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## Juvenile Xanthogranuloma Presenting as Bilateral Non-Infiltrative Extraconal Superior Orbital Tumour in a 27 Year Old Nigerian Woman: Features, Management and Outcome

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### Abstract

**Introduction:** Orbital masses in adults are often caused by systemic diseases or are associated with systemic manifestations. Juvenile xanthogranuloma as a cause is rare and unreported in Africa. We present clinical features, management, and outcomes of bilateral orbital adult onset juvenile xanthogranuloma.

**Case Presentation:** A 27 year old Nigerian woman presented with bilateral upper-lid lumps having lasted 5 months. These increased in size for about 1 month and stopped. Lid swelling was preceded by itchy eyes, redness of conjunctiva, and occasional mild pain. There were no visual or systemic symptoms. The lumps were firm, slightly mobile, not tender, and not attached to skin but rather to deeper structures. There was restriction on up-gaze but no proptosis or diplopia. Hematological, biochemical, and X-ray investigations were normal. Prednisolone tablets 10 mg daily for two weeks were not useful. Tissue biopsy was invaluable in diagnosis of this rare condition and disclosed juvenile xanthogranuloma. Partial surgical excision was done under lidocaine infiltration. No recurrence has occurred in 40 months of follow-up. No systemic disease has manifested.

**Conclusion:** Juvenile xanthogranuloma can present as bilateral superior orbital tumor in adults; functional and cosmetic aims were achieved by sub-total excision.

**Keywords:** bilateral orbital xanthogranuloma, excision

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## Introduction

Xanthomatous diseases are a group of diseases characterized histologically by foamy (lipid laden) histiocytes, lymphocytes, macrophages called Touton giant cells, plasma cells, and some areas of necrosis.<sup>1,2</sup> Components of the histology vary in different portions of the specimen and at different times.<sup>2</sup> These diseases can occur at any age, can affect any organ, and have been associated with haematologic and immunologic disorders.<sup>2-4</sup> The eye and ocular adnexae can be affected by four distinct subtypes of adult xanthomatous disease. These are adult onset juvenile xanthogranuloma, otherwise called adult onset xanthoma (AOX), adult onset asthma with peri-ocular xanthogranuloma (AAPOX), necrobiotic xanthogranuloma (NXG), and Erdheim-Chester disease (ECD).<sup>1</sup> Xanthomatous diseases may manifest as unilateral and less commonly as bilateral orbital masses.<sup>1,2,5,6</sup> These diseases are so uncommon that investigations looking into the causes of orbital masses in a health facility, completed over several years, did not disclose them.<sup>7</sup> It is the first recorded case in this eye care facility, which is over 20 years old and has outpatient contact of about 1600 patients a month. Xanthomatous diseases are therefore generally not considered as first line differential diagnosis of orbital space occupying lesion, giving rise to a delay in diagnosis. Their rarity also results in difficulty in getting a total sense of features, natural history, and best treatment options, even in meta-analysis of extant literature.<sup>1,2,8,9</sup> Contribution to any aspect of knowledge of this disease is therefore welcome. The objective of this communication is to contribute to the knowledge base available about this rare condition. This paper is about juvenile xanthogranuloma occurring as a bilateral non-infiltrative, extra-conal, superior orbital tumor in a 27 year old Nigerian woman. This case occurred in late 2007, with the woman presenting for care at the Guinness Eye Centre (Nnamdi Azikiwe University Teaching Hospital Onitsha, Nigeria) five months later on February 5, 2008. The features, management, outcome, and follow-up for 40 months are presented. Searches were done using Google, Yahoo, Pubmed, Medline, Science Direct, and HealthWorld Online. Searches were conducted on August 15, 2012 using the following keywords: orbital xanthogranuloma; orbital; xanthogranuloma Africa; JXG; AOX; bilateral orbital xanthogranuloma;

juvenile xanthogranuloma; orbital JXG; orbital tumor in Africa. To our knowledge, a similar communication of bilateral orbital adult-onset juvenile xanthogranuloma has not previously been reported in any racial group from Africa.

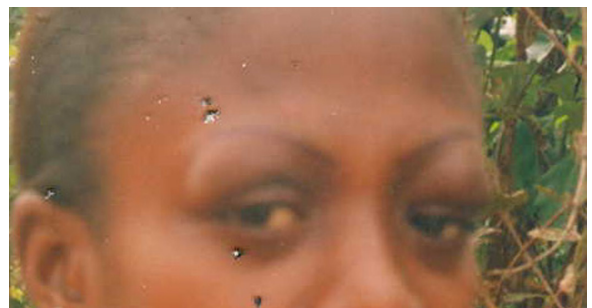
## Case Presentation

Presenting complaint was of upper lid swelling of both eyes for 5 months.

