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## Ultrasound Appearance of Juvenile Xanthogranuloma<sup>☆</sup>



### Imagen ecográfica de xantogranuloma juvenil

Dear Editor:

We present a 7-year-old girl with no past history of interest, who was seen for an asymptomatic lesion that had arisen in the right axilla 3 months earlier and had grown progressively, but that had remained stable after a cycle of cryotherapy in her health center 2 months earlier. Examination revealed a well-defined oval papule in the right axilla. The papule was of yellowish color centrally and more erythematous peripherally. No drainage orifice was present and no material was emitted when pressure was placed on the lesion (Fig. 1).

Color Doppler ultrasound ( Esaote MyLabClass C with an 18 MHz transducer) was performed, showing a well-defined, homogeneous, hypoechoic lesion in the dermis, measuring 6.5 × 3.5 mm, and that depressed the subcutaneous cellular tissue (Fig. 2). No posterior enhancement or lateral shadow was observed. Color Doppler showed no flow within the lesion.

We performed complete excision of the lesion. Histopathology study revealed a diffuse histiocytic proliferation that occupied the full thickness of the dermis (Fig. 3A). The lesion was formed of cells with isomorphic oval nuclei and eosinophilic cytoplasm and foam cells, some of which were multinucleated, including occasional Touton-type cells (Fig. 3B). These cells were accompanied by numerous lymphocytes. No epidermotropism was observed. The diagnosis was xanthogranuloma.

Juvenile xanthogranuloma (JXG) is a benign histiocytic tumor characterized by being most common in the first 2 decades of life. Various classifications place this lesion in the non-Langerhans cell histiocytoses, together with other diseases such as disseminated xanthoma, diffuse eruptive histiocytosis, benign cephalic histiocytosis, and sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease).

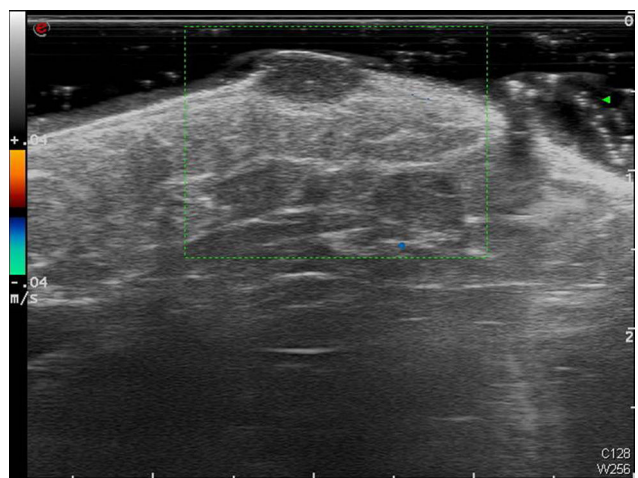
JXG is the most common histiocytic disease of childhood,<sup>1</sup> though its incidence may be underestimated due to the indolent, asymptomatic nature of these solitary lesions and their tendency to resolve spontaneously.

Clinically, it presents as yellowish papulonodular lesions in the skin and other organs, but it is not associated with

metabolic disorders. It is the most common form of non-X histiocytosis and shows no racial or sex differences. Two clinical forms are recognized, both typically asymptomatic. The papular form with firm reddish or yellowish lesions of 2 to 5 mm in diameter, located in the skin or rarely in the mucosas; and the less common, nodular form, which develops as an isolated or small number of round, brownish-red or yellowish lesions of 1 to 2 cm in diameter. The 2 forms can coexist and can arise at any of the sites affected by this disease: lung, heart, gastrointestinal tract, central nervous system, adrenal glands, pituitary gland, bone, bone marrow, kidney, eyes.



