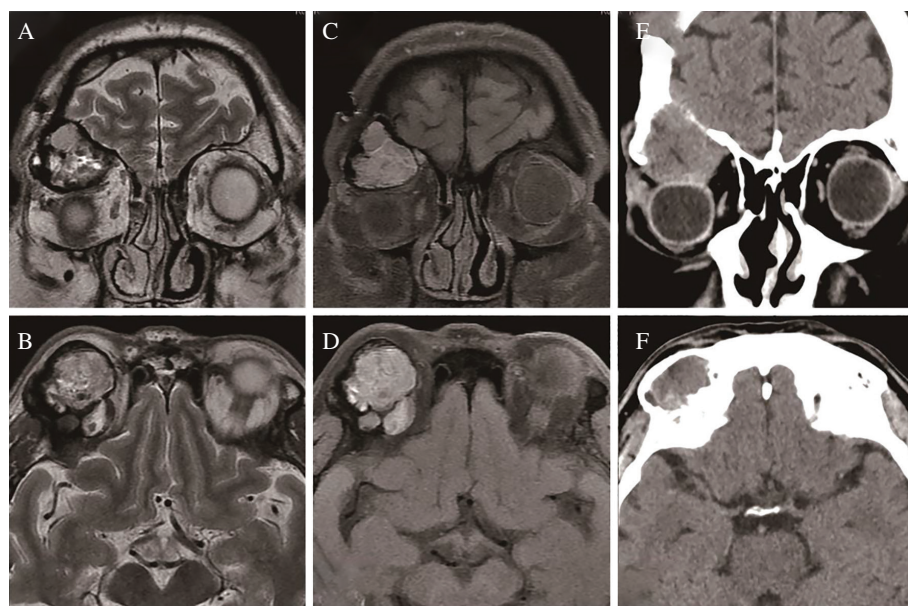


Fig. 1 Preoperative MRI and CT findings. The tumor was demonstrated mixed intensity on T₂-weighted image (WI) (A and B) and T₁-WI (C and D) without contrast enhancement. CT coronal (E) and axial (F) images showed a large heterogeneous soft tissue mass involving the posterolateral orbit of the right eye.

A soft and yellowish lobulated mass covered with membranous tissue was observed at the cranialateral portion in the orbit. Part of the orbital roof had been destroyed by the tumor. The tumor was completely resected via a transcranial orbital approach. Removal of the tumor resulted in a defect of the supraorbital bar. The orbital bar and roof were reconstructed using autogenous frontal and parietal bone (Fig. 2).

Pathologic examination revealed a mixture of inflammatory cells and foam cells with cholesterol clefts. Interstitial fibrosis and multinucleated giant cells were also observed. Immunological staining was positive for CD68 and negative for S100, LCA, and CD1a (Fig. 3). The final pathologic diagnosis was orbital xanthogranuloma.

The displacement of the right eye, and diplopia resolved after the surgery. Lacrimation was subjectively improved. Right eye visual acuity recovered to 20/16. The final diagnosis in our patient was AOX without systemic disease, so no additional treatments were performed. There were no signs of recurrence or systemic disease at follow-up 15 months later.

Discussion

As with most locally growing tumors, surgical removal was deemed the best option for this case of AOX with unilateral orbital involvement. AOX is characterized as local tumor formation in the orbit; this is unlike the other three forms of AXDO that feature systemic disease. Bilateral orbital involvement is generally observed; however, unilateral orbital lesions are also reported, as in our case. Unilateral AOX without systemic disease is considered a good candidate for surgical resection, and therefore avoids steroids and chemotherapeutic agents. In most patients with AXDO, a steroid is used because systemic disease is common. A literature review revealed 12 patients with AOX who had been treated surgically, including our case (Table 1).^{1,5-8)} Patient age ranged from 23 to 79 years, and sex distribution was equal. Four patients (33%) had bilateral involvement. Four patients

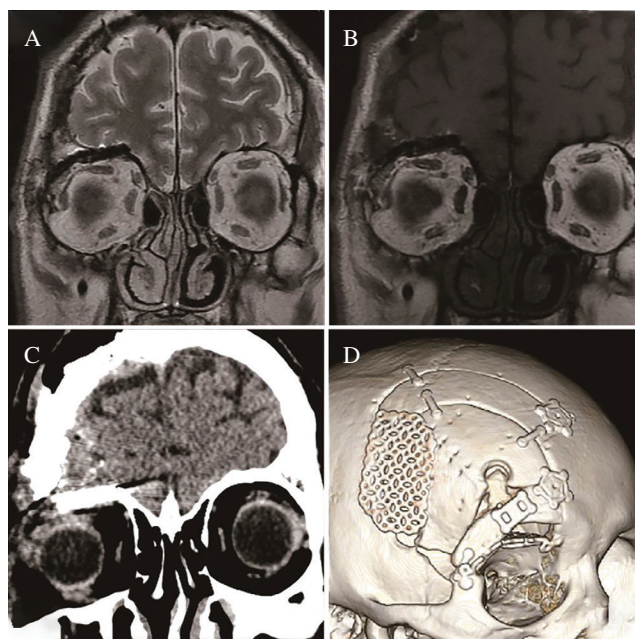


Fig. 2 Postoperative MRI and CT findings. T₂-WI (A), T₁-WI (B) and CT (C) demonstrated total resection of the tumor. An improvement of downward deviation of the right eye was obtained. The reconstruction of the lateral and superior orbital wall and the supraorbital bar was achieved by the autogenous frontal and parietal bone (D).