Patient was well until December 5, to presentation on February 5, 2008, when she noted upper lid swelling in both eyes, the left eye preceding the right by one week. Onset of lump was preceded by itching and redness of conjunctiva, in addition to lid swelling. The swelling progressively increased in size for about 1 month and then stopped. There was associated occasional, mild pain on the lids, but no decrease in vision, no protrusion of the eye ball, no double vision, and no feeling of dryness in the eyes. There was no associated weight loss, excessive sweating, neck swelling, or any other lumps on the body. Systemic reviews were all normal. There was no past history of asthma or any other illness. There was no significant past medical history, except occasional bouts of malaria.

General examination revealed a petite young woman in no obvious distress but with obvious bilateral swelling on both upper lids (see Fig. 1). She was not pale, jaundiced, not emaciated, nor did she have any palpable lymph nodes. Vital signs were normal and there were no signs of any systemic illness. Ocular examination revealed normal visual acuity of 6/6 in both eyes.

Palpable masses were present in the upper lids of both eyes, with the mass in the right eye being slightly bigger than that on the left. The mass on the right upper lid occupied about  $\frac{3}{4}$  of the length of the



**Figure 1.** Showing bilateral superior orbital masses.

space between the globe and the upper orbital margin, and that on the left about  $\frac{1}{2}$  of the length. Masses were firm, mobile, and not attached to skin. The skin covering the masses was not abnormally pigmented. There were no proptosis or globe displacements, and ocular motilities were full except superolaterally in both eyes, where movement was about  $\frac{1}{2}$  of expected motion in the right eye and  $\frac{3}{4}$  in the expected motion in the left eye. There were no pre-auricular or submandibular lymph adenopathy, nor any palpable abdominal masses.

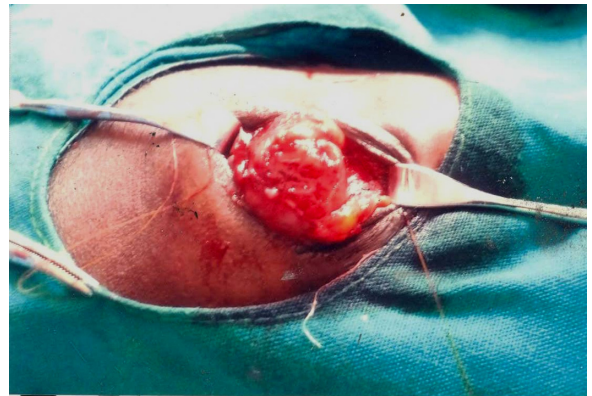
Anterior segment, media segment, and posterior segments were all normal. A diagnosis of orbital tumor was made with differentials of Orbital pseudotumor.

Investigations done included a full blood count and ESR, skull X-ray (Caldwell view), chest X-ray, HIV screening, old and most recent photograph examination, current photograph taken for record (all were normal) and biopsy. There was no hyperlipidaemia abnormality nor any other biochemical abnormality indicative of systemic disease. Details of result are presented below the main body of the manuscript.

Full blood count was done every six months for the first 18 months after surgery, and once yearly since then. No abnormal results have occurred except for occasional malaria parasite in blood film.

Management of this disease was an initial trial of steroids, with a prednisolone tablet dosage of 10 mg daily, for 2 weeks, starting on October 21, 2008. No effect on the tumor mass was detected as judged by observation and palpation.

Excision of tumor by a superior orbitotomy approach was undertaken on December 2, 2008 using local anesthesia that comprised 2% xylocaine with 1/200,000 adrenaline. Each mass was found at surgery to consist of a gray, lobulated, soft rubbery mass situated in the superior part of the orbit, between the muscle cone and the periosteum (Fig. 2), with no evidence of infiltration of surrounding tissue but extending deep into the orbital apex. No prominent blood vessels were found associated and therefore bleeding was minimal and blood loss was an estimated 20 mL. Excision was not complete as the mass was found to extend far into the orbital apex. Difficulty with the posteriorly situated part of the mass, which was in the orbital apex due to its crowded and narrow nature, along with care to avoid the vital structure located in that region and onset of pain in the patient



