A Case of Hunter’s Syndrome
With Ivory-colored Papules

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We report a case of Hunter’s syndrome with characteristic nodules on the upper back. The patient was a 7-year-old Korean boy who presented with ivory-colored papules and nodules on both sides of the scapula, pectoral regions and lateral aspects of the upper arms. These lesions are regarded as pathognomonic cutaneous markers for Hunter’s syndrome. He also presented with truncal hypertrichosis, retarded growth, short neck, round face, claw like contractures of hands, multiple joint contractures, and a clear cornea. Severely elevated glycosaminoglycan levels were present in the patient’s urine samples. The patient’s 5-year-old brother had similar clinical features. (Ann Dermatol 8(4):278–281, 1996).

Key Words: Hunter’s syndrome

Hunter’s syndrome is an X-linked recessive mucopolysaccharide disorder caused by a defect in the metabolism of glycosaminoglycans, which results in incomplete degradation and storage of acid mucopolysaccharides in various tissues. In 1917 Hunter first described the syndrome that was to bear his name when he described two brothers with severe shortness of statures, stiff joints, claw-like hands, hepatosplenomegalies, unusual facies, and peculiar nodular skin lesions over the scapulas. In 1960 McKusick first classified the mucopolysaccharidoses into six types based on the clinical findings, the mode of inheritance, and the mucopolysaccharide found in the urine. The Hunter’s syndrome, mucopolysaccharidosis II, is due to a deficiency in iduronate sulfatase.

Characteristic skin lesions occur in only 20 percent of Hunter’s syndrome. These distinctive lesions are ivory-colored or flesh colored papules and nodules on the upper back that may coalesce to form ridges. In Korean literature, there was only one reported case with skin lesions of Hunter’s syndrome. That case, however, showed linear ulcerative lesions on the left chest and ivory-white colored papules at the periphery of the ulceration which had not been described previously in any literature. Herein we present a case of Hunter’s syndrome with typical skin lesions.

REPORT OF A CASE

A 7.5-year-old boy was admitted to the department of pediatrics, Soonchunhyang university hospital in August, 1995 for evaluation of dysmorphic facial features, joint contracture, and papules on the back. He was the product of a normal pregnancy and delivery. The patient’s 5-year-old brother had the same syndrome, but he did not have papules on his back. For his age, the patient’s height was less than the third percentile, his weight in the 75th percentile, and his head circumference in the 50th percentile. He had mild mental retardation.

Firm, flesh colored, 4-to-10mm papules and nodules were observed over and between both scapulae
Fig. 1. Firm, ivory-colored papules and nodules were seen symmetrically on the scapulae, pectoral regions, and upper arms.

Fig. 2. Coarse facial features, short neck, and large head.

Fig. 3. Claw-like contracture of the fingers.

and lateral aspects of the upper arms (Fig. 1). Some of the papules coalesced to form ridges or a reticular pattern. The lesions first appeared at the age of 2. The patient also presented with generalized downy hypertrichosis. His scalp hair and eyebrows were coarse. Other physical findings included a short stature, large head, short neck, saddle-shaped nose, thick lips, large tongue, thickened

Fig. 4. Loosely arranged collagen fibers in the entire dermis (H & E, ×100).

Fig. 5. Mucinous material in the dermis stained metachromatically with alcian blue (alcian blue, ×200).
ear lobes, broad hands with claw-like contracture of the fingers, and a clear cornea (Fig. 2, 3). There were flexion contractions on the elbow, knee and hip joints. The liver was palpable about 5 cm below the right costal margin.

A karyotype showed the chromosome complement of a normal male (46, XY). The urinary glycosaminoglycan levels were elevated to 620 CPC unit (upper limit of normal range is 173). Roentgenograms showed an enlarged skull, mild kyphosis, short clavicles, pointed proximal ends of the second to fifth metacarpal bones, and tilt of the distal radius and ulna toward each other. EKG and echocardiography revealed normal cardiac function. A biopsy specimen was obtained from a papule on his back. The biopsy specimen showed normal epidermis and loosely arranged collagen fibers in the entire dermis (Fig. 4). Pooling of mucinous material in the entire dermis was stained blue color with alcian blue at both pH 0.5 and 2.0 (Fig. 5).

