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Letters to the Editor, Case letters

Urticarial vasculitis and subcutaneous nodes in the extremities seen in a patient with mucopolysaccharidosis II after hematopoietic stem cell therapy

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Editor

Mucopolysaccharidosis II (MPSII, Hunter syndrome; OMIM 309900) is a rare X-linked recessive lysosomal storage disorder caused by a deficiency of the enzyme iduronate-2-sulfatase (I2S) that leads to the accumulation of glycosaminoglycans (GAGs) within lysosomes throughout the body[1-3]. Hematopoietic stem cell therapy (HSCT) has been indicated for MPSII as a part of standard care [4, 5]. We report a case of MPSII with urticarial vasculitis and subcutaneous nodes in the extremities, in whom GAG accumulation had remained after HSCT.

A 10-year-old boy was referred with urticaria. He had been diagnosed with MPSII from a deficiency in urea I2S activity at the age of 10 months, and enzyme replacement therapy (ERT) had been initiated. He had received HSCT at the age of 2 and ERT was discontinued. However, ERT was resumed due to progressive abnormalities of the craniofacial bones until the age of 9, when no further progress of these symptoms was observed. 6 months after ERT was discontinued, urticarial erythema (Figure 1a) and gonitis with lameness appeared, although pebbly-appearing papules did not appear. Histopathologically, an urticarial erythema on the upper arm showed neutrophil infiltration with nuclear debris around the blood vessels in the superficial and middle dermis (Figure 1c). We diagnosed the erythema as urticarial vasculitis. The erythema improved after the oral administration of epinastine. The gonitis with lameness persisted. We administered prednisolone at 10 mg/day. The gonitis improved, and we tapered and then ceased the oral prednisolone 2 weeks later. Thereafter, a subcutaneous node appeared on the left knee (Figure 1b). A skin biopsy specimen revealed that collagen fibers were disconnected in the subcutaneous node and colloidal iron-positive material was deposited between the disrupted collagen bundles (Figure 1d, e). Electron microscopic observations revealed vacuoles containing flocculent material and ones containing granular or laminated dense bodies in the cytoplasm of fibroblasts in the subcutaneous node (Figure 1f) and in the normal-appearing skin. These vacuoles were more prominent in fibroblasts infiltrating the node on the knee than in the normal-appearing skin. The node on the knee regressed

spontaneously, but similar nodes appeared repeatedly on areas subject to pressure, such as the knees and the elbows.

To the best of our knowledge, there have been no reports of any MPSII patients with urticarial vasculitis or electron microscopic detection of GAG accumulation in a patient's tissue after HSCT. We ultrastructurally confirmed GAG accumulation in the lysosomes of the fibroblasts in the subcutaneous node and the normal-appearing skin of the patient. We speculate that insufficient enzyme activity after HSCT induced the accumulation of GAG in the patient's tissues, including the skin and joints, resulting in nodes on the extremities, and that the nodes regressed spontaneously due to the removal of GAG deposition by residual enzyme activity. The lysosomal dysfunction in neutrophils possibly led to neutrophil activation and resulted in urticarial erythema. The present case suggests that electron microscopic observations of the skin might give us a clue to know the precise timing to restart ERT in patients who have already undergone HSCT treatment.

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Figure legends

Figure 1. Clinical, histopathological and ultrastructural features of the present case.

(a) Urticarial erythema on the upper arm at the patient's initial visit.

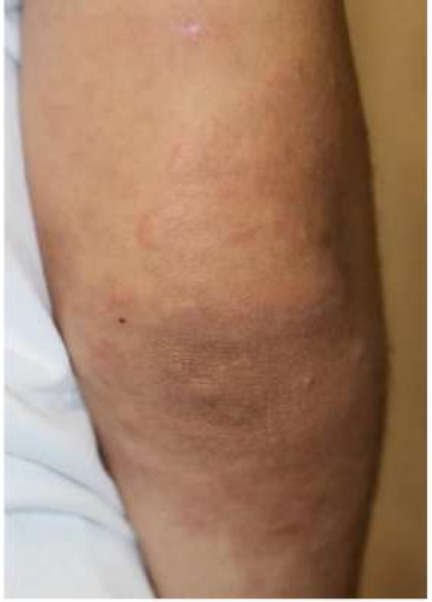
(b) A subcutaneous node (indicated with black dots) appeared on the left knee after the urticarial eruption improved.