**Figure 2.** Still photograph of superior orbitotomy to access the superior orbital adult xanthogranuloma.

**Note:** The reddish yellow to grey lobulated mass protruding from the incision.

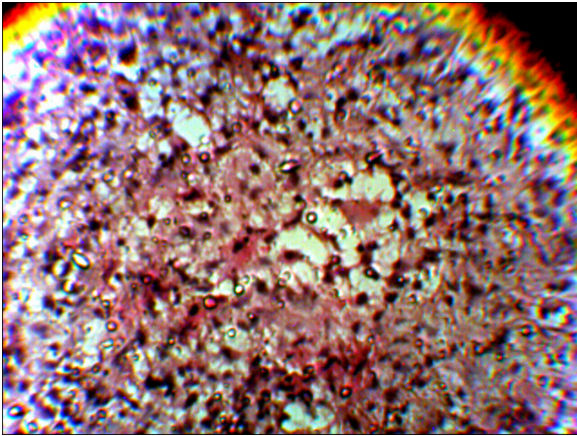
caused removal of the tumor to be limited to only the easily accessible, superficial tumor mass. Estimate is that about 25% of tissue was left in the right orbit, and 10% in the left. Excised tissue from the right orbit measured 3.5 mm by 2.5 mm. Excised tissue from the left measured 3.5 mm by 2 mm (Fig. 3).

Excised matter was sent for histology with the following result (Figs. 4–6).

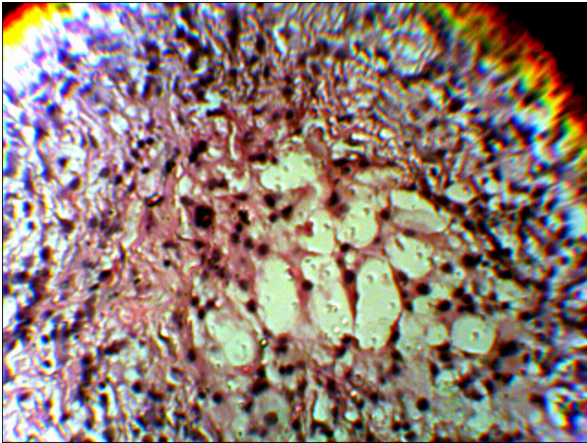


**Figure 3.** The excised masses placed adjacent to a ruler for measurement: right measures three and half mm by two and half mm; and the left measures three and half mm by 2 mm.

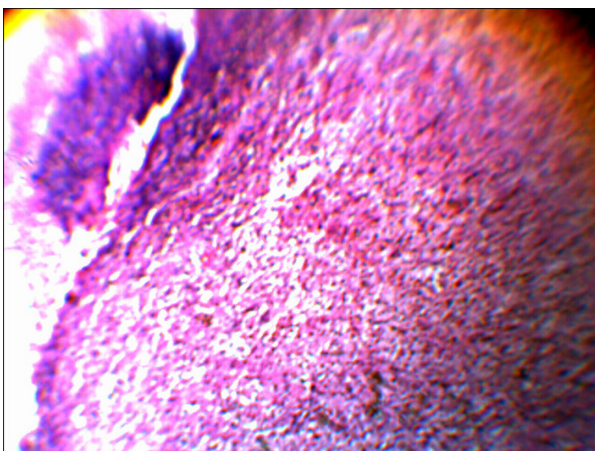




**Figure 4.** Show mainly large foamy cells with both eosinophilic granular abundant cytoplasm and some pale cytoplasm and small blood vessels.



**Figure 5.** Showing large foamy cells with mainly pale cytoplasm and fewer eosinophilic granular abundant cytoplasm.  
**Note:** Some giant looking cells are seen though they are not typically touton-like giant cells.



**Figure 6.** Showing numerous lymphocytes and plasma cells.

## Macroscopy

The specimen consisted of two pieces of grayish white tissue, together measuring  $1.1 \times 0.3 \times 0.2$  cm. The specimen was processed whole.

## Microscopy

A histologic section showed tissue with cells comprised of large, foamy macrophages with eosinophilic, granular, abundant cytoplasm, and others with very pale cytoplasm. Also seen were numerous lymphocytes, plasma cells and small capillary blood vessels. No obvious evidence of malignancy or lymphoproliferative disease was seen in the sample provided. Though no typical toutons giant cells were present, the findings are in keeping with juvenile xanthogranuloma. (Dr. D.C.D. Anyiam, consulting pathologist)

Post op recovery was uneventful and cosmetic was appearance excellent. A review 10 days after surgery showed visual acuity of 6/5 in both eyes and full ocular motility. Follow-up until August 9, 2012 showed no recurrence of orbital mass. However, the patient has on two occasions had episodes of retro-ocular pain, for which a course of prednisolone 10 mg daily for 10 days was prescribed and seemed to resolve. No associated systemic disease, including diabetes mellitus, hyperlipidaemias, and leukaemia, has occurred on review done August 9, 2012.

