

## Three years old child with juvenile hyaline fibromatosis presenting with rectal bleeding

Kapeel Raja,<sup>1</sup> Mohammad Arsalan Khan,<sup>2</sup> Mohammad Mubarak,<sup>3</sup> Zaigham Abbas,<sup>4</sup> Nasir Hassan Luck,<sup>5</sup> Syed Mujahid Hassan<sup>6</sup>

### Abstract

Juvenile Hyaline Fibromatosis is a rare inherited autosomal recessive disorder which is caused by mutation of CMG2 gene on chromosome 4q21. Mutation of this gene protein can disrupt the formation of basement membranes. Hyalinization of various body tissues like skin, joints, and bones leads to development of skin papules, gingival hyperplasia, osteolytic lesions in bones, and joint contractures. We had a case of a 3 years old female child with Juvenile Hyaline Fibromatosis who presented with rectal bleeding. She had a bleeding mucocutaneous lesion in anal canal along with papulonodular lesions on the face, gingival hypertrophy and flexion contractures of small joints of hands and feet. Excision of the anal lesion revealed histopathological features of Juvenile Hyaline Fibromatosis.

**Keywords:** Juvenile Hyaline Fibromatosis, Inherited

autosomal recessive disorder,

### Introduction

Juvenile Hyaline Fibromatosis (JHF) is a rare inherited autosomal recessive disorder<sup>1</sup> which is caused by mutation of gene CMG2 (Capillary morphogenesis protein 2) gene on chromosome 4q21.<sup>2</sup> Mutation of this gene protein disrupts the formation of basement membranes, subsequently hyalinization of various body tissues like skin, joints, and bones and leads to development of skin papules, gingival hyperplasia, osteolytic lesions in bones, and joint contractures. We report here a case of JHF who presented with rectal bleeding due to a mucocutaneous tissue in anal canal which made this report distinct from the others already reported in literature.

### Case Report

A three years old female child presented with history of

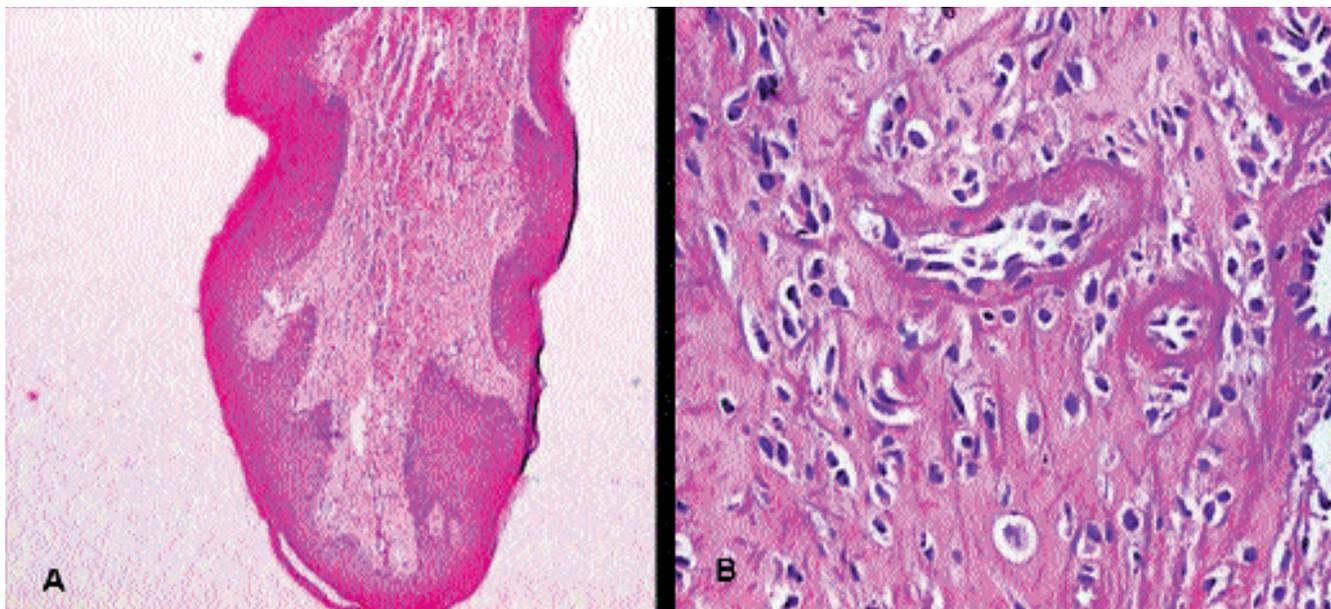


**Figure-1:** (A) Depressed nasal bridge and ear deformity (large right ear & small left ear). (B) Flexion contractures of small joints of both hands. (Picture taken after permission of patient).

