CASE REPORT

Juvenile xanthogranuloma presenting as a large neck mass and ocular complications: a diagnostic and therapeutic dilemma

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SUMMARY

Juvenile xanthogranuloma is a non-Langerhans cell histiocytosis that originates from dendritic cells. Dendritic cells can accumulate in the skin of the head, neck, trunk, arms and legs. They may also involve other tissues such as the bones, lung, liver, heart, bone marrow, central nervous system, spleen and large intestine in rare cases. We report a rare case of juvenile xanthogranuloma in a 16-year-old girl who presented with a neck mass and left-sided ptosis 2.5 months previously. Excisional biopsy of the neck lesion revealed proliferated histiocytes admixed with numerous eosinophils and multinucleated giant cells that simulate eosinophilic granuloma; however, the histiocytes were negative for CD1a, CD123 and S-100 protein and positive for CD68 and CD14. The course of the disease led to treatment of the patient with chemotherapy, followed by low-dose radiotherapy.

BACKGROUND

Juvenile xanthogranuloma (JXG) is an uncommon non-Langerhans histiocytic disorder that mostly affects the skin.[1] Extracutaneous sites such as the central nervous system, eye, salivary glands, larynx, heart, liver, spleen, colon, retroperitoneum, kidney, adrenal glands, bone and mucous membranes may also be involved, although this is rare.[1–9] JXG presents as single or multiple, 1–20 mm size, tan/orange colour, papulonodular, well-demarcated cutaneous lesions, frequently located on the head and neck of infants and small children.[1–3] Cutaneous lesions are self-limiting and usually regress spontaneously over time, although sometimes they do require treatment, but systemic involvement is rare.[4 7 8] Only a few literature reviews have been published about the pathogenesis, prognosis and treatment guidelines of this condition.[1] The eye, especially the uveal tract, is the most frequent site of involvement in an extracutaneous manifestation.[3 5 6] Cutaneous JXG is seen 1.5 times more frequently in male children than in female children, but the extracutaneous predilection rate has not been reported.[9] The similarity of symptoms with Langerhans cell histiocytosis causes confusion in clinical and pathological diagnosis. We report a case of extracutaneous JXG with a rare clinical presentation in a 16-year-old girl, and then briefly discuss the manifestations of the disease by looking at the radiological, clinical and histopathological characteristics.

CASE PRESENTATION

A 16-year-old girl was admitted to the otorhinolaryngology ward with a swollen red left eye and a fast-growing neck mass with ptosis 2.5 months previously. On physical examination, it appeared as a non-tender, mass-like lesion, measuring approximately 5 cm in diameter at levels II and III, on the left side of her neck. The patient explained that 3 months prior to the appearance of the neck mass, amber-coloured fluid (tears) were leaking from her left eye. Her medical history revealed that she suffered from absence seizures from the age of 4 years. She was not currently on any medication for this disorder.

INVESTIGATIONS

On ultrasonography, an ill-defined heteroechoic mass-like lesion in the anterior aspect of the left sternocleidomastoid (SCM) muscle and multiple small lymph nodes measuring up to 10 mm (short axis diameter) on both sides of the carotid spaces were seen. The mass showed internal blood flow on colour Doppler ultrasonography and a minimal pressure effect on the left internal jugular vein. A CT scan showed a solid heterogeneous mass-like lesion measuring 5×10 cm in the mid portion of the anterior aspect of the left SCM muscle extending to the lower aspect of the left parotid gland superoposteriorly and to the left thyroid lobe medially.

Also, multiple small lymph nodes measuring up to 1.1×0.8 cm in the anterior aspect of the left SCM muscle and on both sides of the carotid spaces were depicted (figure 1). Furthermore, axial T1-weighted gradient echo MRI of the orbits

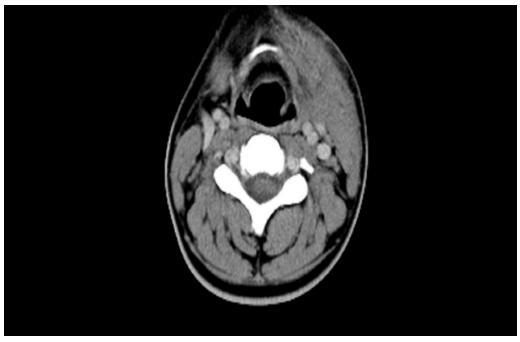

Figure 1 CT scan showing a solid heterogeneous mass-like lesion measuring 5×10 cm in the anterior aspect of the left sternocleidomastoid muscle.

