

Case Report

Xanthoma disseminatum: report of one case

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Abstract: An 8-year-old female had generalized papules and nodules for more than 6 years. Urine routine, blood lipid level, and cranial CT were normal. Histopathology of the lesion revealed that it consisted of abundant short spindle-shaped and epithelioid cell proliferation with foam cells and Touton giant cells. On immunohistochemistry, cells were CD68, CD31, and Ki-67<3% positive but were non-reactive to CK-pan, CD1a, and S-100. Diagnosis: xanthoma disseminatum.

Keywords: Xanthoma disseminatum, differential diagnosis, treatment

Introduction

Xanthoma disseminatum (XD) is currently considered to be a rare benign manifestation of non-Langerhans cell histiocytosis (NLCH). It is reported that the population infected with XD is between 5 months and 70 years old, most of whom are younger than 25 years old [1]. The main manifestation is the yellow-brown papule nodules that are symmetrically distributed on the face, trunk, and limb folds. Herein, we report a case of XD treated by us.

Report of a case

Child female, 8 years old. Onset was around 1 year old. Many small papules and nodules on the trunk and limbs. At the age of 5, generalized papules and nodules appeared on the whole of the body. She underwent partial resection of large skin lesions in other hospitals and took oral Chinese medicine for 1 year. After treatment failed she came to our hospital.

The child is 8 years old. Generalized papules and nodules occurred in batches and were distributed all over the body without visceral involvement. At present, oral Chinese medicine has been discontinued. The child and her sister were identical twins, but her twin sister did not have similar symptoms. There was no eating of

a high fat diet. None of the family members had hyperlipidemia.

Physical examination: no obvious abnormality was found in the system examination. Dermatological examination: papules and nodules of different sizes distributed on the trunk and limbs, with a diameter of about 0.5-1.3 cm which were higher than the skin surface. Multiple yellowish-brown papules and nodules were scattered on the neck. Multiple symmetrical yellowish-brown papules were scattered on the axilla and hip. Multiple yellow papules and nodules were scattered on the perianal area and medial thighs. The rashes were no tenderness and no discoloration. The skin between rashes was normal (**Figure 1A-C**). The skin of her twin sister was normal (**Figure 2**).

Laboratory and auxiliary examinations: blood and urine routine examination, liver and kidney function, blood lipid and blood glucose, cranial CT, chest X-ray, abdominal color doppler ultrasound, and other examinations were normal. One piece of skin tissue from the right waist band was taken. Histopathology showed that the lesion was composed of abundant spindle and epithelioid cells with foam cells and Touton giant cells (see **Figure 3**). On immunohistochemistry, CD68, CD31, and Ki-67<3% were positive, but CK-pan, CD1a, and S-100 were