<sup>1,4-6</sup>Department of Hepatogastroenterology, <sup>2</sup>Department of Nephrology, <sup>3</sup>Department of Histopathology, Sindh Institute of Urology and Transplantation, Karachi, Pakistan.

**Correspondence:** Kapeel Raja. Email: kapeelraja@yahoo.com

per rectal bleeding for one and a half year. Bleeding, was intermittent, one to two episodes in a day, moderate in amount, red in colour, fresh, painless, and was associated with feeling of something coming out of the anus; She had two siblings, who were normal. On



**Figure-2:** (A) Low-power photomicrograph showing a polypoid fragment of anal lesion. Stroma shows many small blood vessels. (H&E stain,  $\times 50$ ). (B) High-power photomicrograph showing abundant hyaline, glassy, material deposited in the interstitial spaces and in blood vessel walls. This material was negative for amyloid stains. There are also interspersed fibroblasts and macrophages in the background. (H&E stain,  $\times 400$ ).

general physical examination she was found to have normal IQ, with depressed nasal bridge (Figure-1), left small ear and right large ear, multiple large, pink-coloured papules of variable size present around the nose, chin, and behind the right ear lobe (Figure-1). A small subcutaneous nodule of half cm size was present below the chin and two large one cm each nodules were also seen at right parietal-temporal region. Flexion Contractures were present in small joints of hands and feet bilaterally. On rectal examination a soft mucocutaneous lesion around 4-5mm were palpable in the anal canal. Flexible sigmoidoscopy was normal. Excisional biopsy of lesion confirmed features of Juvenile hyaline fibromatosis (Figure-2). Biopsy showed amorphous, hyaline, glassy material deposited in the interstitial spaces and in blood vessel walls. There was an abundance of stroma with a relative paucity of cellular elements. Numerous macrophages were seen in the vicinity of the deposits. On special staining, the deposits were seen to be periodic acid-Schiff (pas)-positive, Congo red-negative and Alcian blue-negative. CD68 and vimentin were positive. X-rays of hands and feet, showed generalized osteopenia, and contractures of the small joints with no periosteal reaction. X-rays skull revealed osteopenia with no lytic lesion. Systemic examination did not reveal any abnormality. Complete blood count, renal function tests, liver function tests, blood sugar, and electrolytes were within normal limits.

## Discussion

Juvenile hyaline fibromatosis is a rare disorder of connective tissue which is associated with abnormal synthesis of hyaline, a collagen like substance. Poretic syndrome hyalinosis, systemic juvenile, murray-poretic syndrome, and molluscum fibrosus are known synonyms of juvenile hyaline fibromatosis.<sup>3</sup> JHF was first described in 1969 by Drescher et al.<sup>4</sup> So far less than 70 cases of JHF have been reported worldwide.<sup>5</sup> The prevalence of JHF is unknown. It usually affects one or more siblings. At birth the infant is normal. The disease progresses from gingival hypertrophy to papulonodular lesions to contractures and osteolytic lesion in bones, from the neonatal period to 4 years of age.<sup>1</sup> As the name suggests, the disorder commonly occurs in infants, but is also rarely seen in adults. Partial expression of disease is common.<sup>6</sup> There is equal male to female ratio. JHF is caused by mutation of gene ANTXR2 (also known as the CMG2 gene) on chromosome 4q21.<sup>2</sup> ANTXR2 gene encodes a transmembrane protein (capillary morphogenesis protein) that is induced during capillary morphogenesis. The ANTXR2 gene provides instructions for making this protein which is involved in the formation of tiny blood vessels (capillaries) and maintaining the structure of basement membranes. Mutation of this gene protein disrupt the formation of basement membranes, allowing the hyaline substance to leak through and build up in various body tissues like skin, joints, and bones leads to

development of skin papules, gingival hyperplasia, osteolytic lesions in bones, and joint contractures. Histology shows the deposition of an amorphous, eosinophilic hyaline material in the extracellular spaces of the dermis around the blood vessels. There is an abundance of stroma with a relative paucity of cellular elements. The dermis contains a few inflammatory cells and widely scattered spindle cells disposed in a densely eosinophilic background.<sup>3</sup> The deposits are PAS-positive and Alcian blue-negative.

