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INHERITED SYSTEMIC HYALINOSIS A CASE REPORT

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Abstract : Inherited Systemic Hyalinosis , a rare autosomal recessive disorder is characterized by hyaline deposits in the papillary dermis and other body tissues like joints, bones, and internal organs. Severe form is infantile systemic hyalinosis which die in early childhood. Milder form is juvenile hyaline fibromatosis which survive into adulthood. The prevalence of infantile systemic hyalinosis is unknown. Fewer than 20 people with this disorder have been reported worldwide so far. A 5 month old male child born of third degree consanguinous marriage presented with complaints of paucity of movement of all limbs since birth. Child had joint contractures at both elbow and knee joints and hyperpigmented thickening over the bony prominence. The child was diagnosed as a case of infantile systemic hyalinosis, a severe form of inherited systemic hyalinosis based on clinical features,hyaline material accumulation in skin biopsy and radiological finding.

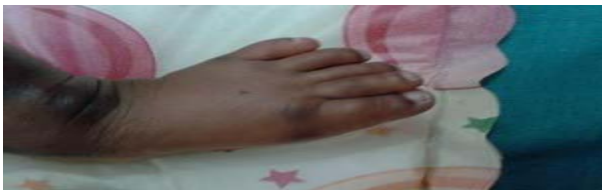
Keyword : Inherited Systemic Hyalinosis, Hyaline material accumulation

Case report :

A 5 month old first order male child born to a third degree consanguinous parents presented with complaints of paucity of movement of all limbs since birth. Baby was always keeping limbs in flexed posture. There was difficulty in extension and crying during passive movements. There was history of diminished fetal movements from 8 months. Baby born by Full term LSCS (Indication: Oligohydramnios, Breech presentation). There was history of developmental delay. Social smile attained at three and half months. Head control not attained. On examination he was Lying in frog like position. Hyperpigmented thickenings were noted over knuckles, ankles and malleolar areas . Joint contractures were noted at both elbow & knee joints . Failure to thrive present. Plagiocephaly of skull was noted. Vitals were stable. Cardiovascular system, respiratory system, abdomen were normal.

Knuckle Pigmentation

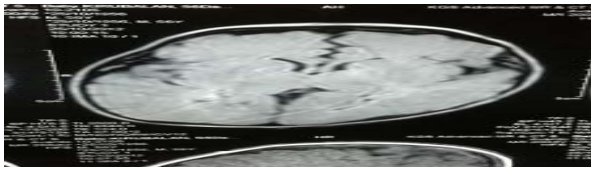
Malleolar Pigmentation

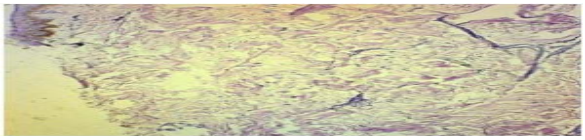


Ankle Pigmentation

Skull radiograph revealed osteolytic lesion 2.7 x 1.8 cm in occipital bone. MRI brain revealed non synostotic plagiocephaly in left postero temporo parieto occipital region and mild thinning of corpus callosum with dilatation and splaying of lateral ventricles. Light microscopy of skin biopsy section showed structure of skin with normal epidermis and underlying dermis with hyaline material accumulation. The hyaline material appeared as an amorphous eosinophilic substance that was periodic acid-Schiff (PAS) positive. USG Abdomen, ECHO were normal.

MRI with plagiocephaly





Diagnosis was made out based on clinical features, skin biopsy and radiological finding. The child was given symptomatic and supportive care. Careful physiotherapy was given. Child had not turned up for further follow up.

DISCUSSION:

Inherited Systemic Hyalinosis typically presents at birth or in infancy with thickened skin, hyperpigmented macules over bony prominences, pain or excessive crying with movement, prog ressive joint contractures often with severe motor disability. Skin nodules, pearly papules of the face and neck, fleshy lesions especially over perioral and perianal area are common. Gingival hypertrophy, hepatomegaly may be present. Most patients develop a condition called protein-losing enteropathy which results in severe diarrhoea, failure to thrive and cachexia. Patient often do not survive beyond early childhood due to chronic diarrhoea and recurrent infections. Cognitive function is preserved; however, cases of delayed development have been reported. Inherited systemic hyalinosis is inherited as an autosomal recessive pattern. Both severe and mild forms are caused by mutations in anthrax toxin receptor 2 gene (ANTRX2) on chromosome 4q21. Mutations disrupt the formation of basement membranes, allowing a clear (hyaline) substance to leak through and accumulate in various parts of the body. Diagnosis is based on clinical findings, Skin biopsy, Intestinal biopsy, skeletal x-rays and molecular genetic testing. Diagnosis based on clinical findings is hyper pigmented skin over bony prominence, frog like posture, progressive contractures, pain or excessive crying and gingival thickening. Other skin manifestations include skin nodules and pearly papules common on the face and neck. Fleshy lesions may appear in the perianal region. Unusual facies - A depressed nasal bridge, ear malformations (large ears, low-set ears, and pre auricular skin tags), coarse facial appearance may be present. Failure to thrive occurs due to chronic diarrhoea and protein-losing enteropathy.

Skin biopsy: Light microscopy demonstrates hyaline material accu mulation in the dermis. The hyaline material appears as an amorphous eosinophilic substance that is periodic acid-Schiff (PAS) positive. It is thought to contain glycoproteins and collagen. The spindle-shaped fibroblasts dispersed in abundant amounts of hyaline material render a "chondroid appearance." Electron microscopy demonstrates cells filled with fine, fibrillary material with an enlarged endoplasmic reticulum and Golgi apparatus. Intestinal biopsy specimen: In individuals with prominent gastrointestinal symptoms specimen shows villous atrophy, edema, lymphangiectasia, and hyalinosis Skeletal radiographs may reveal osteopenia, periosteal reaction, and lucent lesions. MRI of the brain is unremarkable Molecular Genetic Testing - ANTXR2 gene, the capillary morphogenesis gene-2, is the only gene in which mutations are currently known to cause inherited systemic hyalinosis. Differential Diagnosis include Farber disease, I –cell disease, Pseudo hurler polydystrophy , Winchester syndrome , Infantile myofibromatosis and Stiff skin syndrome Pain is managed by Nonsteroidal anti-inflammatory drugs (NSAIDs) and opiates. Gentle handling, splinting of affected joints may provide comfort. Joint contractures are typically progressive. Physiotherapy should be performed with care. For failure to thrive early consideration should be given to nasogastric tube or gastrostomy tube feeding. Protein-losing enteropathy is treated with adequate hydration and albumin infusions. Infections are treated in a standard manner based on the site of infection and causative agent. Skin nodules, gingival thickening, perianal masses - For problematic lesions surgical excision is an option, but lesions may recur. Genetic counselling: Laboratories offering molecular genetic testing for prenatal diagnosis of inherited systemic hyalinosis are listed in the Gene Tests Laboratory Directory.

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