

## Infantile systemic hyalinosis: A case report

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### Abstract

Infantile systemic hyalinosis (ISH) is a rare, progressive, autosomal recessive disorder characterized by connective tissue involvement as hyaline deposition in the skin, gastrointestinal tract, muscles, glands, and other organs. We report a child with this rare condition presenting with growth retardation, joint contractures, and intractable diarrhea. Though genetically analyzed, ISH still remains as a poorly understood disease raising concerns during diagnosis and treatment.

**Key words:** *Capillary morphogenesis protein 2, Infantile systemic hyalinosis, Periodic acid schiff test*

Infantile systemic hyalinosis (ISH) is a rare autosomal recessive disease of the connective tissue characterized by generalized deposition of hyaline material in the skin, gastrointestinal tract, muscles, glands, and other organs. Till 2009, fewer than 20 patients with ISH were reported [1]. In 1873, Murray used the term “molluscum fibrosum” for this condition [2] and then in 1962, Puretic et al. reported a case under the name of mesenchymal dysplasia [3]. The term systemic hyaline fibromatosis was introduced by Ishikawa and Hori in 1964 [4].

### CASE REPORT

A 13-month-old female child was referred to our center with complaints of restricted movements of all the four limbs and progressive contractures of the joints for 3 months. The child was normal till 8 months of age when her mother noticed reduced spontaneous movements of the limbs associated with severe pain while handling. Within a few months, the child developed loose stools, abdominal distension, bilateral pedal edema, and protrusion of mass per rectum. There was no history of convulsions or hoarseness of voice.

The child was born at full term following an uneventful pregnancy by normal vaginal delivery. There was no history of consanguinity and no other family members were affected with the similar disorder. Her intra-natal and postnatal period were unremarkable. She was small for his age with both weight (4 kg) and length (62 cm) below the 3<sup>rd</sup> percentile, and head circumference was 43 cm. Though irritable, child was responsive to his surroundings. Developmental assessment revealed motor and speech developmental delay with normal social adaptive domains.

On physical examination, the child was pale, sick-looking, and irritable with abnormal coarse facies. She had low set ears, small palpebral fissure, broad forehead, and sparse lusterless hair as a part of his craniofacial dysmorphism. She also had perianal nodules with ulceration and gingival hypertrophy. She had tense shiny skin with multiple bluish plaques over elbow, dorsum of the hand, and ankle with multiple joint contractures involving bilateral ankle, knee, wrist, and elbow joints.

On laboratory investigations, complete blood count (hemoglobin - 11.8 mg%, total leukocyte count 11,700 cells/mm<sup>3</sup>, and platelet count - 2.99 lakh/mm<sup>3</sup>) and peripheral smear was normal. His renal and liver function tests were within normal limits except the presence of the hypoalbuminemia. Stool routine examination and microscopy were inconclusive. Abdominal ultrasound revealed mild hepatomegaly with ascites, increased renal cortical echogenicity and loss of corticomedullary differentiation.

Skin biopsy from the papule near the elbow joint revealed normal epidermis covered by the thick orthokeratotic corneal layer, dermis had features of normal adnexa with focal lymphocytic aggregates near the sweat ducts at the interface with subcuticular fat. The periodic acid-Schiff positive material was noted in the dermis near the subcuticular fat favoring the diagnosis of ISH. However, a gastrointestinal biopsy was not done.

Thus, the diagnosis of ISH was made on the basis of clinical features and skin biopsy. Symptomatically treatment was started with intravenous antibiotics, analgesics, and physiotherapy. Albumin infusion was also given to correct hypoalbuminemia.



**Figure 1: Showing sick-looking, irritable child with abnormal coarse facies, low set ears and tense shiny skin over lower limbs**



**Figure 2: Infant with tense shiny skin with multiple bluish plaques over elbow, dorsum of the hand, and ankle with multiple joint contractures involving bilateral ankle, knee, wrist, and elbow joints.**

However, the child gradually deteriorated and succumbed to death within 7 days of hospitalization.

## DISCUSSION

ISH is a fatal disorder usually presents during the first months of life, especially first six months with widespread involvement of the joints, skin, gastrointestinal tract, and other parts. It is a disorder of synthesis of glycosaminoglycans with a resultant abnormality in collagen synthesis. The gene responsible for this condition has been mapped on chromosome 4q21. A mutation in the gene encoding ANTRX2/capillary morphogenesis protein 2 (CMG2) is responsible for expression of this disease. CMG2 is a transmembrane protein which is induced during CMG. This protein CMG2 has an extracellular region that contains a Von Willebrand type A domain that shows strong binding to laminin and collagen IV, both of which are markedly induced in endothelial cell morphogenesis. If a mutation affects the laminin sites, a severe form of ISH occurs [5,6].

Clinically, joints usually are the first involved areas with swelling, pain, and limited range of motions disabling the

patients. Bones start to become osteoporotic and prone to multiple bone fractures. Skin is another involved part which becomes thickened and covered by purplish papules especially gathered on face, neck, and ears. The scattered fibrous nodules on the chest wall, hypertrophic gum, and prominent nodules around the anus are the other manifestations of involved skin [7]. In view of the hyaline deposition in the intestinal walls, these patients have protein losing enteropathy and intermittent diarrhea that lead to short stature, failure to thrive, severe malnutrition, infection and septicemia, and death [8]. Mean duration of survival in such patients is around 11 months [1]. Antenatal diagnosis of the condition can be made by screening of the fetus for the responsible mutations, and genetic counseling should be done as there are 25% chances of development of this disease in offsprings.

There is no specific treatment available. Early surgical excision is recommended for those lesions with a cosmetic problem or functional impairment. However, there are chances of recurrence following surgical excision. NSAIDs and opioids may be helpful to alleviate the pain. Oral D-penicillamine has also been used in some cases and has shown improvement in joint mobility and flexibility. Dimethyl sulfoxide, ketotifen, and calcitriol have also been tried with variable results [1].

## CONCLUSION

ISH is a very rare condition presenting in early life with growth failure, painful reduced movements of the limbs with joint contractures, characteristic skin manifestations. As the prognosis of ISH is poor, awareness, and early recognition aids in better supportive therapy for the child.

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