Original Article

Solitary juvenile xanthogranuloma with tibial involvement: a case report

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Abstract: Juvenile xanthogranuloma (JXG) is a rare disease that is part of a spectrum of histiocytic dendritic cell disorders. Most patients present with a solitary cutaneous lesion; however, others present with extracutaneous manifestations or even with systemic involvement. We present the first report of an 11-month-old girl in whom was diagnosed a unifocal extracutaneous JXG involving the tibia. Histological and immunohistochemical staining results are presented. A review of the literature on these unusual lesions is conducted, along with discussion of their differential diagnosis and key aspects of the patient’s evaluation, management, and pathological diagnosis.

Keywords: Juvenile xanthogranuloma, Langerhans cell histiocytosis, tibia

Introduction

Juvenile xanthogranuloma is typically a benign, self-limited histiocytic disorder of infancy and early childhood manifesting as single or multiple cutaneous lesions [1-3]. The first report documenting single, and occasionally multiple, cutaneous lesions occurring in infants and showing spontaneous involution was written by Adamson in 1905 [4]. In 1954 Helwig and Hackney proposed the name “juvenile xanthogranuloma” to define cutaneous lesions that arise from fibrohistiocytes [5]. Extracutaneous manifestations of JXG without systemic involvement are uncommon, and isolated JXG involving the tibia is extremely rare [6]. There have been only one report documenting tibia involvement by JXG [7]. Here, we report an 11-month-old patient who presented with a large mass eroding the left tibia, which to the best of our knowledge is the first solitary JXG case in the left tibia, and make a systematic review about the relevant literatures. The clinical and radiological presentations as well as our management strategy in this unique case are discussed.

Case report

History and examination

An 11-month-old girl was presented to our hospital due to more than 5 months of straight ten complication obstacle of left low limb. The child had left lower limb curled up with obvious pain and excessive cry since trauma about 5 months ago. X-ray examination from other hospital showed lesions in left proximal tibia, suggesting suspicious aneurysmal bone cyst or osteosarcoma. The child was undergone bone biopsy for left proximal tibia in other hospital, and was diagnosed as atypical Langerhans cells histiocytosis and suspicious osteoclastoma. The child was discharged without special treatment, and admitted to our hospital for further treatment. Physical examination at admission: no rash, subcutaneous bleeding or nodules, or scar was seen; the left lower limb was flexed inward; there was swelling and deformity in the left upper and middle tibia, with smooth surface and unclear boundary; there was no drainage, abscess, or rupture; there was no fluctuation; the surface skin temperature was normal; there was tenderness and bone friction feeling in the lesion site, which was inactive. The adjacent joints were of flexibility, without abnormal activities. And no obvious abnormality was examined in the rest limbs. Blood routine examination showed leucocyte of 5.37×10⁹/L, eosinolhs of 0.06×10⁹/L, platelet normal of 403×10⁹/L, alkaline phosphatase of 94 U/L; and the kidney function was normal.
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Figure 1. FDG PET scan shows an intensely metabolically active soft tissue mass in the left leg (arrows).

Radiological studies

Whole body PET-CT (Figure 1) showed no lesions in other parts of the body. Anteroposterior and lateral X-ray film of the left tibiofibula showed bone destruction at upper tibia. Plain CT scan (Figure 2) and 3D deconstruction of the special part in left lower limb (Figure 3) showed patchy dissolved bone destruction area in the upper segment of left tibia, and no hardness was seen in lesions edge bone. Density of crumb soft tissue was seen in destruction area. Part of the soft tissue was protruded into the surrounding soft tissue, where watery density was seen, with CT value of 39.4 Hu; B ultrasound at left tibia suggested low echo of 4.8×4.3×3.9 cm with unclear boundary and irregular form in left upper and middle tibia.