A case of xanthoma disseminatum

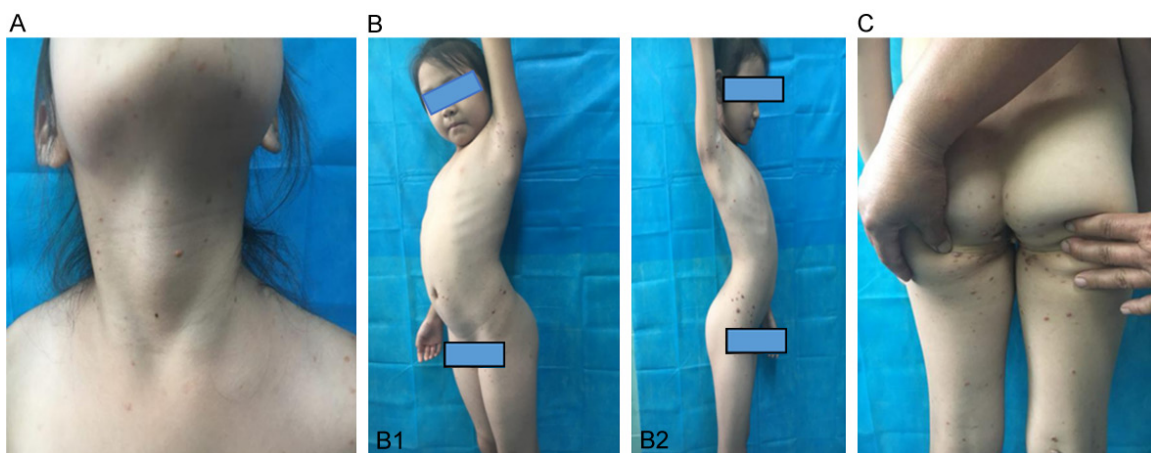


Figure 1. A. Multiple yellowish-brown papules and nodules were scattered on the neck. B. Multiple symmetrical yellowish-brown papules were scattered on the axilla and hip. C. Multiple yellow papules and nodules were scattered on the perianal area and medial thighs.

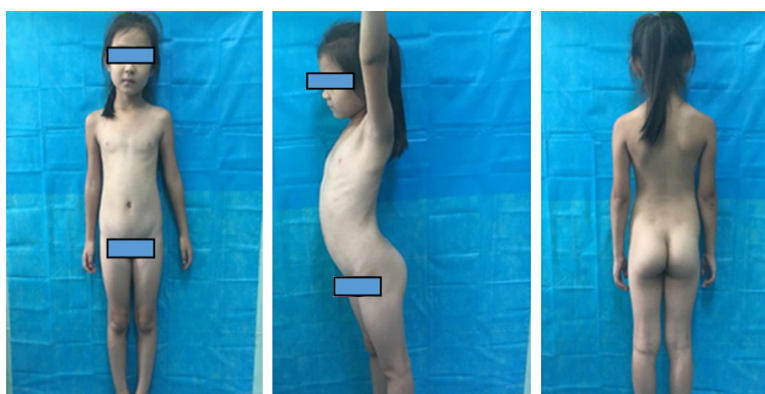


Figure 2. Pictures of the twin sister. The skin was normal.

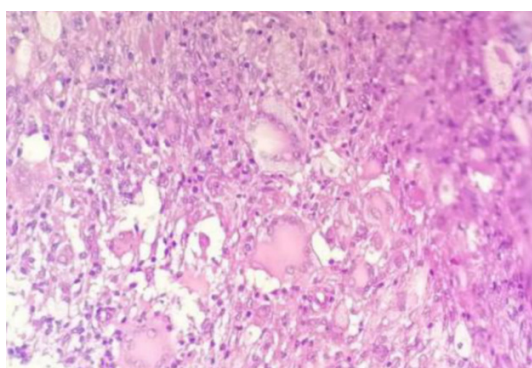


Figure 3. At high magnification, there were many Touton giant cells, foam cells, and eosinophils (H&E, 200 \times).

negative (see **Figure 4**). Xanthoma disseminatum (XD) was diagnosed by pathology combined with clinical considerations.

This case of cutaneous xanthoma disseminatum has not been associated with diabetes insipidus, laryngeal mucosal involvement, or occult diabetes mellitus, but should be closely followed up in the future.

Discussion

Xanthoma disseminatum, also known as Montgomery syndrome, is a rare non-Langerhans cell-derived benign histiocytosis disease with unknown etiology. The disease occurs most frequently in men, ranging in age from 8 months to 85 years, but 60% of patients develop the disease before the age of 25 years [2]. At present, there have been no reports of similar cases of twins. One twin has been sick since childhood and the other is normal, which deserves further study. The common triple clinical manifestations of typical patients are cutaneous xanthoma, mucosal xanthoma and diabetes insipidus. Cutaneous xanthoma usually occurs in the wrinkles of the face and the proximal extremities, such as groin, axilla, neck, elbow fossa, popliteal fossa, and so on. It is characterized by extensive yellow, brown-yellow papules or nodules, initially scattered, and then flaky. About 40%-50% of the patients had mucosal lesions, including oral, nasopharyngeal, respiratory, anal, or conjunctiva. About 50% of patients complicated

