Giant Juvenile Xanthogranuloma Co-Occurring with Langerhans Cell Histiocytosis

A 7-year-old, male, Japanese patient with autism spectrum disorder presented with a soft tissue mass located in the left center of his back. According to his family, the mass had grown progressively from 1 year prior to presentation from a cutaneous nodule which was present at birth. A physical examination revealed a pedunculated, multinodular mass with surface ulceration (Figure 1). Magnetic resonance imaging demonstrated a lobulated, solid tumor with heterogeneous signal intensity, suggesting internal necrosis and hemorrhage. The tumor had low T2 signal intensity, hyperintensity on diffusion-weighted sequence, and a low apparent diffusion coefficient (mean apparent diffusion coefficient value 0.7×10^{-3} mm^2/s). After antibiotic treatment for cellulitis, which caused a transient fever and increased exudates from the lesion, complete resection of the mass was performed. The resected mass measured $7.5 \times 7 \times 4$ cm and weighed 102.4 g. Histopathological analysis revealed diffuse infiltration of the skin by foam cells and Touton-like multinucleated giant cells as well as inflammatory cells, including lymphocytes and eosinophils (Figure 2). Immunohistochemistry revealed pathognomonic cells in the dermis which were CD68 and CD163-positive and CD1a, S-100, and Langerin-negative. However, a small population of medium-sized, CD68 and CD163-negative, CD1a, S-100, and Langerin-positive histiocytes with an irregular, notched nucleus was observed. Based on these findings, juvenile xanthogranuloma (JXG) with small foci of Langerhans cells was diagnosed. Whole body computed tomography ruled out metastasis, and no recurrence was observed for 1 year after surgical resection.

JXG is the most common form of non-Langerhans cell histiocytosis and usually occurs in infants younger than the age of 1 year.[1,2] Giant JXG, defined as a lesion larger than 2.0 cm, is rare within the JXG subgroup.[3] Although the majority of solitary, cutaneous lesions in JXG demonstrate spontaneous regression, total surgical excision is recommended in cases of growing, soft tissue masses in which malignancy cannot be ruled out.[4] In fact, a retrospective review of giant JXG cases revealed that 60% of patients underwent surgical resection.[3] In our case, the lack of spontaneous regression by the age of 7 years and the risk of the lesion becoming a source of infection prompted the choice of surgical excision.

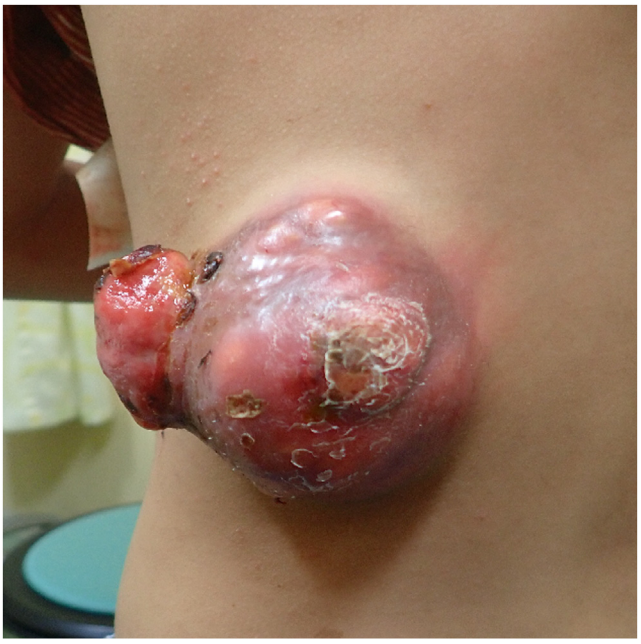

Figure 1. Pedunculated, multinodular mass with surface ulceration before resection.

Several previous studies have described JXG co-occurring with Langerhans cell histiocytosis (LCH), including cases in which 1 preceded the development of the other.[5,6] Changes in phenotype observed after chemotherapy suggest that a different cytokine environment may modulate the final cell fate.[7] These findings support the hypothesis of the existence of a common cell precursor of these 2 histiocytoses, both of which develop as a consequence of misdirected differentiation programs in myeloid dendritic cell precursors.[8] Although our patient did not have a history of chemotherapy, changes in environmental factors modulating the cytokine profile within the tumor or additional genetic/epigenetic events may have resulted in a mixed phenotype and tumor enlargement.[9] In previous cases of co-occurring LCH and JXG, the presence of multiple lesions or systemic involvement prompted systemic therapy. However, in the present case, the localization of the nodule and the absence of an extracutaneous lesion enabled complete resection and led to a favorable outcome without systemic therapy, as with localized LCH.

