

Pebbling of skin: Cutaneous marker of Hunter syndrome

Sir,

Hunter syndrome or mucopolysaccharidoses type II (MPS II) belong to a group of lysosomal storage disorder caused by the deficiency of iduronate-2-sulfate leading to decreased degradation of mucopolysaccharides. It is characterized by accumulation of glycosaminoglycans within lysosomes of various organs including the skin. It is inherited as an X-linked recessive disorder, and hence, seen only in males. Hunter syndrome is the only type of MPS that has distinctive skin lesions described as “pebbling” of skin.^[1] We describe this case of Hunter syndrome to highlight this distinctive skin lesion that serves as a cutaneous marker in early diagnosis.

A 7-year-old male term child, born of nonconsanguineous marriage by normal vaginal delivery, presented with asymptomatic skin colored raised lesions on the upper back, chest, and arms from past 4 years. The lesions first appeared on the upper back and slowly progressed over the years to involve the chest and both arms. Developmental milestones were delayed with speech abnormalities. He had normal intelligence. The child had recurrent upper respiratory tract infection and was operated for umbilical hernia 2 months back. Family history was noncontributory. General physical examination revealed short stature, coarse facial features, thick eyebrows, puffy eyelids, depressed nasal bridge, wide nostrils, thick lips, protuberant abdomen, broad hands, stubby fingers, and claw-like contractures of the distal interphalangeal joints [Figure 1]. He had contractures of elbow joints with widening of bilateral wrist. Cutaneous examination showed multiple, firm skin-colored papules and nodules measuring 0.5 cm × 1 cm to 1 cm × 2 cm presenting bilaterally and symmetrically in a reticular pattern over the scapulae, posterior axillary line, lateral aspect of upper arms, and pectoral region, giving the appearance of pebbled skin [Figure 2a-d]. Hypertrichosis was seen on the trunk and extremities. Systemic examination showed hepatosplenomegaly. Systolic murmur was present. Ophthalmological examination was normal. Complete blood counts and renal and liver function test were normal. 2D echocardiography revealed moderate aortic regurgitation, mild mitral regurgitation, and left ventricular hypertrophy with normal left ventricular function. Nerve conduction study showed motor axonal neuropathy of bilateral median nerves. Lateral skull radiography showed J-shaped sella turcica with thickened skull. Hand radiography showed proximal tapering of metacarpal bones. Enzyme analysis showed deficiency of iduronate sulfatase, 0.04 nmol/4 h/mg (Normal values: 15-57 nmol/4 h/mg) confirming the diagnosis of Hunter syndrome (Type B). Parents did not give consent to do a skin biopsy, hence, it was not performed.



Figure 1: Coarse facial features, depressed nasal bridge, wide nostrils, bushy eyebrows, and thick lips

There are two phenotypes of Hunter syndrome. Type A is the severe classic form that clinically presents as severe mental retardation and death and usually occurs by adolescence as a result of cardiorespiratory failure.^[2] Type B is the milder form that presents with normal intelligence, skeletal abnormalities, less prominent features, and survival into adulthood. Classical cutaneous feature described as “pebbling of skin” is present in both phenotypes. It is described as firm, skin colored to ivory white papules and nodules that coalesce to form ridges in a reticular pattern, distributed symmetrically between the angles of scapulae, posterior axillary lines, pectoral region, nape of neck, and lateral aspect of upper arms and thighs.^[1,3,4] Histopathological examination shows mucin deposition in the dermis. Other skin lesions include mongolian spots and scleroderma-like appearance on hands. Management of this condition is mainly palliative and is based on signs and symptoms. Treatment includes enzyme replacement therapy, bone marrow transplantation, fibroblast transplantation, and serum or plasma infusion gene therapy. Enzyme replacement therapy with idursulfase has shown resolution of skin lesions.^[5] In our case, the child was not on any treatment.



Figure 2: (a) Firm, skin colored papules presenting symmetrically on the pectoral region. (b) closer view showing papules and nodules coalesced to form ridges. (c and d) papules and nodules presenting bilaterally and symmetrically on scapular region extending to lateral aspect of the upper arm

Other differential diagnosis to be considered for such distinctive skin lesions are connective tissue nevi, localized amyloidosis, and papular mucinosis. Connective tissue nevus can occur at different sites as compared to the patterned distribution of skin lesions in Hunter's syndrome. Lack of inflammation and pruritus would rule against amyloidosis. Mucinosis presents as translucent firm papules and nodules.^[1] "Pebbled skin" is a pathognomic sign of Hunter syndrome and is not seen in other types of MPS. Recognition of this entity can provide a clue to diagnose milder forms of the disease as it can be the earliest clinical feature, which helps in counseling the family.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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