(33%) had hypercholesterolemia or hypertriglyceridemia. All four types of AXDO may be associated with dyslipidemia;²⁾ however, AOX is only rarely associated with serious systemic findings.

A transcranial orbital approach was used in our patient to obtain a wide operative field that would allow total resection of the orbital xanthogranuloma. Six of the 12 reported patients underwent total resection. However, there was no report of orbital xanthogranuloma being treated by transcranial surgical resection. Five (83%) of the six patients who underwent total

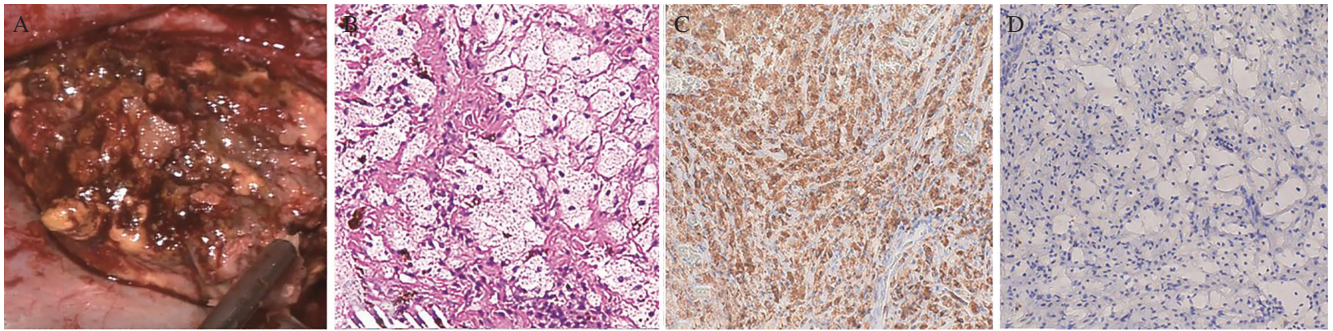


Fig. 3 Intraoperative findings and Pathological examination. A soft and yellowish lobulated mass covered with the membranous tissue was observed at the cranial lateral portion in the orbit, a part of the orbit roof was destructed (A). A mixture of the inflammatory cells, foam cells with cholesterol clefts, a part of interstitial fibrosis and multinucleated giant cells were observed on hematoxylin–eosin stains (B). Immunological staining revealed CD68-positive (C) and S100-negative (D) cells in the tumor.

Table 1 Surgical cases of adult-onset xanthogranuloma in the orbit

Author, Year	Age/ Sex	Laterality	Systemic findings	Treatment			Follow-up	Recurrence	Outcome
				Extent of resection	Approach	Others			
Zeynel et al., 2003	23/F	Bilateral	Hypercholesteremia	Total (1 st Tx)	N/A	Radiation, Steroid (1 st Tx)	8 years	Without	Alive
	41/F	Unilateral	Hypercholesteremia	Total	N/A		6 years	Without	Alive
	79/F	Unilateral	Hyperglyceridemia, hyperparathyroidism, hypercalcemia	Partial	N/A		12 months	Without	Alive
	38/F	Bilateral	None	Partial (1 st Tx)	N/A	Steroid (1 st Tx) Radiation (2 nd Tx)	10 years	With	Alive
	79/M	Unilateral	N/A	Total	N/A		Lost to follow-up		
Ramesh et al., 2007	47/M	Unilateral	None	Total	The medial transcaruncular		30 months	Without	Alive
Shimizu et al., 2010	52/F	Unilateral	None	Total	Anterior through the lower eyelid		2 years	Without	Alive
Kiratli et al., 2015	29/M	Bilateral	Autoimmune sialadenitis, microproteinuria	Partial (1 st Tx)	N/A	Steroid (1 st Tx)	29 months	Without	Alive
	55/M	Bilateral	Retinitis pigmentosa, hypertension, type 2 diabetes	Partial (1 st Tx)	N/A	Steroid (2 nd Tx)	23 months	Without	Alive
	57/M	Unilateral	Hilar lymphadenopathies, β 2 microproteinuria	Partial (1 st Tx)	N/A	Steroid (2 nd Tx)	62 months	Without	Alive
Michael et al., 2017	47/F	Unilateral	None	Partial (1 st Tx) Partial (2 nd Tx)	N/A	Steroid, methotrexate (2 nd Tx)	8 years	With	Alive
Tamada et al., 2018	52/M	Unilateral	Hypercholesteremia, hyperglyceridemia	Total	Trancranial		8 months	Without	Alive