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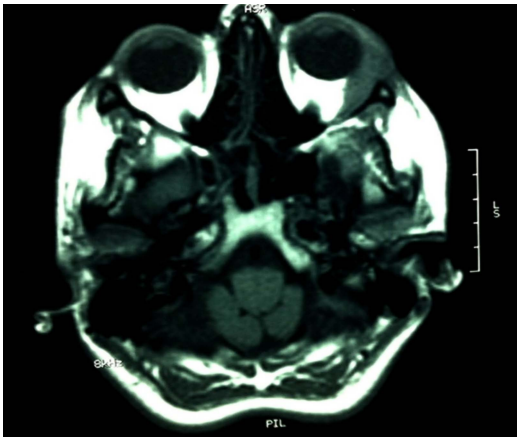
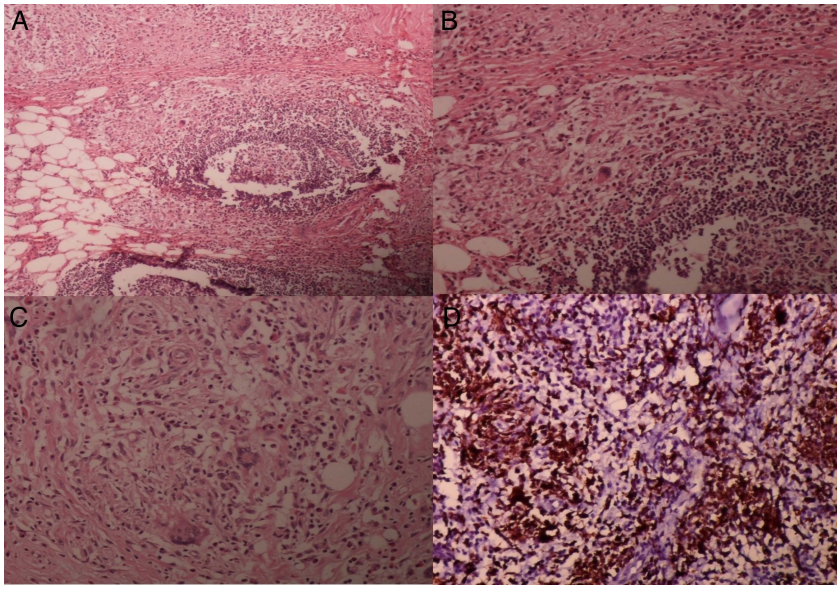


Figure 2 Axial T1-weighted gradient echo MRI demonstrates a swelling and inflammation of the periseptal and extraconal soft tissue of the left orbit.