## Discussion

### Difficulty in diagnosis-due to rarity

The occurrence of a bilateral, slowly progressive, not markedly painful, and almost symmetrically-spaced mass lesion in the superior orbit of a young adult patient would not normally evoke the suspicion of xanthomatous disease. It would instead indicate other conditions, primarily because of the rarity of this condition.<sup>1</sup> Adult-onset bilateral orbital juvenile xanthogranuloma is even more uncommon and, to the authors' knowledge, has not been reported from Africa. The first reported case of a similar condition was by Nasr and colleagues in 1991.<sup>10</sup> Subsequent reports by Elner et al<sup>8</sup> and Malhotra et al<sup>5</sup> were dissimilar to the current report by the concomitant presence of tissue infiltration, associated skin lesions, or occurrence of systemic symptoms. The reason was that most of their series included other variants of xanthomatous disease in which these associations



occur—Erdheim-Chester disease (ECD), adult onset asthma with periocular xanthogranuloma (AAPOX), or necrobiotic xanthogranuloma (NBX). Adult onset xanthogranuloma (AOX) on the contrary is not usually associated with these other features,<sup>2</sup> frequently leading to an initial erroneous differential diagnoses. The phenomenon of erroneous initial differential diagnosis of this condition, as occurred in this patient, has been described previously by other investigators as a not unusual occurrence in bilateral orbital masses without associated systemic symptoms.<sup>7,9</sup> Because of these more commonly occurring conditions, an initial diagnosis of bilateral orbital xanthogranuloma is difficult to make on history and clinical examination alone.

### Useful investigations in AOX

Although they may be considered integral evaluation tools, sophisticated imaging and biochemical and genetic studies may not be feasible in poorer countries. Best practices in disease management are therefore in large measure dependent on what is feasible in an environment. Investigators have documented various tests in the evaluation of orbital xanthogranuloma,<sup>9,11</sup> but in poor countries the tests are not available or affordable, and cost/benefit consideration renders many tools impractical for most patients. MRI and CT would be useful imaging methods to determine extent of lesion, infiltration, and bony erosion in the patient in this study, but they were not available. Some practitioners may have reservations with any consideration of orbital surgery without more extensive sophisticated imaging tests such as CT and MRI or biochemical tests. These are valid concerns if such tools are available. However, X-ray, the only available imaging technique, was deployed to determine presence of bony erosion into the sinuses or cranial cavity, which had important implications for surgical excision of the tumor. It was determined to be adequate for the task and no bony erosion was noted. The simple hematological and biochemical investigations done were the only tools available and were considered adequate. Review of several old photographs were undertaken to better understand time of onset and subsequent progression of this disease. What is considered the golden standard<sup>9</sup>—biopsy—was done to obtain a histological specimen for analysis, and this informed

the decision to proceed with surgical exploration and excision.

### Treatment modalities and result

Treatments deployed for orbital xanthomatous diseases include steroid<sup>1,8</sup> anti-tumor agents like metotrexate, radiation, cyclosporine, immunotherapy, laser application and surgery.<sup>1,2,6</sup> However, the rarity of this disease has resulted in insufficient data for an evaluation of the efficacy of various modes of treatment, or even an evolution of what may be considered conventional, standard, or usual treatment. Oral administration of prednisolone 10 milligram a day for two weeks in this patient was of no use in decreasing the size of the tumor nor did it prove effective in relieving the sensation of pressure in the orbit. Elner and colleagues documented regression of lesions on intra-lesional injection of long acting steroids like triamcinolone,<sup>8</sup> although adverse effects of this practice have been noted and therefore called for caution.<sup>12,13</sup> Absence of systemic symptoms in this patient, together with the isolated and discrete nature of the lesion, made utilization of systemic therapy inappropriate.

Surgery as a mode of therapy was considered more suitable. Factors in this determination included the fact it was considered simple and decisive and the fact it did not involve administration of expensive and unaffordable drugs that would require monitoring and management of side and adverse effects. The same approach was also utilized in a similar case reported by Murthy et al.<sup>6</sup> Bilateral superior orbitotomy and surgical excision of the tumor was done during the same surgical session using perilesional infiltration of xylocaine 2%, with adrenaline 1/200 000, a procedure which has not been documented previously for this condition.