In summary, we presented a rare case of giant JXG co-occurring with LCH. Complete surgical resection should be attempted for a histopathological diagnosis and as definitive therapy for this type of rapidly growing, pediatric tumor. ■

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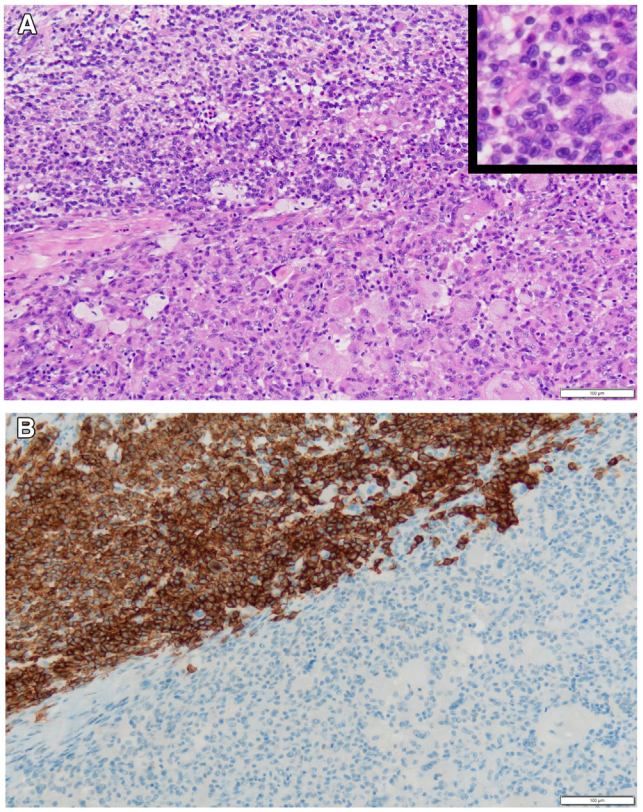

Figure 2. **A,** Foam cells and Touton-like giant cells were observed. The inset shows Langerhans cells with an irregular, notched nucleus. **B,** Small foci of Langerhans cells were observed. (**A,** Hematoxylin-eosin staining, × 200; **B,** CD1a staining, × 200).

Data Statement

Data sharing statement available at www.jpeds.com.

Declaration of Competing Interest

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Hiroshi Hayashi, MD
Department of Hematology/Oncology
Tokyo Metropolitan Children's Medical Center
Tokyo, Japan

Atsushi Makimoto, MD, PhD
Department of Hematology/Oncology
Tokyo Metropolitan Children's Medical Center
Tokyo, Japan
Department of Laboratory Medicine
Tokyo Metropolitan Children's Medical Center
Tokyo, Japan

Kentaro Matsuoka, MD, PhD
Department of Laboratory Medicine
Tokyo Metropolitan Children's Medical Center
Tokyo, Japan

References

1. Weitzman S, Jaffe R. Uncommon histiocytic disorders: the non-langerhans cell histiocytoses. Pediatr Blood Cancer 2005;45:256-64.
2. Hernandez-Martin A, Baselga E, Drolet BA, Esterly NB. Juvenile xanthogranuloma. J Am Acad Dermatol 1997;36:355-67: quiz 368-359.
3. Ladha MA, Haber RM. Giant juvenile xanthogranuloma: case report, literature review, and algorithm for classification. J Cutan Med Surg 2018;22:488-94.
4. Cypel TK, Zuker RM. Juvenile xanthogranuloma: case report and review of the literature. Can J Plast Surg 2008;16:175-7.
5. Yu H, Kong J, Gu Y, Ling B, Xi Z, Yao Z. A child with coexistent juvenile xanthogranuloma and Langerhans cell histiocytosis. J Am Acad Dermatol 2010;62:329-32.
6. Martín JM, Jordá E, Martín-Gorgojo A, Beteta G, Monteagudo C. Histiocytosis with mixed cell populations. J Cutan Pathol 2016;43:456-60.
7. Strehl JD, Stachel K-D, Hartmann A, Agaimy A. Juvenile xanthogranuloma developing after treatment of Langerhans cell histiocytosis: case report and literature review. Int J Clin Exp Patho 2012;5:720-5.
8. Berres M-L, Allen CE, Merad M. Chapter five pathological consequence of misguided dendritic cell differentiation in histiocytic diseases. Adv Immunol 2013;120:127-61.
9. Allen CE, Parsons DW. Biological and clinical significance of somatic mutations in Langerhans cell histiocytosis and related histiocytic neoplastic disorders. Hematology 2015;2015:559-64.