Infantile systemic hyalinosis: A case report and review of literature

Bhushan Madke, Vidya Kharkar, Sunanda Mahajan, Siddhi Chikhalkar, Uday Khopkar

Department of Dermatology, Seth GS Medical College and KEM Hospital, Parel, Mumbai, India

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

Access this article online

Website: www.idoj.in

DOI: 10.4103/2229-5178.73250

Quick Response Code:

Address for correspondence:
Uday Khopkar, Department of Dermatology, OPD 117, 1st Floor, Old OPD building, Seth GS Medical College and KEM Hospital, Parel, Mumbai-400 012, Maharashtra, India.
E-mail: drkhopkar@gmail.com

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.[1] 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.[2] 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.[3] The management of hyalinosis at present is not well established and survival beyond 3 years of life is exceedingly rare.[4]

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, baby was well and weighed about 2.7 kg. Within a few days 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).

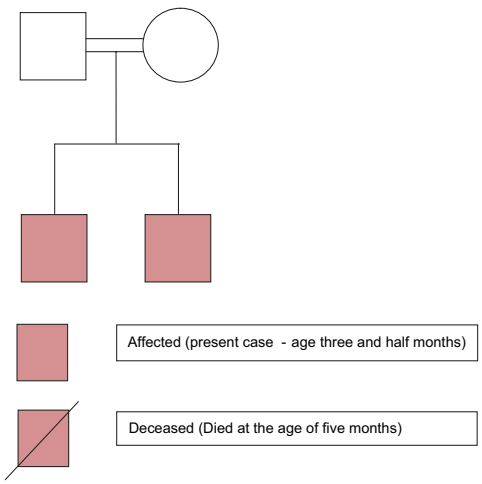


Chart 1: Pedigree

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.[5] ISH is one of the differentials for infantile stiff skin syndromes, others

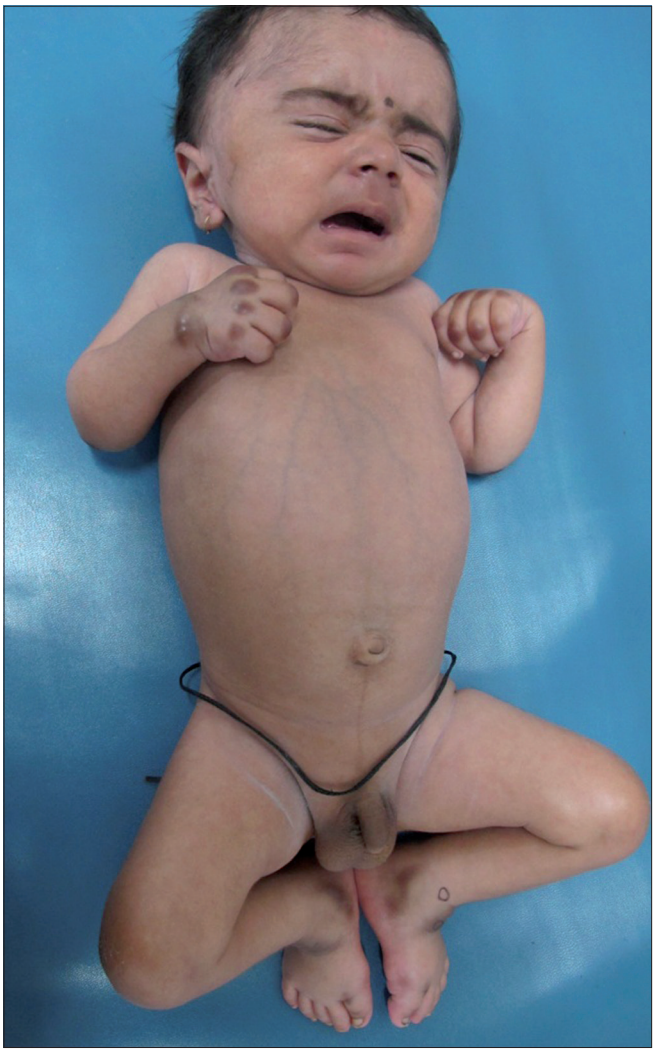


Figure 1: Brownish papulonodular lesions on bony prominences. Note the joint contracture at the elbow. Also seen is the abdominal distension with dilated overlying veins

