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Hunter Syndrome with Extensive Mongolian Spots

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Dear Editor:

Hunter syndrome is an X-linked disorder of lysosomal iduronate-2-sulfatase deficiency, generally presenting with cardiac disease, joint contracture, recurrent respiratory infection, and various degrees of central nervous system involvement[1]. Yet, diagnosis of the mild form of Hunter syndrome tends to be delayed because these specific abnormalities are sometimes not observed[1]. Cutaneous manifestations of Hunter syndrome can be very important early diagnostic clues. The most frequent lesions are firm ivory-white papules in symmetrical areas, but extensive Mongolian spots have been reported only in a few patients[2,3].

A 4-year-old boy presented with an 8-month history of pebbly papules on the trunk and upper arms and multiple round- to oval-shaped patches of blue-gray hyperpigmentation on the back since birth (Fig. 1A～C). He had relatively normal intelligence but a speech delay. On physical examination, coarse facial features, flattened nasal bridge, and shortened neck were observed (Fig. 1D). Also, he had a slightly limited range of motion in his elbow, knee and shoulder joints. Echocardiography showed moderate eccentric mitral regurgitation, and hepatosplenomagaly was revealed by an abdominal computed tomography. Biopsy of an ivory-colored papule showed loosely arranged collagen fibers and mucin accumulation compared to normal tissue (Fig. 2). Laboratory findings showed deficiency in peripheral blood lymphocytes iduronate-2-sulfatase activity. Based on these clinicopathological findings, Hunter syndrome was diagnosed. The patient was treated with enzyme replacement therapy (ERT) using idursulfase for 8 months. After ERT, improvement in papular cutaneous lesions, serial cardiopulmonary exercise testing and reduction of urinary excretion of glycosaminoglycans were observed.

Only 13% of patients with Hunter syndrome show asymptomatic, ivory-colored papules and nodules that coalesce to form ridges in a reticular pattern ("pebbling" of the

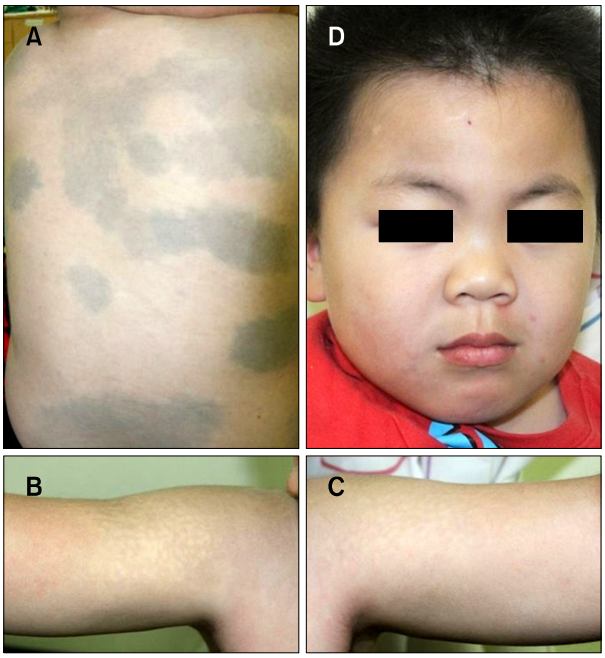

Fig. 1. (A) Extensive round and oval patches of blue-gray hyperpigmentation on the back. (B, C) Numerous firm, ivory-colored papules with a pebbly appearance on both arms. (D) A coarse face, flattened nasal bridge, and shortened neck.