Treatment

Currently, there is no standard treatment for JXG, we gave the child the chemotherapy (1.2 mg of vindesine, 5 mg of prednisone, tid) with regard to Langerhans cells histiocytosis. The mass was once decreased and the child was in condition so she discharged. But 2 months later, her parents found that the mass in the left proximal tibia was increased, though the child did not fell obvious pain or numb in toes. We hence decided to give the child osteotomy and bone grafting (artificial bone) on the right fibula, lesion curettage and bone grafting (right fibula and artificial bone) on the left tibia, Kirschner wire internal fixation, plaster external fixation on the both lower limbs (Figure 4). A yellowish gray subcutaneous mass with the size of 5×4×3.5 cm was seen during the operation. The child was well recovered and discharged one week after operation. The child was visited twice after operation, and was closely followed up for 6 months. The child was well recovered, and no signs of relapse were seen (Figure 6).

Pathology

Pathological examination on surgically removed specimen: HE staining mainly showed histocyte-like cells; few of them were swelled, with small nucleoli; multinucleated giant cells (Touton cell) were distributed between them; small patchy of foamy cells can be seen but no obvious eosinophils or other white cells (Figure 7). Immunohistochemical staining showed that the tumor cells were CD68 (+), S-100 (scattered +), CD1a (-), CD4 (+), CD38 is (+), CD21 (-). Both the morphologic and immunophenotypic features were compatible with a diagnosis of JXG.

Discussion

JXG was first reported by Adamson [4]. It is a rare lesion of non-Langerhans cell histiocytosis [8], which is mostly common in infants and children’s skin. Children younger than 6 months with JXG often appear multiple rash in the head and neck, characterized by scattered red and yellow dome-like papules and nodules. For cutaneous JXG, only skin rather than other system is involved. For systemic JXG, rash can be present or not, and organs beyond skin may be involved, especially the eyes [9]. Iris is the most common affected, which may cause symptoms such as glaucoma and anterior chamber bleeding. It can affect the liver, spleen, lung, brain and other organs, with higher mortality. It can also affect the heart, retroperitoneum, nervous system, ovaries, adrenal gland, and bone. Most of the JXG that involves bone is a systemic disease, in which only one case is reported involving the tibia [7]. With no rash present, a whole body PET-CT (Figure 1) shows no lesions in other part of the body in this case. It is a rare isolated lesion in the tibial shaft (Figure 2). To our knowledge, this was the first case reported in English literatures.

Histologically, diffuse invasion of a large amount of tissue cells accompanied with a small
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Figure 2. Preoperative CT scan showed a large mass with osteolytic defect in the left tibia. A-F. Axial View. G, H. Transverse View.
Figure 3. Preoperative three-dimensional reconstruction of CT scan demonstrated bone destruction of the left tibia.
amount of lymphocytes and eosinophils can be seen in the skin in the early stage of JXG. Some tissue cells have light and hollow cytoplasm, and the nucleus is small in round or ovoid shape without atypia. In some cells, the nuclear groove and an unclear nucleus can be seen, which are often absent in Touton cells. Invasion of foam cells, foreign body giant cells and Touton giant cells can be seen in mature stage. The nucleus of Touton cell is garland-like, which is the typical characteristic for juvenile xanthogranuloma. A lot of fibroblasts are visible at the late stage, and fibrosis replaces the infiltration. JXG lesions beyond skin have different histological characteristics with JXG occurred in the skin, which are easy to be confused with Langerhans cell histiocytosis (LCH) [10]. Microscopically, the tumor cells are rich in cytoplasm, which is light and eosinophilic or fine granular-like. The nucleoli are round or kidney-shaped. Most of the cells are mononuclear, and some can see two or three unclear nucleoli. The number of Touton cells is obviously reduced than skin JXG lesions or even missing, and inflammatory cells are also rare. The differential diagnosis relies on immunohistochemical study: JXG expresses CD68, lysozyme and FXIIIa, but not CD1a; LCH expresses S-100 protein and CD1a, but not CD68, lysozyme and FXIIIa. CD1a is a relatively specific marker for LCH, which is not expressed in non-LCH diseases. Birbeck granules found under electron microscope are LCH [11]. In this case, the immunohistochemical results were CD68 (+), CD4 (+), CD38 (scattered +), S-100 (scattered +), CD1a (-), CD21 (-). These are in consistent with JXG characteristics. But there is one reported case [12] that the patients

Figure 4. Postoperative X-ray examination. A. left leg; B. right leg; C. lower limbs.