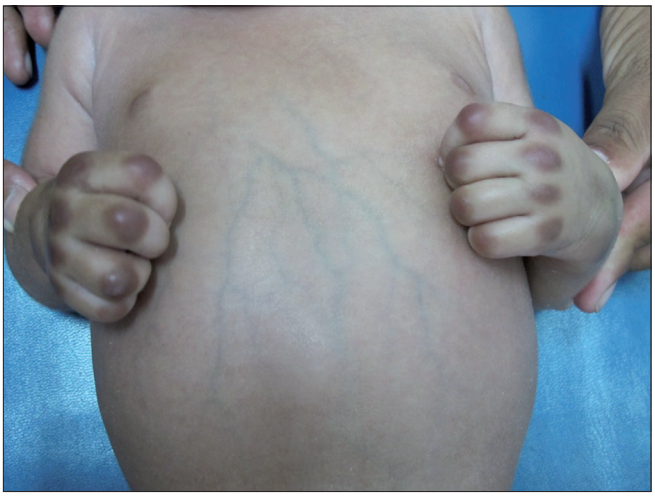


Figure 2: Close-up of papulonodules on knuckles and metacarpophalangeal joints

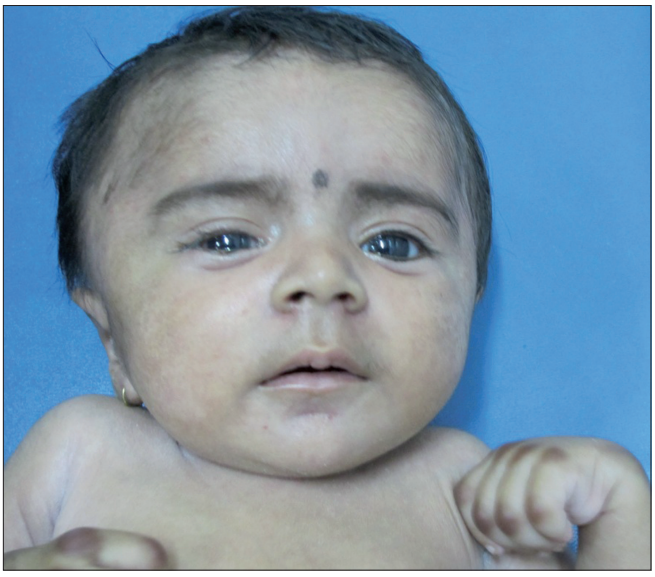


Figure 3: Note the presence of increased facial hairs and clear watery discharge from both the eyes

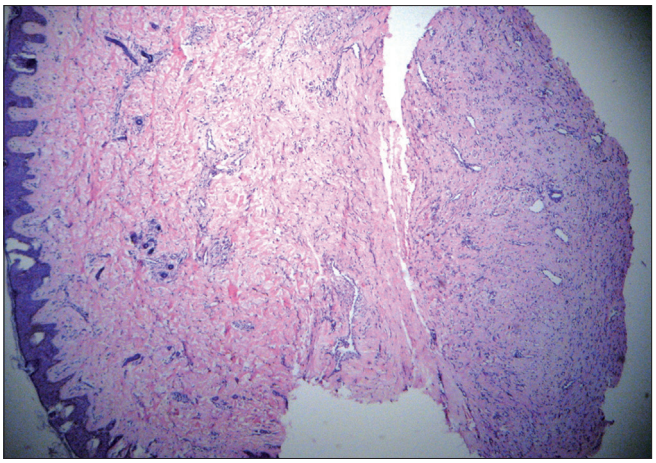


Figure 4: Biopsy section from papulonodular lesion, showing amorphous material in the deeper dermis with few ectatic blood vessels (H&E, ×10)