(c) Neutrophil infiltration with nuclear debris around the blood vessels in the superficial and middle dermis of the urticarial erythema on the knee (hematoxylin-eosin [HE], original magnification × 400).

(d) Collagen bundles are disconnected in the subcutaneous node (HE, original magnification × 400).

(e) The deposition of colloidal iron-positive material is seen in the space between the disconnected collagen fibers (colloidal iron stain, original magnification × 400).

(f) Ultrastructurally, lysosomes containing granular or laminated dense bodies (arrowheads) and vacuoles containing flocculent material (arrows) are seen in the cytoplasm of fibroblasts in the subcutaneous node on the knee. Scale bar: 1 μm.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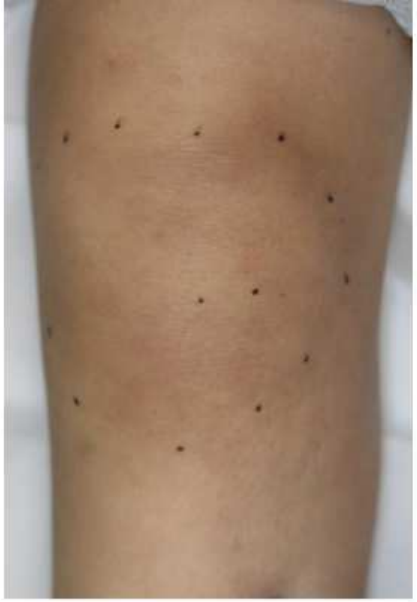
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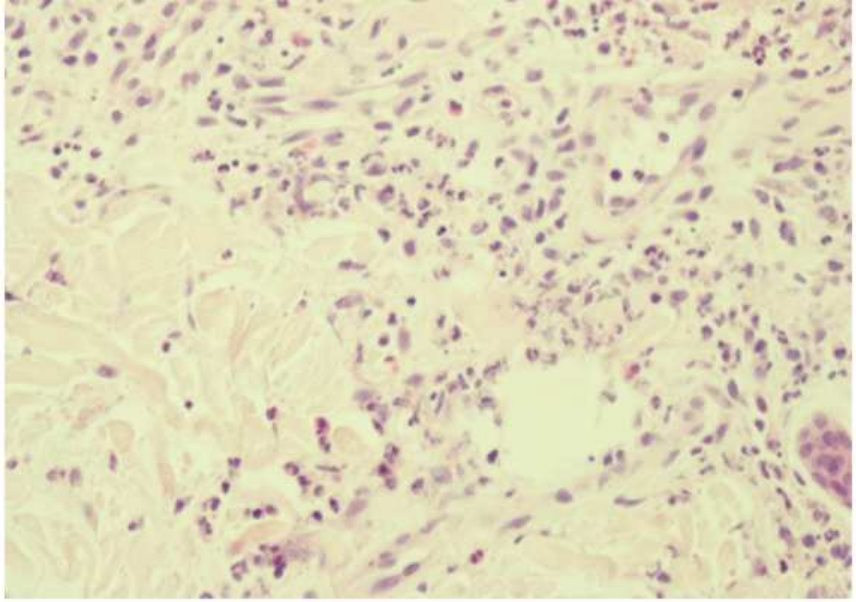
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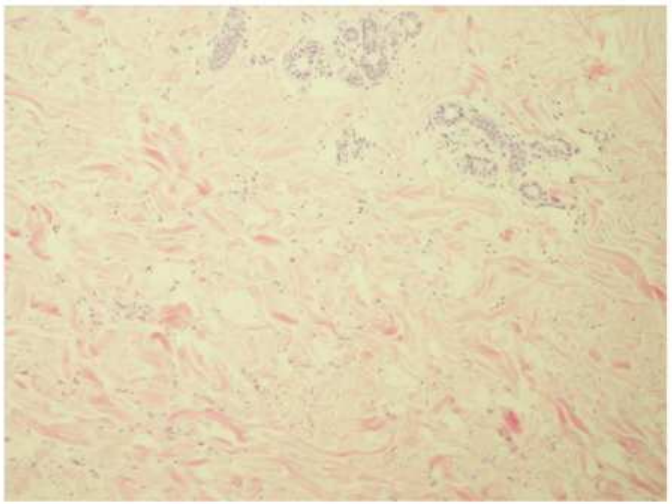
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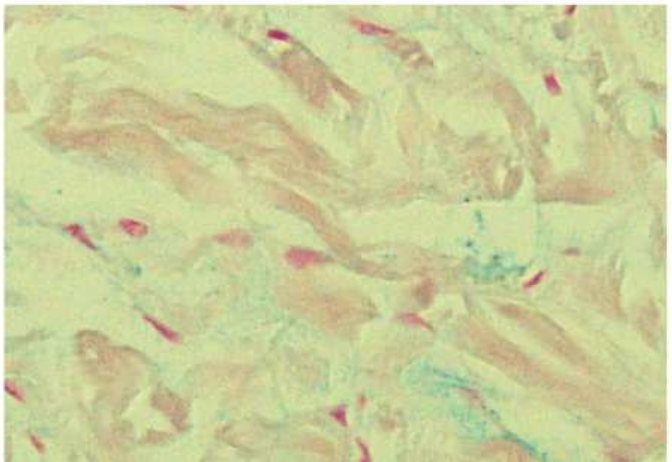
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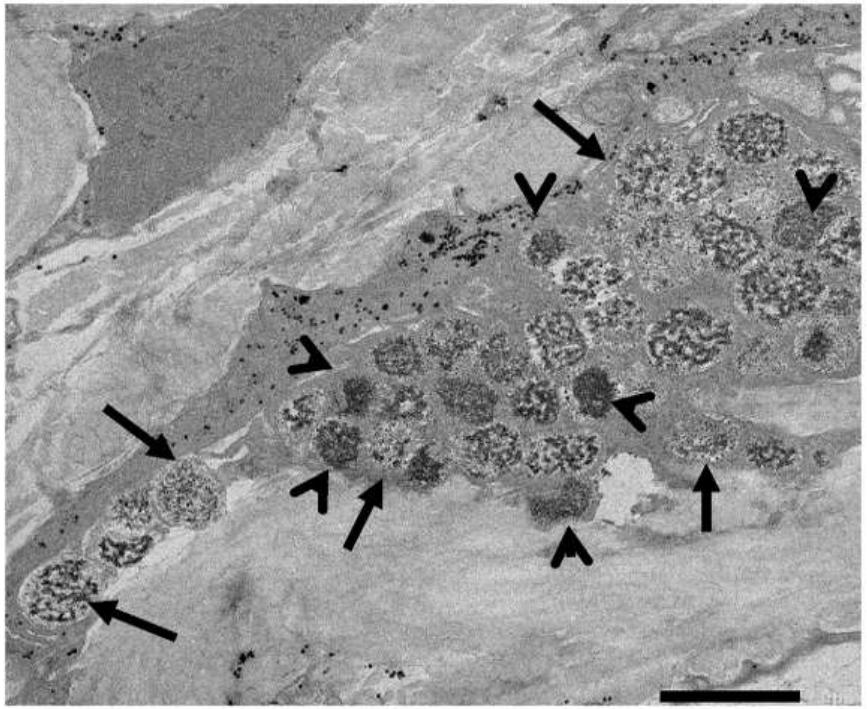
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