**DISCUSSION**

The mucopolysaccharidoses (MPSs) are lysosomal storage disorders that result from the deficiency of one of ten specific lysosomal enzymes. These storage diseases are composed of a heterogenous group of disorders characterized by the intralysosomal accumulation of mucopolysaccharides, progressive mental and physical deterioration.

Young and Harper reported the incidence of Hunter’s syndrome in the United Kingdom to be 1 in 132,000 live male births from 1955 to 1974. In contrast, Schaap and Bach reported a much higher incidence of Hunter’s syndrome in Israel of 1 in 67,500 live male births. All the mucopolysaccharidoses except Hunter’s syndrome are inherited as an autosomal recessive trait. Hunter’s syndrome is a classical X-linked recessive inherited disease. Clinical manifestations of Hunter’s syndrome in females are exceedingly rare with only a few cases reported.

There are two forms of Hunter’s syndrome according to clinical severity. Type A is a severe form with a life expectancy of 14-15 years and much earlier onset. Type B is a mild form with a life expectancy of 30-50 years and physical features similar to, but not as severe as those of type A. The mild and severe forms of Hunter’s syndrome can only be separated on clinical grounds, since the level of enzyme activity is similar in both forms.

The many primary systemic manifestations of Hunter’s syndrome include macrocephaly, thickened and deformed skull and thick and dense cranial base and orbital roofs with the premature closing of sagittal and lambdoidal sutures. Very prominent frontal bossing and temporal bulges, as well as changes in the skull can be present. Skeletal abnormalities include an enlarged chest with flaring ribs and short stature. These children exhibit hepatosplenomegaly due to the accumulation of dermatan and heparan, which also cause cardiac valvular disease and thickening of the coronary arteries. Death usually occurs due to cardiac or respiratory arrest.

Hunter and Dorfman reported problems with tonsil and adenoids leading to frequent and severe respiratory infections. Recurrent otitis media and hearing impairment are common. Carpal tunnel syndrome and joint stiffness are also common and can result in loss of hand function. The gingival tissues are hyperplastic, hypertrophic, and enlarged, while the tongue is thickened and macroglossic. The teeth are small and shortened. Patients can have severe retinal degeneration, but the cornea characteristically remains clear. The observations of clear corneas have been used to distinguish Hunter’s syndrome from other mucopolysaccharidoses that present with corneal clouding.

Greatly elevated levels of mucopolysaccharides are present in the serum and urine. A low level of iduronate sulfatase, assayed from cultured skin fibroblasts or leukocytes, is diagnostic of Hunter’s syndrome. As our case showed increased urinary excretion of glycosaminoglycans, we could suspect that our case was mucopolysaccharidosis.

The skin in all types of MPS usually appears thickened and inelastic. However, the only type in which distinctive cutaneous lesions are found frequently, though not invariably, is MPS II, Hunter’s syndrome. The only distinctive skin change of Hunter’s syndrome is the firm, flesh-colored to ivory-white papules and nodules, which may coalesce to form ridges or a reticular pattern. These lesions occur in symmetrical areas between the angles of the scapulas and posterior axillary lines, the pectoral regions, the nape of the neck and/or the lat-
eral aspects of the upper arms and thighs. This is the only physical finding that establishes the diagnosis. Thus, the presence of a clear cornea and ivory-colored papules on the back and lateral aspects of the upperarms of our patient confirmed the diagnosis of Hunter’s syndrome. They appear before 10 years of age, and may spontaneously disappear.19 Unfortunately, the cutaneous lesions of the Hunter’s syndrome are seen in both severe and mild form of Hunter’s syndrome and cannot be used to differentiate a benign from a rapid course.

Histopathologic findings of the papular lesion demonstrated normal epidermis and adnexal structures. Extravasation and pooling of mucinous material in the dermis stained positively with alcian blue at pH 2.0 and 0.5.

No definite treatment is available for patients with an MPS, although a variety of experimental therapies have been attempted. Bone marrow transplantation in MPSs appear to improve the visceral disease, although the time course of improvement and extent in different organs remains to be determined.13

The presence of ivory-colored papules on the back, chest, or arms of a patient with a suspected mucopolysaccharidosis confirms the diagnosis of Hunter’s syndrome. Thus, careful physical examination including whole body surface is as important as biochemical or enzymatic assays.

REFERENCES