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CASE AND RESEARCH LETTERS

Adult Onset Langerhans Cell Histiocytosis Diagnosed With Xanthoma-like Plaque[☆]



Placas similares a xantomas como forma de presentación de una histiocitosis de células de Langerhans en un paciente en edad adulta

To the Editor,

Langerhans cell histiocytosis (LCH) is a rare, clonal disorder of immature Langerhans cells that can involve various organs and especially the skin, bone, lungs and pituitary gland. The disease is most commonly seen in infants, children and is rare in adulthood.^{1,2} Skin limited Langerhans cell histiocytosis in adults is even less common.^{2,3}

A 73-year-old male patient presented to our clinic complaining of a patch on his back that had appeared about a year ago and gradually enlarged. There was nothing of significance in his medical history. Although he had a 15 pack/year cigarette-smoking history, he had stopped smoking 30 years prior to his diagnosis. The dermatologic examination revealed xanthoma-like plaques on his back, that had composed with the accumulation of yellow-orange papules on an erythematous background, and erythematous papules (Fig. 1). Skin biopsy was taken for differential diagnosis of diffuse plane xanthoma. Histopathological examination revealed dense clusters of Langerhans cells with an eosinophilic cytoplasm, grooved or lobular nucleus; histiocytes with abundant pale cytoplasm, multinucleated giant cells and lymphocytes in the dermis (Fig. 2). Langerhans cells stained the positive for CD1a, CD207 (langerin) and S100 (Fig. 3a-3b). The diagnosis of LCH skin involvement was confirmed with histological and immunohistochemical analysis of skin biopsy. BRAFV600E mutation was been detected in skin tissue sample.

Computed tomography (neck, thorax, abdomen, pelvic), also pituitary magnetic resonance scan failed to demonstrate systemic involvement. The patient was diagnosed with LCH skin involvement. He was referred to pulmonology, medical oncology, hematology and endocrinology departments and there was no extracutaneous involvement.

Treatment was started with topical corticosteroids and PUVA treatment with oral 8-Methoxypsoralen (8-MOP). The patient had photosensitivity reaction to PUVA after 46 sessions and treatment was changed to UVA with topical 0.1% 8-MOP gel. Phototherapy resulted with healing of the erythematous papules, erosions and thinning of the yellow-orange plaques (Fig. 1). The sixth month follow-up thoracic computed tomography image revealed parenchymal involvement consistent with LCH. Bronchoalveolar lavage investigation showed a large number (90%) of histiocytes and a small number of polymorphonuclear leukocytes. The patient was diagnosed with multi-systemic LCH and started methotrexate treatment, in the first week with a 5 mg test dose and then as 20 mg per weekly. The patient was stable with methotrexate treatment for 6 months.

The diagnosis of LCH is based on clinical and histopathological evidence with microscopic examination and immunohistochemical features of langerhans cells.^{1,4} Detection of LC markers CD1a and CD207 (langerin) is essential to confirm diagnosis and evaluation of Birbeck granules on electronic microscopy has been using less frequently.⁴ In this case CD1a and CD207 were positive with immunohistochemical investigation of the cells, with eosinophilic cytoplasm and grooved or lobular nucleus.

Skin lesions of LCH can be limited to a single anatomic region or generalized, and consist of diffused papules, nodules or plaques, and can mimic seborrheic dermatitis in addition to prurigo nodularis, eczema, psoriasis, candidiasis or intertrigo.^{1,5} Since skin involvement can be the initial symptom of systemic disease, these patients should be evaluated in terms of multi-organ involvement.^{6,7} Our patient had atypical lesions, xanthoma-like plaques and erythematous papules on his back and waist.

Clinical evidence of LCH vary based on the affected organ or system, from self-healing disease to chronic recurrences and it may resulted in patient being underdiagnosed.¹ Podjasek et al reported a LCH case, followed-up with a misdiagnosis of inflammatory intestinal disease, was diagnosed with skin lesions and had gastrointestinal, lung and liver involvement. Skin biopsy may be valuable for diagnosis of LCH.⁷ Our case developed lung involvement about 8 months after he was first diagnosed with LCH skin involvement. Additionally, lung involvement of LCH is more frequently in adults and strongly associated with smoking.⁴

BRAFV600E mutation has been detected in approximately half of LCH samples. Recently, it is suggested to research BRAFV600E mutation in all samples with difficult cases.⁴ In our case, we detected BRAFV600E mutation in skin tissue sample.

[☆] Please cite this article as: Boyuk E, et al. Placas similares a xantomas como forma de presentación de una histiocitosis de células de Langerhans en un paciente en edad adulta. Actas Dermosifiliogr. 2020;111:71–73.

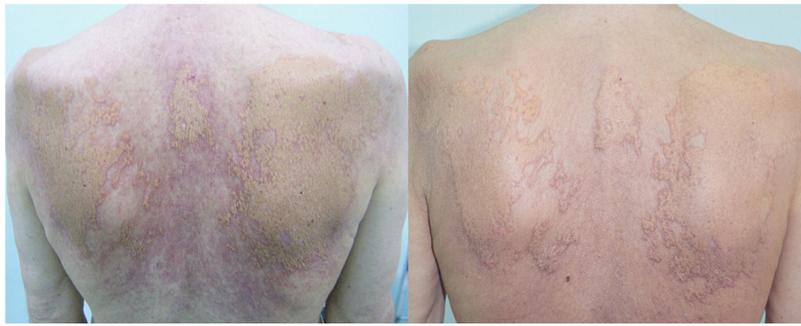


Fig. 1 Xanthoma-like plaques on trunk, that had composed with the accumulation of yellow-orange papules on an erythematous background, and erythematous papules. Phototherapy resulted with healing of the erythematous papules, erosions and thinning of the yellow-orange plaques.