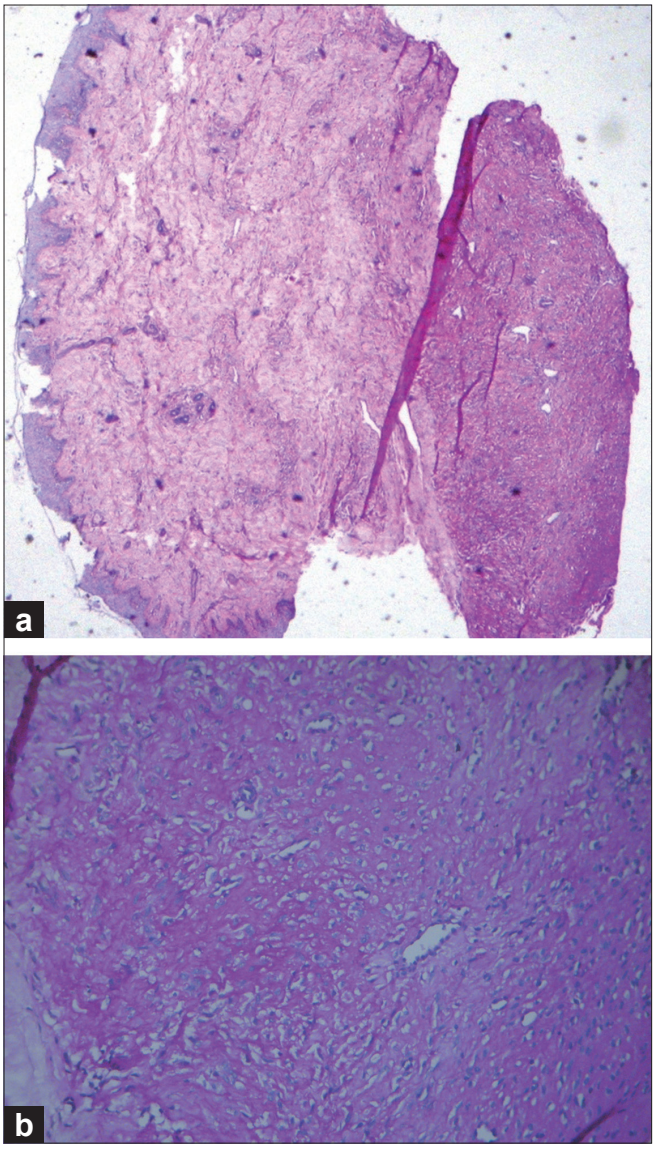


Figure 5: (a and b) Periodic acid Schiff positive diastase resistant eosinophilic material in the deeper dermis (×10 and ×40, respectively)

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 chondrotin 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.

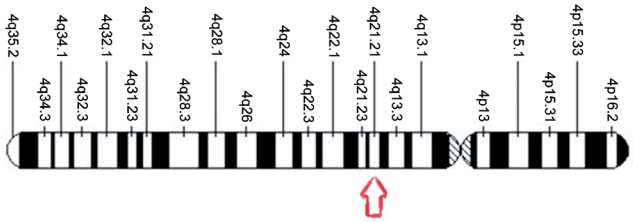
The gene responsible for hyalinosis has been mapped to chromosome 4q21.21 and deletion mutations in CMG2 (capillary morphogenesis gene 2)/ anthrax toxin receptor 2

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

Skin	ISH	JHF	Our case
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.[11] Thus, it has been said that both ISH and JHF are allelic and they belong to spectrum of same disorder.[12]



Diagrammatic representation of chromosome 4 showing the locus of CMG2 gene (red arrow)

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.[10] 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.

REFERENCES

1. Huan YC, Xiao YY, Zheng YH, Jang W, Yang YL, Zhu XZ. Infantile systemic hyalinosis: a case report and mutation analysis in a Chinese infant. Br J Dermatol 2007;156:575-612.
2. Glover MT, Lake BD, Atherton DJ. Clinical, histologic, and ultrastructural findings in two cases of infantile systemic hyalinosis. Pediatr Dermatol 1992;9:255-8
3. Shin HT, Paller A, Hoganson G. Infantile systemic hyalinosis. J Am Acad Dermatol 2004;50:61-4.
4. Dhingra M, Amladi S, Savant S, Nayak C. Juvenile hyaline fibromatosis and infantile systemic hyalinosis: Divergent expressions of the same genetic defect? Indian J Dermatol Venereol Leprol 2008;74:371-4.
5. Landing BH, Nadorra R. Infantile systemic hyalinosis: report of four cases of a disease, fatal in infancy, apparently different from juvenile systemic hyalinosis. Pediatr Pathol 1986;6:55-79.
6. Finlay AY, Ferguson SD, Holt PJA. Juvenile hyaline fibromatosis. Br J Dermatol 1983;108:609-16
7. Lubec B, Steinert I, Breier F, Jurecka W, Pillwein K, Fang-Kircher S. Skin collagen defects in a patient with juvenile hyaline fibromatosis. Arch Dis Child 1995;73:246-8.
8. Urbina F, Sazunic I, Murray G. Infantile Systemic Hyalinosis or Juvenile Hyaline Fibromatosis? Pediatr Dermatol 2004;21:154-9
9. Yesudian P, Janaki VR, Thambiah AS. Juvenile hyaline fibromatosis. Int J Dermatol 1984;23:619-20.
10. Sahn EE, Salinas CF, Sens MA, Key J, Swiger FK, Holbrook KA. Infantile systemic hyalinosis in a black infant. Pediatr Dermatol 1994;11:52-60
11. Hanks S, Adams S, Douglas J, Arbour L, Atherton DJ, Balci S, *et al*. Mutations in the gene encoding capillary morphogenesis protein 2 cause juvenile hyaline fibromatosis and infantile systemic hyalinosis. Am J Hum Genet 2003;73:791-800.
12. Dowling O, Difeo A, Ramirez MC, Tukel T, Narla G, Bonafe L, *et al*. Mutations in capillarymorphogenesis gene-2 result in the allelic disorders juvenile hyaline fibromatosis and infantile systemic hyalinosis. Am J Hum Gen 2003;73:957-66.

Source of Support: Nil, **Conflict of Interest:** None declared