demonstrated a swelling and oedema of the periseptal and extraconal soft tissue in the lateral side of the left orbit, without involvement of the surrounding bones, paranasal sinuses, nasopharynx or the retropharyngeal space (figure 2). No other positive findings were observed in a thoracoabdominal CT scan. Fine-needle aspiration cytology from the neck lesion was negative for malignancy. The patient underwent deep neck mass resection. In the surgical approach to the lesion, an incision at the site of the left SCM muscle was performed (10 cm in length) and the platysma muscle was opened; then, the dissection was continued up to the anterior aspect of the left SCM. The left carotid sheath also was exposed where the left jugular vein and left carotid artery were visible. The left XII cranial nerve in the posterior triangle space of the neck was saved. The attached mass was released from the surrounding muscles precisely. At the III level and jugulodigastric area, there were few lymph nodes that seem relatively larger than normal, so they were dissected. The facial vein and middle thyroid vein were ligated and separated from the lesion. The lesion was resected by saving the XI, XII and X cranial nerves. The resected mass and lymph nodes were sent to the pathology ward. The received specimen from the neck lesion measured 5×3.5×2.5 cm and was grossly greyish coloured with an elastic consistency. Histopathological examination showed fibroadipose vascular connective tissue severely infiltrated by inflammatory cells, mostly eosinophils, neutrophils and lymphoplasma cells, admixed with numerous multinucleated giant cells, some of which were Touton-like cells, along with many histiocytic-like cells. Prominent lymphoid follicles were also visible, and these were infiltrated by Touton giant cells and eosinophils (figure 3A–C). Inflammatory cells were spread throughout the bundles of skeletal muscle tissue, with large areas of fibrosis. Prominent blood vessels were also seen throughout the lesion. Histopathological examination of the lymph nodes showed reactive lymphoid follicle hyperplasia, and the neck lesion was suggestive of eosinophilic granuloma or JXG. To make a differential diagnosis, immunohistochemical studies were conducted and the histiocytes were positive for CD68 and CD14 (figure 3D), but were negative for CD1a, S-100 protein and CD123 (figure 4). Based on H&E staining and immunohistochemical studies, a diagnosis of JXG was confirmed.

DIFFERENTIAL DIAGNOSIS

In a differential diagnosis of mass-like lesions with an infiltration of eosinophils, and lymphoplasma cells, admixed with multinucleated giant cells, eosinophilic granuloma, granulocytic sarcoma, angioimmunoblastic lymphadenopathy, tuberculosis, Rosai-Dorfman disease and, in rare cases, JXG should be considered. In eosinophilic granuloma, histiocytes have nuclei with a coffee bean appearance, and they also have a positive reaction for CD1a, CD123 and S-100 protein. In tuberculosis, well-formed granuloma lesions with central caseating necrosis are present, and PCR confirms the diagnosis. Granulocytic sarcoma is an uncommon tumour composed of myeloblasts, immature eosinophilic series and multinucleated giant cells, in which the myeloid series have a positive reaction for CD117, CD68 and CD33. In Rosai-Dorfman disease, there is pronounced dilation of the lymph sinuses, which are occupied by lymphocytes, plasma cells and numerous histiocytes containing large amounts of neutral lipids and numerous lymphocytes within their cytoplasm (emperipolesis). These histiocytes strongly show a positive reaction for S-100 protein. In JXG, histiocytes which are non-Langerhans type have a positive reaction to CD68 and



Figures 3 (A) Fibroadipose connective tissue infiltrated by eosinophils, histiocytes and multinucleated giant cells, with lymphoid tissue (H&E staining, objective ×10). (B) Numerous eosinophils are seen inside the lymphoid follicle and connective tissue (H&E, objective ×20). (C) Numerous multinucleated giant cells, that some of them are Touton-like (H&E, objective ×20).(D) Histiocytes have a positive reaction to CD68 (immunohistochemical staining, objective ×20).

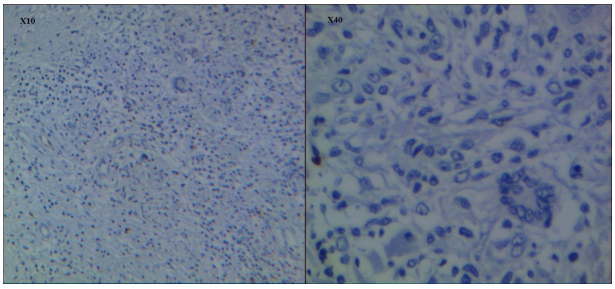


Figure 4 Histiocytes have a negative reaction to S-100 protein (immunohistochemical staining, objective ×10 and ×40).

CD14, but they are negative for CD1a, CD123 and S-100 protein.