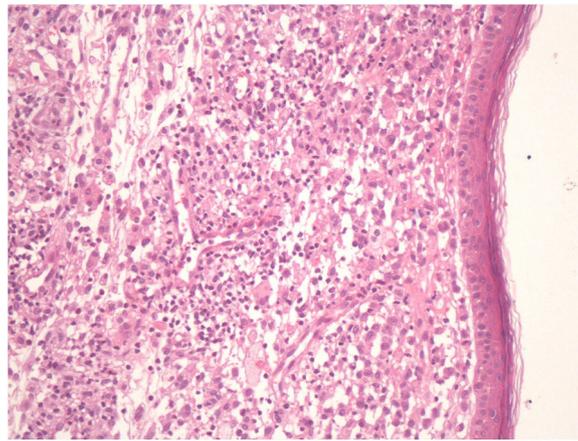


Fig. 2 Langerhans cells with an eosinophilic cytoplasm, grooved or lobular nucleus, histiocytes with abundant pale cytoplasm and lymphocytes in the dermis.

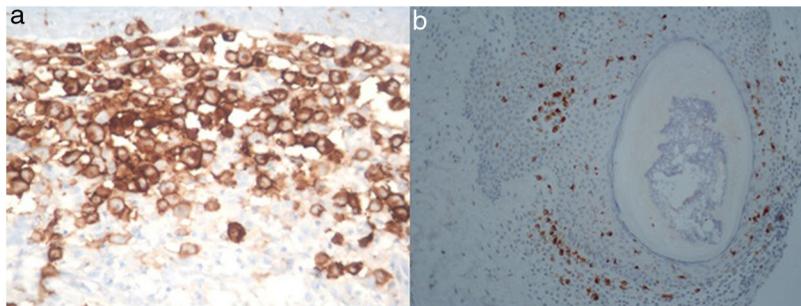


Fig. 3 Immunohistochemistry showed CD1a (3a) and CD207 (3b) expression by the cells with eosinophilic cytoplasm and grooved or lobular nucleus.

LCH may affect any organs and revised classification contains 4 subtypes of LCH depending on the number of organs or systems involved, lung involvement and involvement of risk organs (liver, spleen and bone marrow).⁴ Treatment recommendations are determined according severity of disease.¹ The treatments used include topical and systemic steroid treatment, phototherapy, topical nitrogen mustard, azathioprine and methotrexate.^{1,8} In our case erythematous papules, perilesional erythema and eroded areas resolved with PUVA treatment but the xanthoma-like plaques showed thinning.

LCH in adults is difficult to diagnose as it is rare and skin involvement can vary in appearance. Skin biopsy is significant to diagnose skin involvement. It can be the initial sign of multi-systemic LCH although the condition can rarely be limited to the skin. Close follow-up of adult-onset LCH patients with skin involvement is therefore essential in terms of future potential multi-organ involvement.

Conflict of interest

The authors declare that they have no conflict of interest.

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14 February 2018 12 June 2018

<https://doi.org/10.1016/j.adengl.2019.11.003>

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Familial Eruptive Pseudoangiomatosis: 2 Recurring Cases[☆]



Pseudoangiomatosis eruptiva familiar: 2 casos de presentación recurrente

To the Editor

Eruptive pseudoangiomatosis is an uncommon skin disease of unknown etiology that is increasingly reported in children. The condition may be preceded by a prodrome comprising fever and respiratory or gastrointestinal symptoms during the days before onset of the skin lesions. The rash is characterized by the appearance of multiple asymptomatic reddish-violaceous papular lesions that present with a specific peripheral whitish halo and that disappear on diascopy. The lesions are found mainly on areas exposed to sunlight and resolve spontaneously without residual marks after 10–15 days.

Histopathology usually reveals vascular dilatations with endothelial cells that project toward the vascular compart-

ment, together with a perivascular infiltrate and no signs of vasculitis, capillary proliferation, or extravasated erythrocytes. While not disease-specific, these histological findings are consistent with the diagnosis in a patient with a compatible clinical picture.

We report the case of a 7-year-old girl with no history of interest who was referred to our clinic with an episode of asymptomatic erythematous lesions that had appeared more than 1 week earlier. The lesions affected the face and arms. She had a 2-year history of similar outbreaks. These were self-limiting and had gradually increased in frequency from 3 episodes per year to 1 per month. The episodes were not preceded by systemic symptoms, and no clear triggers were identified.

The patient's grandmother, who was aged 55 years, had experienced similar episodes, with lesions in the form of self-limiting flares, from the fourth decade of life. The number of lesions increased gradually, and the episodes became more frequent (1–2 per month at the time of consultation). These were located on the face, arms, and thorax. The patient had a history of rheumatoid arthritis diagnosed at age 40 years (after onset of the symptoms) and had received treatment for infiltrating ductal carcinoma at age 53 years (tamoxifen, anti-inflammatory drugs, and low-dose prednisone). Neither of the patients had presented symptoms before onset of the rash or during the rash.

In both patients, examination revealed reddish-wine colored papules measuring 2–3 mm in diameter. Most were surrounded by a peripheral hypochromic halo and blanched on diascopy (Fig. 1). The girl's lesions were located mainly

[☆] Please cite this article as: García-Harana C, del Boz-González J, Padilla-España L, Rodríguez-Lobalzo S, de Troya-Martín M. Pseudoangiomatosis eruptiva familiar: 2 casos de presentación recurrente. *Actas Dermosifiliogr.* 2020;111:73–75.