Features found on surgical exploration of this tumor included an absence of bone erosion or infiltration into the skull bones, periosteum, the cranial cavity, or any other orbital tissue, which in contrast to juvenile xanthogranuloma are commonly documented features of adult onset juvenile xanthogranuloma.<sup>4,6,9,14-17</sup> Absence of local infiltration was of great benefit in excising this lesion.

Several features from the surgical procedure on this patient are of noted. First, debulking was





effective and not total excision is not necessary if total excision is either impractical or poses considerable risk of damage to surrounding structures. This is evidenced by no recurrence of the tumor in over 40 months and acceptable cosmetic appearance. Other workers have noted the same fact.<sup>3</sup> Secondly, the surgery was done under local infiltration anesthesia. This should be the preferred option except in exceptional circumstance which make general anesthesia, with its higher associated risks, necessary. Lastly, bleeding during surgery was minimal, since the tumor was observed to be devoid of large blood vessels. Visibility for dissection was excellent, requiring only an occasional gauze swab dab to dry surgical area, whereas juvenile xanthogranuloma of the iris are significant causes of bleeding even without trauma.<sup>18</sup>

## Conclusion

Isolated juvenile xanthogranuloma occurring bilaterally in the orbit of a young female adult Nigerian was presented. The diagnosis was done through biopsy. Excision was completed by a simple surgical procedure and was not complete. The result is judged to be good because of a lack of recurrence of the tumor in 40 months of follow-up.

## Author Contributions

OMC performed the surgery, analyzed and interpreted patient's data, and was the major contributor in writing the manuscript. ADCD completed the histopathological work and reporting. Both authors read and approved the current manuscript.

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## Competing Interests

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## Disclosures and Ethics

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## Results of Investigation

FBC on 22/02/08 result: Hb 10.0 g/dL;  
WBC- $9.6 \times 10^9/L$ ; N-50%; E-1%; B-0%; L-46%;  
M-3%

ESR-15 mm/first hr  
Blood film—normal

Results on 26/02/08

PCV-35  
WBC- $8.6 \times 10^9/L$ ; N-80; E-6; B-0; L-14;  
Platelets-adequate  
ESR-96 mm/1st hour

Results 14/10/08

PCV-28  
WBC- $7.5 \times 10^9/L$ ; N81; E-2; B-0; L-16; M-1  
Platelets- $7.5 \times 10^9/L$ ; Morphology-normal  
Blood film-anisocytosis, macrocytosis, hypochromia,  
malaria parasite++

Urinalysis was done by means of dipstick—Meditest-  
Combi 9 by MACHEREY-NAGEL Duren-

Detailed result of urinalysis done 26/08/2008

Colour-amber  
Blood-negative  
Urobilinogen-normal  
Bilirubin-normal  
Nitrite-negative  
Protein-negative  
Sugar-negative

Skull Xray was normal,

HIV screening was negative [17/10/08]

LIPID PROFILE DONE 9/08/2012

Total cholesterol-4.8 mmol/L  
LDL-3.5 mmol/L

HDL-1.2 mmol/L

Fasting tryglicerides-1.2 mmol/L

Most current blood count done on follow-up on  
9/02/2012

PCV-35  
WBC- $9.6 \times 10^9/L$ ; N-60%; E-1%; B-0%; L-36%;  
M-3%

Platelets- $7.5 \times 10^9/L$ ; Morphology-normal

ESR-15 mm/first hr

Blood film—normal

JUVENILE XANTHOGRANULOMA (UPPER  
EYELID SOFT TISSUE MASS).

MCROGRAPH PICTURES: DCD ANYIAM Dept  
of histopathology, NAUTH, NNEWI

MACROSCOPY: Specimen consists of two pieces of  
grayish white tissue together measuring  $1.1 \times 0.3 \times$   
0.2 cm. Processed whole.

MICROSCOPY: Histologic sections show tissue with  
cells comprising mainly of large foamy macrophages  
with eosinophilic granular abundant cytoplasm  
and others with very pale cytoplasm. Also seen are  
numerous lymphocytes and plasma cells and small  
capillary blood vessels. No obvious evidence of  
malignancy or lymphoproliferative disease is seen in  
the sample provided. Though no typical toutons giant  
cells are present, the findings are in keeping with a  
juvenile xanthogranuloma.

LEFT UPPER EYELID SOFT TISSUE MASS:  
JUVENILE XANTHOGRANULOMA.