TREATMENT

We have not had any earlier cases of JXG with extracutaneous manifestations in our centre. Therefore, owing to the problematic clinical presentations of this case, and a few previously published case reports in the literature, along with a lack of standard treatment, our team, including an oncologist and a radiotherapist, recommended careful follow-up of the patient. During the follow-up, epiphora of the patient was continued and no sign of improvement was observed. The patient also reported with neck mass pressure to the adjacent soft tissues. Based on the tumour board's recommendations, chemotherapy was initiated with: tablet prednisone 50 mg daily for 2 months, and vincristine 1.4 mg/m^2 (2 mg) for 9 weeks (four courses). After the administration of vincristine, the patient presented with neuropathy, and therefore treatment was changed to three courses of intravenous injection of cyclophosphamide 750 mg/m^2 for 3 weeks. She tolerated these medications better, although after completion of chemotherapy she opted for low-dose radiotherapy (5 courses of 10 gray radiation).

OUTCOME AND FOLLOW-UP

After 4 months, her general condition had improved and eye complications had subsided except ptosis.

DISCUSSION

JXG is an uncommon dermatological disease originating from dermal dendrocytes, which are non-Langerhans cell histiocytes.[1–9] This condition was first reported by Rudolf Virchow in 1871 and then in 1905 by Adamson.[10] JXG presents as single or multiple papulonodular skin lesions, ranging in size from 1 to 20 mm in diameter; they usually have a benign outcome, are self-limited and rarely require treatment. Infants and young children are affected predominantly; however, it may also occur in adulthood.[2 8 9] The skin of the head, neck and trunk are the most common sites of involvement, but involvement of extracutaneous organs such as the brain, eye, spleen, bones, central nervous system, heart, liver, adrenal glands and mucus glands have also been reported.[1–9] Although the cause of the disease is not clear, some believe that overproduction and accumulation of dendritic cells could lead to various symptoms based on location.[1 2] JXG is sometimes misdiagnosed or spontaneously regresses in children, so it seems that the incidence rate is higher than the number of reported cases. Our case presented with a large mass-like lesion in the left neck, ptosis and leaking amber-coloured tears, which might be a rare manifestation. In reported cases, eyes were the most common site of extracutaneous involvement and almost 50% of the patients with ocular involvement also suffered from skin lesions, in comparison with our patient who did not have any cutaneous lesions.[3 6] Involvement of the iris may lead to heterochromia, uveitis, spontaneous hyphema and secondary glaucoma, whereas our presented case did not have these symptoms. As a result, her eye complications might be due to oedema of the periseptal and extraconal soft tissue of the left orbit; moreover, the ptosis could be due to the involvement of the subcutaneous eyelid tissue. We did not biopsy from the lesion of the periorbit to document the invasion because there was the possibility of high risk of severe complications. Histopathological characteristics of the disease are based on the infiltration of histiocytes, large amounts of eosinophils and multinucleated giant cells, some of which were Touton type.[1–10] Histiocytes in JXG do not have the characteristics of Langerhans cell histiocytes, which have a positive reaction for CD123, CD1a and S-100 protein, but dendritic histiocytes of JXG have a positive reaction to CD14, CD68 and factor XIIIa.[2 5 6] We encountered problems with the treatment of our case, because proven, established treatments were not available in the texts or literature reviews and there is a lack of comprehensive studies in this regard. Based on published case reports and the tumour board recommendations, we treated our patient with chemotherapy and this was followed by low-dose radiotherapy. The response to treatment was acceptable.

Learning points

- In differential diagnosis of soft tissue masses, with infiltration of numerous eosinophils, histiocytes and multinucleated giant cells, rare causes such as juvenile xanthogranuloma (JXG) should be considered.
- Immunohistochemical studies play an important role in differentiating eosinophilic granuloma (subtype of Langerhans cell histiocytosis) from JXG, where histiocytes originate from dendritic cells that are positive for CD68 and CD14 and negative for CD123, CD1a and S-100 protein.
- In rare conditions, JXG may involve deep soft tissues and invade adjacent organs and cause mass effect symptoms.
- Despite dendritic cells commonly accumulating in the skin tissue, they could also involve other organs such as the lung, bones, liver, heart, bone marrow, central nervous system, spleen and large intestine.
- However, cutaneous forms of JXG with or without organ involvement are curable and respond to surgical resection without chemoradiotherapy, or even regress spontaneously, but deep located lesions with complications on serious organs such as eyes need chemotherapy and radiotherapy for regression of the lesions and therefore resolving the symptoms.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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