**Figure 1** A solid yellowish-erythematous papule of 7 mm diameter in the right axilla.

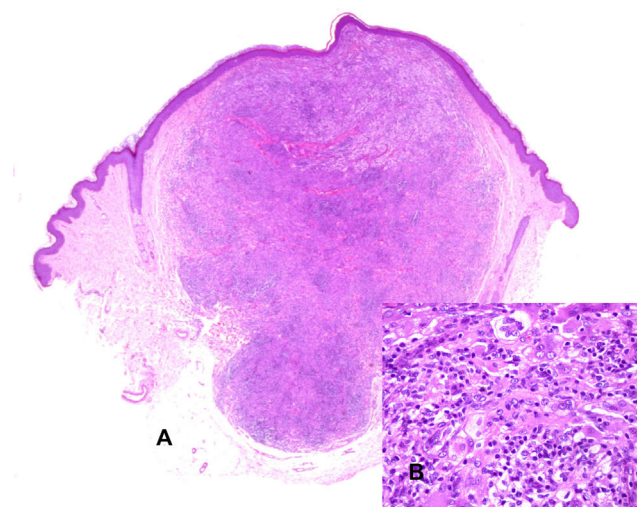


**Figure 2** High-frequency (18 MHz) Doppler ultrasound image showing a well-defined, homogeneous, hypoechoic lesion measuring 6.5 × 3.5 mm in the dermis, with no blood flow internally.

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**Table 1** Ultrasound Features of Lesions Common in Childhood.

	Juvenile Xanthogranuloma	Pilomatrixoma	Infantile Hemangioma	Dermoid Cyst	Dermatofibroma
Gray scale	Homogeneous, hypoechoic, dermal	Five types described. <sup>2</sup> Hyperechoic areas. Posterior acoustic shadow	Hypoechoic, formed of a more or less homogeneous stroma (more stroma than channels)	Deep hypoechoic lesion with linear hyperechoic images internally	Homogeneous, with poorly defined borders, dermal
Color Doppler	No vascularity	No vascularity except type 5 <sup>2</sup>	Abundant vascularity	No vascularity	Occasionally vascular



**Figure 3** A, A diffuse histiocytic proliferation occupies the full thickness of the dermis. Hematoxylin and eosin, original magnification  $\times 20$ . B, At higher power, the proliferation is seen to be formed of cells with isomorphic oval nuclei and eosinophilic cytoplasm, together with foam cells, some of which are multinucleated, including occasional Touton-type cells. Hematoxylin and eosin, original magnification  $\times 400$ .

The differential diagnosis of JXG when it presents as a solitary lesion, as in our patient, should include Spitz nevus, cystic lesions, and certain adnexal tumors, such as pilomatrixoma.

The definitive diagnosis of JXG is made on histopathology, which, in early lesions, shows a monomorphic infiltrate of histiocytes that contain no lipids and that can occupy the full thickness of the dermis, or at least the upper half of the dermis. Mature lesions contain foam cells and Touton-type giant cells, located particularly in the superficial dermis and at the border of the infiltrate, and fibrosis may be observed. Lymphocytes, neutrophils, and eosinophils may sometimes also be seen. Immunohistochemistry shows that the histiocytes in the infiltrate usually express CD68, CD163, Factor XIIIa, and CD4 and are negative for protein S-100,<sup>3,4</sup> which facilitates their differentiation from Langerhans cell histiocytosis and Rosai-Dorfman disease.

Although the definitive diagnosis of JXG is histological, we consider that ultrasound can be a useful noninvasive diagnostic tool. The ultrasound findings in our patient were

very similar to those of an earlier description of the ultrasound image of JXG in an adult, which showed a lesion in the dermis with no posterior enhancement or lateral shadow.<sup>5</sup>

The sonographic differential diagnosis of JXG should include other vascular lesions such as infantile hemangioma, in which greater vascularity is usually observed on Doppler and more marked epidermal alterations are present, induced by the underlying lesion.<sup>5</sup>

The ultrasound image of JXG can be differentiated from epidermal and other cysts because those cystic lesions are usually anechoic or hypoechoic with anechoic bands.<sup>6</sup> Tumors that arise from the hair matrix, such as pilomatrixomas, present sonographically as hypoechoic lesions with different degrees of internal echogenicity, producing a posterior acoustic shadow.<sup>7</sup>