Infantile systemic hyalinosis (infantile hyaline fibromatosis, infantile hyalinosis)<sup>3</sup> is a severe form of JHF, with more severe joint involvement, joint contractures and thickened skin. Infants are affected within the first few weeks or months of life. Recurrent purulent infections, diarrhoea and severe osteoporosis are observed in the first year of life. Severe joint limitation and pain lead to immobility and respiratory insufficiency. Feeding problems, malnutrition and protein-losing enteropathy are caused by the thickening and hyaline infiltration of intestinal walls. Death occurs secondary to sepsis with renal, respiratory and heart failure, usually by the age of two years.<sup>7,8</sup>

One study has reported that patients with severe forms of JHF with persistent diarrhoea died in early infancy due to infections.<sup>9</sup> In our reported case, there was no history of hyalinosis in siblings, and course of JHF was slowly progressive and absence of systemic features differentiated it from rapidly fatal form of JHF.

No specific treatment is available for JHF. Early surgical excision is recommended by some authors for those lesions that either present a significant cosmetic problem or produce some degree of functional impairment.<sup>10</sup> But it may be followed by recurrences.<sup>11</sup> Intralesional steroids may reduce the size of early lesions temporarily. Capsulotomy of joints may also show some temporary, symptomatic relief. Radiotherapy is ineffective in JHF<sup>10</sup> Gingival overgrowth may be treated with partial gingivectomy. Some oral and topical agents including D-penicillamine has been used in some cases<sup>9</sup> there are

some therapeutic trials with dimethyl sulfoxide, ketotifen, and calcitriol.<sup>10</sup> patients with JHF typically have severe physical limitations, but most individuals have normal intelligence and live into adulthood. The parents were counseled about the progressive nature of the disease and the 25% chance of development of disease in future offspring. The patient is currently undergoing physiotherapy for the improvement of muscle strength.

## Conclusion

In summary, JHF is a rare inherited autosomal recessive disorder. Our case presented with rectal bleeding due to anal lesion in addition to typical skin lesions along with joint contracture and gingival hypertrophy.

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## References

1. Landing BH, Nadorra R. Infantile systemic hyalinosis: report of four cases of disease, fatal in infancy, apparently different from juvenile systemic hyalinosis. *Pediatr Pathol* 1986; 6: 55-79.
2. Rahman N, Dunstan M, Teare MD, Hanks S, Edkins SJ, Bignell GR, et al. The gene for juvenile hyaline fibromatosis maps to chromosome 4q21. *Am J Hum Genet* 2002; 71: 975-80.
3. Mancini G, Orange A, Hollander J, Levy M. Fibromatosis, hyalinosis and Stiff Skin syndrome. In: Harper J, Oranje A, Prose N, editors. *Textbook of Pediatric Dermatology*. 2nd ed. Oxford: Blackwell 2006; pp 951-4.
4. Miyake I, Tokumaru H, Sugino H, Tanno M, Yamamoto T. Juvenile hyaline fibromatosis. Case report with five years follow-up. *Am J Dermatopathol* 1995; 17: 584-90.
5. Gupta LK, Singhi MK, Bansal M, Khullar R, Jain V, Kachhawa D. Juvenile hyaline fibromatosis in siblings. *Indian J Dermatol Venereol Leprol* 2005; 71: 115-8.
6. Larralde M, Santos-Munoz A, Calb I, Magarinos C. Juvenile hyaline fibromatosis. *Pediatr Dermatol* 2001; 18: 400-2.
7. Shin HT, Paller A, Hoganson G, Willner JP, Chang MW, Orlow SJ. Infantile systemic hyalinosis. *J Am Acad Dermatol* 2004; 50: S61-4.
8. Glover MT, Lake BD, Atherton DJ. Clinical, histologic and ultrastructural findings in two cases of infantile systemic hyalinosis. *Pediatr Dermatol* 1992; 9: 255-8.
9. Urbina F, Sazunic I, Murray G. Infantile systemic hyalinosis or juvenile hyaline fibromatosis? *Pediatr Dermatol* 2004; 21: 154-9.
10. Quintal D, Jackson R. Juvenile hyaline fibromatosis: A 15-year follow-up. *Arch Dermatol* 1985; 121: 1062-3.
11. Finlay AY, Ferguson SD, Holt PJ. Juvenile hyaline fibromatosis. *Br J Dermatol* 1983; 108: 609-16.