Infantile systemic hyalinosis: A case report and review of literature

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ABSTRACT

We report a case of infantile systemic hyalinosis in a 3.5-month-old male child born out of consanguineous marriage. He presented with multiple brownish raised lesions over bony prominences. He had also developed difficulty in movement of limbs and as a result developed severe flexion joint contractures. There was history of similar complaints in elder sibling who died at the age of 5 months due to repeated episodes of pneumonia. Skin biopsy from one of the papulonodular lesions showed increased amount of amorphous hyaline matrix, which was Periodic Acid Schiff positive with scattered fibroblasts. Though classical, we report this case for its rarity in western India.

Key words: Infantile systemic hyalinosis, papulonodular skin lesions, contractures

INTRODUCTION

Infantile systemic hyalinosis (ISH; Online Mendelian inheritance in Man 236490) is a rare autosomal recessive disease that usually presents at birth or within the first few months of life. The main clinical features of ISH include diffusely thickened, inflexible skin, papular skin lesions, hyperpigmentation over the metacarpophalangeal joints of the hands and malleoli, gingival hyperplasia, perianal nodules, limitation of joint motility, osteoporosis of bones, bone fractures, short stature, persistent diarrhea, and failure to thrive. The condition is characterized by deposition of amorphous hyaline material very similar to collagen VI in various tissues like skin, gastrointestinal tract, cardiac muscle, adrenals, skeletal muscles, lymph nodes, spleen, thyroid, and adrenal glands. The management of hyalinosis at present is not well established and survival beyond 3 years of life is exceedingly rare.

CASE REPORT

A 3.5-month-old male child was brought for skin lesions on bony prominences. Our patient was the second offspring born out of a consanguineous marriage. He was born at term by vaginal delivery. At the time of birth, parents noticed that the baby had difficulty in moving both the limbs and used to cry excessively during handling. Then, within a few weeks of life, parents also noticed that baby had developed multiple brownish colored raised lesions on knees, elbows, knuckles and ankles. Detailed enquiry revealed that there were frequent episodes of loose motions which were treated symptomatically by the pediatrician with oral rehydration solution (ORS). There was history of similar complaints in another elder sibling, who had died at the age of 5 months due to repeated episodes of chest infection (Pedigree Chart 1).
Examination revealed that the baby had severe flexion joint contractures at both elbow and knee joints and as a result had developed flexural intertrigo [Figure 1]. Skin over both the thighs, legs, arms and forearms was indurated. There were multiple hyperpigmented nodular lesions of size 2–3 cm on knuckles, knees, ankles [Figure 2]. Scalp showed greasy scales and mild erythema. Abdomen was distended with undue prominence of overlying veins secondary to malnutrition and repeated episodes of diarrhea. General examination showed macrocephaly, excessive facial hair and eye discharge [Figure 3]. Complete blood count showed hemoglobin (11.8 g/dl), total leukocyte count of 6700/mm$^3$ with differential count of P 62%, L 35%, E 03% and serum chemistry (blood urea nitrogen: 16 mg/dl, serum creatinine: 0.7 mg/dl, serum glutamate oxaloacetate transaminase (SGOT): 20 IU/l, serum glutamate pyruvate transaminase (SGPT): 25 IU/l) were within normal range for age. Abdominal ultrasound revealed no major abnormality. Differential diagnosis of deposition disorder, hyalinosis and stiff skin syndrome was entertained. Skin biopsy from one of the papulonodular lesions showed increased amount of amorphous eosinophilic material in the dermis on hematoxylin and eosin staining with a few ectatic blood vessels [Figure 4]. Periodic acid Schiff (PAS) staining showed intensely eosinophilic amorphous material occupying the deeper dermis with hyperplasia of the fibroblasts [Figure 5a and b]. The deposited material did not stain with either Alcian blue or Masson's trichrome, thus ruling out mucopolysaccharidosis and collagen deposition disorder, respectively.