Figure 5. Postoperative X-ray 1 month after surgery showed Callus formation (arrows) and no residue or recurrence of the tumor. A. left leg; B. right leg.
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developed LCH at first and recovered after treatment but appeared JXG after a year and a half, suggesting that there is a relationship between these two kinds of disease, or they are the different stages of the same disease [13]. Typical X-ray characteristics of osteoclastoma of bone in long bone show eccentricity in bone end, osteolysis, dilatable bone destruction, and soap bubble changes. Besides multinucleated giant cell, polygon, ovoid, round or spindle mononuclear cells are visible in pathological examination. Lysozyme and CD68 can be expressed, while S-100 and NSE are not expressed [14]. Elevated alkaline phosphatase is detected in serological examination. In this case, the serum alkaline phosphatase is normal. Xanthoma histological characteristics are given priority to hyperplastic foamy tissue cells, most of which are multinucleated giant cells. Extracellular cholesterol crystal deposition is visible [15].

JXG is a benign hyperplastic disease, which is a self-limited disease. Most of the skin lesions can be faded and stabled within a few years, and can be removed when necessary [1]. Systemic JXG affects multiple organs, with signs of malignant tumor. For severe cases, it can be life-threatening [16]. Janssen et al., through calculation on cloning ratio of Humara gene and DNA of JXG lesions, proved that JXG was a proliferation of clone cells. It is a kind of cloned hyperplasia of tissue cells or dendritic cells like LCH. This provides the theory support for the treatment of JXG. There is the report on systemic JXG which has obvious curative effect by the treatment for LCH [17]. So for systemic JXG, the treatment for LCH can be referenced. Once diagnosed as systemic JXG, the involvement of the patients needed to be evaluated, at the same time, the related inspection of the malignant tumor should be improved. This case is the JXG occurs in the tibial shaft beyond the skin. No organ is involved in whole body PET-CT (Figure 4). The child was given preoperative chemotherapy (1.2 mg of vindesine, 5 mg of prednisone, tid) based on treatment for LCH. The mass was once decreased and the child was in condition so she discharged. But 2 months later, the mass was increased again. She was transferred to surgical treatment. The child was given lesion curettage, osteotomy and bone grafting (artificial bone) on the right fibula, lesion curettage and bone grafting (right fibula

Figure 6. Postoperative X-ray 5 months after surgery showed Callus formation (arrows) and no residue or recurrence of the tumor. A. left leg; B. right leg; C. lower limbs.

Figure 7. Monomorphic histiocytic cells with characteristic admixed eosinophils, Touton giant cells (arrows), and cells with intracytoplasmic microvesicular lipid, no prominent cytological atypia or mitotic figures were identified (H&E, original magnification ×200).
and artificial bone) on the left tibia, Kirschner wire internal fixation, plaster external fixation on the double lower limbs (Figure 4). The child was good in general condition without recurrence at the review of 5 month postoperatively (Figure 6), and the curative effect was satisfied. The child was closely followed up for 16 months. No residual lesions or relapse were seen.

In conclusion, juvenile xanthogranuloma is a rare type of hyperplastic diseases of non-Langerhans histiocytes. It is mainly differentially diagnosed with Langerhans cells histiocytosis. The lesion affecting bone is relatively rare, which needs to be identified with tumor diseases. Surgical removal and additional chemotherapy is an effective method for treatment of isolated or localized lesions, and the prognosis is good.

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Disclosure of conflict of interest

None.

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