Solivetti et al.<sup>2</sup> described 5 ultrasound images of pilomatrixomas that varied from a completely calcified lesion, in which only the posterior acoustic shadow was observed (type 1) to one with a pseudoneoplastic, hypoechoic appearance, with increased vascularity on Doppler (type 5). The ultrasound features of basal cell carcinoma (BCC) differ from those of JXG in that BCC is a hypoechoic lesion that contains hyperechoic spots within its substance.<sup>8,9</sup> Table 1 summarizes the ultrasound characteristics of other tumors and lesions that are common in childhood.<sup>10</sup>

We have presented a patient with JXG that was excised surgically and we have correlated the clinical and histopathological features with the ultrasound findings on 3 images of the lesion.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

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## Oral Ivermectin to Treat Papulopustular Rosacea in an Immunocompetent Patient<sup>☆</sup>



### Tratamiento con ivermectina oral en un paciente inmunocompetente con rosácea pápulo-pustulosa

Dear Editor:

Papulopustular rosacea is a chronic inflammatory disease characterized by erythematous, papular, and papulopustular lesions on the face with variable ocular involvement. Various antimicrobial treatments such as erythromycin, metronidazole, permethrin, and oral tetracyclines have proven effective, as well as topical immunomodulators and, in severe cases, oral isotretinoin.<sup>1</sup> However, despite the varied therapeutic arsenal available, rosacea can be difficult to treat in some patients.

Our patient was a 44-year-old man who had had facial rosacea since age 30 years and no other past history of interest. Over the course of his illness, the patient had received treatment with retinoids and topical immunomodulators, oral cloxacillin, and repeated cycles of doxycycline, with only partial and/or transient improvement. Physical examination revealed diffuse erythema and a moderate number of papuloerythematous lesions on both cheeks and the dorsum of the nose (Fig. 1A). After obtaining informed consent from the patient, we recommended treatment with a single 250 µg/kg dose of oral ivermectin and specifically instructed

the patient not to apply any topical treatment. After 2 weeks, significant improvement was observed and the disease has remained in complete remission for 6 months after treatment (Fig. 1B).

The etiology and pathogenesis of rosacea is not fully understood. It is thought to be caused by a combination of factors, including augmented immune response, neuroimmune dysregulation, and vasoregulatory alterations.<sup>2</sup> There is growing evidence that *Demodex* mites play a role in the etiology and pathogenesis of rosacea. The density of *Demodex* organisms has been found to be greater in areas affected by rosacea than in healthy skin, and these mites have been found in a significant proportion of patients with rosacea.<sup>3</sup> Good response to acaricidal agents has been reported.<sup>1</sup> In addition, *Demodex* mites have started to gain recognition as one of the numerous factors that trigger the expression of Toll-like receptors 2 (TLR-2), giving rise to the exacerbated immune response observed in patients with papulopustular rosacea.<sup>3</sup> Ivermectin is an antiparasitic agent that has been widely used since 1988 for oral treatment of filariasis and other parasitic infections. Ivermectin not only has an antiparasitic effect but also has an immunomodulatory and anti-inflammatory effect by inhibiting the lipopolysaccharide-induced production of cytokines.<sup>4</sup> The use of topical ivermectin for the treatment of rosacea was approved by the US Food and Drug Administration in 2014 and by the European Medicines Agency in 2015. Oral ivermectin has also been successfully used, without formal indication, in the treatment of demodicosis, in both immunosuppressed<sup>5</sup> and immunocompetent patients.<sup>6</sup> Oral ivermectin has also been used, with satisfactory results, in 2 healthy patients with papulopustular rosacea; in 1 case, the patient received 3 mg/d for 8 days in association with 5% topical permethrin 3 times a week,<sup>7</sup> and in the other case, a child with severe oculocutaneous rosacea received a single dose of 250 µg/kg.<sup>8</sup>

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