A case of xanthoma disseminatum

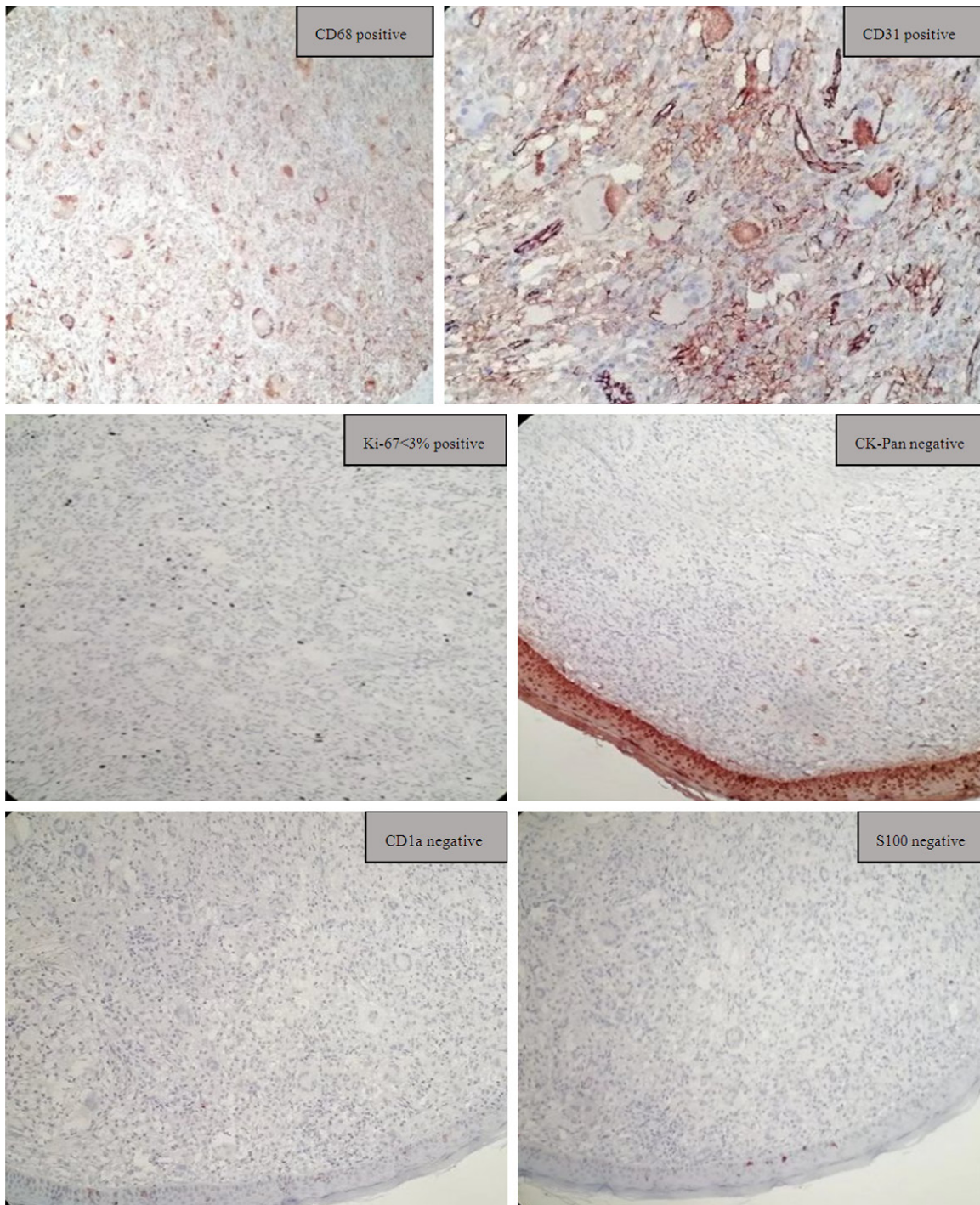


Figure 4. Immunohistochemical staining of the waist skin lesions (SP, 200×).

with diabetes insipidus, clinical manifestations of polydipsia and polyuria, but the symptoms are mild and mostly temporary, can be relieved with the disappearance of skin lesions [3]. Blood lipid levels are more normal and some patients have cholesterol elevation. By histopa-

thology, dense mononuclear cells and polynuclear cells can be seen in the dermis. In the early stage, a large number of tissue cells in the dermis accompanied by a small number of lymphocytes and eosinophils can be seen. In the mature stage, foamy tissue cells and Touton

giant cells can be seen, accompanied by lymphocytes, plasma cells, and eosinophils.