**DISCUSSION**

ISH was first described in detail by Landing in 1986. ISH is one of the differentials for infantile stiff skin syndromes, others

![Figure 1: Brownish papulonodular lesions on bony prominences. Note the joint contracture at the elbow. Also seen is the abdominal distension with dilated overlying veins](image1)

![Figure 2: Close-up of papulonodules on knuckles and metacarpophalangeal joints](image2)

![Figure 3: Note the presence of increased facial hairs and clear watery discharge from both the eyes](image3)
being Winchester’s syndrome, congenital fascial dystrophy (stiff skin syndrome), infantile restrictive dermopathy, and juvenile hyaline fibromatosis (JHF). The pathogenesis of these hyalinosis syndromes remains obscure at present, but increased chondroitin synthesis has been demonstrated by skin fibroblasts in systemic hyalinosis.[6] A few studies have demonstrated abnormal metabolism of type III collagen.[7] Few authors have debated about the existence of two separate disorders, namely, JHF and ISH.[8] Attempts have been made to differentiate between ISH and JHF.[9,10] Comparison has been made between our case and the two hyalinosis [Table 1].

ISH presents in early life with growth failure, painful, reduced movements of the limbs with joint contractures and osteoporosis, diffuse as well as nodular thickening of skin, gingival hyperplasia, severe chronic diarrhea, multiple sepsis and ultimately death.[2] Survival beyond 3 years of life is rare and recurrent chest infections due to impaired chest wall movement is the leading cause of death. Histopathology or electron microscopy of skin tissue is needed to establish the diagnosis in addition to typical clinical findings.

Histopathology of typical papulonodular skin lesion shows deposits of a homogeneous, eosinophilic amorphous material that is PAS positive in the papillary and reticular dermis. In our case, diagnosis was established with the help of typical skin changes and on routine histopathology.

The gene responsible for hyalinosis has been mapped to chromosome 4q21.21 and deletion mutations in CMG2 (capillary morphogenesis gene 2)/ anthrax toxin receptor 2

Table 1: Clinical features of ISH, JHF and the present case

| Feature                        | ISH  | JHF  | Our Case |
|-------------------------------|------|------|----------|
| Skin                          | +    | +    | +        |
| Papular skin lesions          | +    | +    | +        |
| Thickened skin                | +    | −    | +        |
| Gingival hyperplasia          | +    | +    |          |
| Perianal nodules              | +    | +    | −        |
| Large nodules/tumors          | −    | +    |          |
| Hyperpigmented plaques        | +    | −    | +        |
| Joints and bones              |      |      |          |
| Joint contractures            | +    | +    |          |
| Osteoporosis/osteopenia       | +    | +    |          |
| Osteolysis                    | +    | +    |          |
| Others                        |      |      |          |
| Persistent diarrhea           | +    | −    | +        |
| Recurrent infections          | +    | −    |          |
| Visceral involvement          | +    | −    |          |
| Short stature                 | +    | −    |          |
| Prolonged survival            | −    | +    | *        |

ISH: Infantile systemic hyalinosis, JHF: juvenile hyaline fibromatosis
(ANTXR2) have been documented in patients with both JHF and ISH. Thus, it has been said that both ISH and JHF are allelic and they belong to spectrum of same disorder.

Management of hyalinosis is unrewarding for the treating physician and at present, there are no well-established treatment guidelines. There are frequent episodes of breakthrough infections, especially bacterial pneumonia and diarrhea, which need hospitalization and administration of parental antibiotics. A few reports have documented the use of d-penicillamine with some improvement in joint mobility as a result of its inhibitory effect on collagen maturation. Troublesome nodules can be surgically excised, but chance of recurrence is high. Joint contracture needs to be addressed aggressively to maintain ambulation and requires dedicated physiotherapy staff. To conclude, systemic hyalinosis is still less understood entity of ground substance biology and poses a diagnostic as well as therapeutic dilemma for the treating physician.

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