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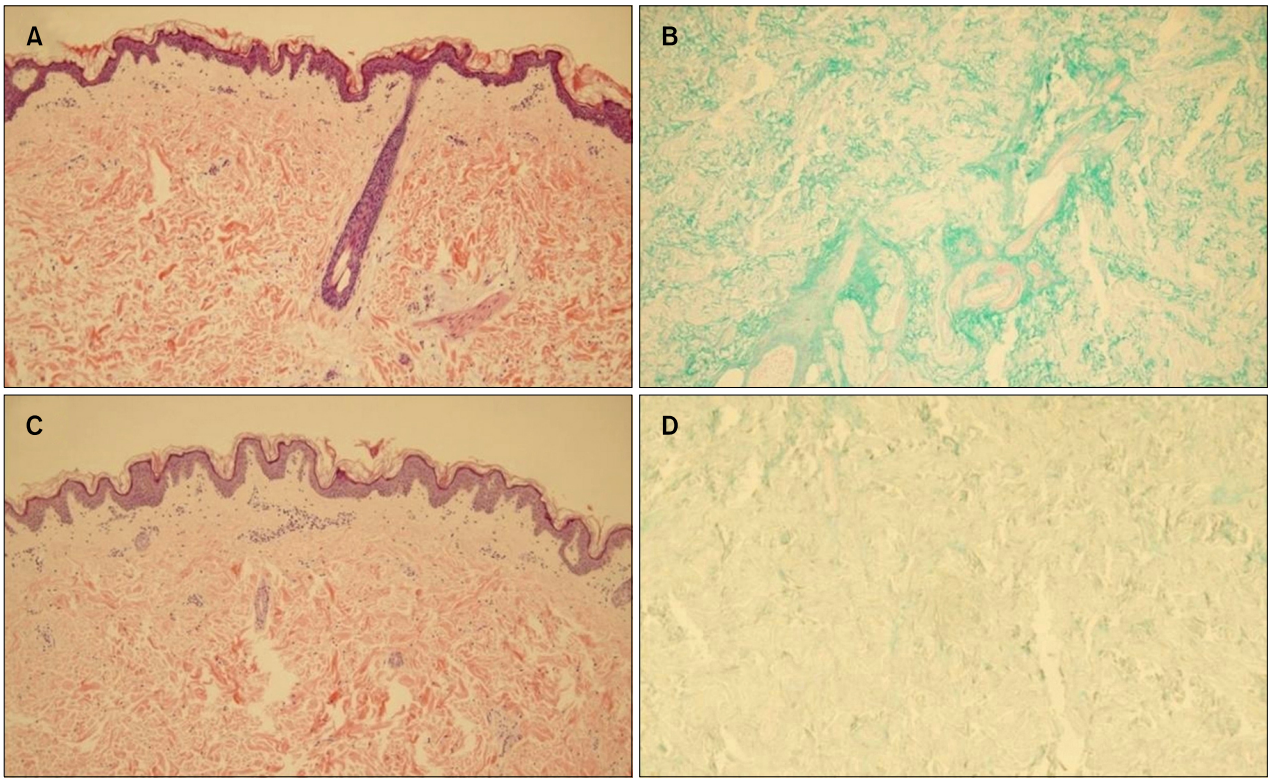

Fig. 2. A biopsy specimen from an ivory-colored papule showing (A) loosely arranged collagen fibers and (B) mucin accumulation (A: H&E, ×100; B: Alcian blue pH 2.5, ×100) compared to (C, D) normal tissue (C: H&E, ×100; D: Alcian blue pH 2.5, ×100).

skin)[4]. This unique cutaneous finding is important in Hunter syndrome diagnosis; however, it is difficult for dermatologists to diagnose the milder form of Hunter syndrome because these cutaneous lesions, which can act as the earliest sign, generally appear before 10 years of age. Occasionally, extensive Mongolian spots have been observed in patients with inborn errors of metabolism, including gangliosidosis and Hurler syndrome[3]. In Hunter syndrome, Mongolian spots are observed on typical location of classic Mongolian sports such as lumbosacral regions, buttocks and back, but they are multiple, extensive and do not fade[3]. ERT has been shown efficacies for variety symptoms of Hunter syndrome and early diagnosis is needed for patients who might have treatment with ERT[5]. In conclusion, a differential diagnosis of inborn errors of metabolism including Hunter syndrome can be considered in infants with extensive Mongolian spots. More importantly, careful examination of pebbly papules and extensive Mongolian spots would be helpful for early diagnosis of Hunter syndrome.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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