In this case, the onset of the disease at a young age was as follows: the rash was manifested as multiple yellow-brown papules and nodules of varying sizes in the trunk and limbs, with advanced progression and no abnormal blood lipids. Histopathology revealed that the lesion was composed of abundant short spindle and epithelioid cell hyperplasia with foam cells and Touton giant cells. Immunohistochemistry showed that CD68, CD31, Ki-67<3% (+), CK-Pan, CD1a, and S100 (-) combined with clinical manifestations and histopathology, result in a clear diagnosis of xanthoma disseminatum. This disease needs to be differentiated from juvenile xanthogranuloma, progressive nodular histiocytoma, generalized eruptive histiocytoma, multicentric reticular histiocytosis, and eruptive xanthoma. ① The most similar to this disease is juvenile xanthogranuloma (JXG), which occurs in people more than 2 years old. Skin lesions exist independently. Generally, these lesions can disappear completely in 3-6 years. They are self-limited and rarely involve mucosa with diabetes insipidus. The two are usually indistinguishable in histopathology [4]. ② Progressive nodular histiocytoma is characterized by progressive development of brown-yellow papules or lilac nodules on the face, trunk, and limbs. It is asymmetrically distributed, solid and round, disseminated but not fused, and most of the wrinkles and joints are not involved. Histologically, foam cells are seen in superficial skin rashes. Nodular rash is characterized by diffuse infiltration of histiocytes and multinucleated giant cells with spindle-shaped "storiform" distribution in the deep dermis [5]. In this case, the rash was mainly distributed in the folds and distributed symmetrically. Combined with biopsy, the disease can be excluded. ③ Generalized eruptive histiocytoma is more common in adults and the rash is more common in the proximal trunk and extremities, presenting as a symmetrical distribution of bright red papules with self-limitation. Histopathologically, there are no Touton giant cells and a large number of tissue cells and a small number of lymphocytes infiltrated the dermis. It can be excluded by clinical manifestations and histopathology. ④ Multicentric reticular histiocytosis is more common in adults, mostly in females, and is often accompanied by

joint lesions. The skin lesions are mainly papules and nodules, which are hard and brown-red or yellowish. Typical pathological manifestations are infiltrations of histiocytes and multinucleated giant cells, and the cytoplasm of multinucleated giant cells is "frosted glass". ⑤ Eruptive xanthoma usually occurs on the upper trunk, buttocks, and extensions of limbs, and can involve lips and oral mucosa. It can quickly fade away without leaving any trace. Most of them were accompanied by hyperlipoproteinemia. The patient has a long course of disease, progressive development, and normal blood lipids, which can exclude eruptive xanthoma.

According to natural course and outcome, XD was divided into three clinical types by Caputo [6]: ① lasting existence (the most common and the most stable); ② self-healing (rare); ③ progressive development with organ dysfunction (rare). The treatment of this disease is difficult and there is no satisfactory treatment at present. Surgical resection, laser, freezing, or electrocautery can improve the local appearance, but cannot control the development of the disease [7]. Various treatments which can improve the condition have been reported in the literature, including glucocorticoid, compound betamethasone, cyclophosphamide, vincristine, azathioprine, methotrexate, and antimalarial drugs. Kang L et al. [8] reported that 3 cases of cladribine successfully treated progressive xanthoma disseminatum, the skin lesions of the patients were significantly improved. Follow-up after withdrawal of the drug showed that the skin lesions and mucosa were further improved; and diabetes insipidus could also be improved. Sawatkar et al. [9] reported that imatinib can treat XD safely and effectively. The treatment of xanthoma disseminatum deserves further study and exploration.

Acknowledgements

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and with the national research committee and with the Helsinki declaration and its later amendments or comparable ethical standards. The study was performed according to the Declaration of Helsinki and was approved by the ethics committee of the Second Affiliated

Hospital of Shandong First Medical University. Written informed consents were obtained from all the subjects recruited into our study.

Disclosure of conflict of interest

None.

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