Tx: Treatment.

resection survived without recurrence. The remaining one patient was lost to follow-up. Seven patients underwent partial resection as the first or second treatment, and five (71%) of them needed additional treatment. Two (28%) of these seven patients had recurrent lesions during 8–10 years of follow-up. The remaining five patients survived without recurrence over 12–62 months of follow-up. The two patients who developed recurrence underwent additional treatment with steroids, radiation, or methotrexate. Partial resection (including biopsy) is rarely recommended for treatment of AXDO because of the risk of early relapse after surgery (in <1 year in the most cases).²⁾ Total resection using a transcranial orbital approach allows a wide and shallow surgical field and is a valid treatment for orbital xanthogranuloma in the absence of severe systemic disease. In addition, there are no cosmetic concerns due to incising in the hair. There is also the merit that autogenous bone can be collected for reconstruction, as in our case. Tumor resection might be expected to increase the likelihood of long-term survival without recurrence.

No adjuvant therapy was required in the present case. The most common treatment used to obtain local control of the disease is systemic steroid therapy. Administration of a steroid has been reported to be an effective treatment option for AXDO with systemic complications. However, this strategy might have temporal effects. Moreover, some patients have not responded to systemic corticosteroids.^{2,3)} Multimodality treatment, such as a combination of systemic steroids with chemotherapy, radiotherapy, and surgery, is now recommended.²⁾ Radiation to the orbit in combination with systemic corticosteroids has proven successful in some cases of AXDO, although exacerbation of cutaneous lesions has been reported.²⁾ Chemotherapy using methotrexate may be efficacious when systemic corticosteroids alone have failed.³⁾ Additional studies are required to establish a standard therapy for orbital xanthogranuloma.

No recurrence was observed in our patient after 15 months of follow-up. All of the 12 reported cases remained alive

after follow-up periods ranging from 12 months to 10 years (mean 4.0 years). Screening for systemic disease and long-term follow-up are necessary, even in patients with AOX, because late-onset hematologic malignancies can occur. In past reports, the interval to development of a hematologic malignancy varied from 1 to 25 years after the onset of orbital xanthogranuloma.^{9,10)}

Conflicts of Interest Disclosure

The authors report no conflicts of interest concerning the materials or methods used in this study or the findings specified in this article.

References

- 1) Murthy R, Honavar SG, Vemuganti GK, Naik M, Burman S: Isolated giant xanthogranuloma of the orbit. *Indian J Ophthalmol* 55: 156–158, 2007
- 2) Ortiz Salvador JM, Subiabre Ferrer D, Pérez Ferriols A: Adult xanthogranulomatous disease of the orbit: clinical presentations, evaluation, and management. *Actas Dermosifiliogr* 108: 400–406, 2017
- 3) Guo J, Wang J: Adult orbital xanthogranulomatous disease: review of the literature. *Arch Pathol Lab Med* 133: 1994–1997, 2009
- 4) Suzuki H, Wanibuchi M, Komatsu K, et al.: Erdheim–Chester disease involving the central nervous system with the unique appearance of a coated vertebral artery. *NMC Case Rep J* 3: 125–128, 2016
- 5) Shimizu F, Taneda H, Sato H, Kato A, Takeo N, Fujiwara S: A case of orbital xanthogranuloma treated by surgical excision. *Case Rep Dermatol* 2: 110–115, 2010
- 6) Kiratli H, Kiliç M, Tarlan B, Söylemezoglu F: Adult orbital xanthogranulomas: clinical features and management. *Eur J Ophthalmol* 25: 288–292, 2015
- 7) Karcioğlu ZA, Sharara N, Boles TL, Nasr AM: Orbital xanthogranuloma: clinical and morphologic features in eight patients. *Ophthalmic Plast Reconstr Surg* 19: 372–381, 2003
- 8) Davies MJ, Whitehead K, Quagliotto G, Wood D, Patheja RS, Sullivan TJ: Adult orbital and adnexal xanthogranulomatous disease. *Asia Pac J Ophthalmol (Phila)* 6: 435–443, 2017
- 9) Jakobiec FA, Mills MD, Hidayat AA, et al.: Periocular xanthogranulomas associated with severe adult-onset asthma. *Trans Am Ophthalmol Soc* 91: 99–125; discussion 125–129, 1993
- 10) Ugurlu S, Bartley GB, Gibson LE: Necrobiotic xanthogranuloma: long-term outcome of ocular and systemic involvement. *Am J Ophthalmol* 129: 651–657, 2000

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