



CLOVE Syndrome- Case Report of a rare Congenital Disorder

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Abstract

Congenital lipomatous overgrowth, vascular malformations and epidermal nevi (CLOVE) syndrome is a recently delineated rare congenital disorder that comprises of vascular malformations (typically truncal), dysregulated adipose tissue, scoliosis and enlarged bony structures (typically of the legs) without progressive or distorting bony overgrowth. This recent delineation distinguishes it from Proteus syndrome, a disorder that comprises localized, progressive, postnatal overgrowth with bony distortion, dysregulated adipose tissue, cerebriiform connective tissue, linear epidermal nevus, hemimegalencephaly and other manifestations¹.

Introduction

CLOVE (S) is an acronym that describes a rare syndrome of Congenital Lipomatous Overgrowth due to dysregulated adipose tissue, Vascular malformations (typically truncal) and Epidermal nevi. The (S) denotes scoliosis or skeletal abnormalities like enlarged bony structure (typically of the legs) without progressive or distorting bony overgrowth that have been noted infrequently in subsequent cases.² Central nervous system manifestations include hemimegalencephaly, dysgenesis of the corpus callosum, neuronal migration defects and consequent seizures. CLOVES is caused by postzygotic activating mutations in PIK3CA.³ Proteus syndrome, congenital lipomatous overgrowth, vascular malformations, epidermal naevi

(CLOVE) syndrome and isolated hemihyperplasia (IHH) are disorders that occur sporadically and comprise malformations of various tissues with asymmetrical overgrowth. Diagnosis of these syndromes is difficult because of the variability of symptoms. Difficult diagnosis, varied symptoms and continuous disfiguring overgrowth require concerted multidisciplinary interventions and postoperative care.⁴ We describe a 3 year old first born male child of nonconsanguineous and otherwise healthy and young parents who presented to us with unilateral linear verrucous pigmented epidermal nevus and associated skeletal, ocular and dental abnormalities which corresponded to CLOVES syndrome.

Case Report

A 3-year-old male child presented with pigmented skin lesion over one half of the body present since birth and progressive enlarging abdomen. He was the first child born to non-consanguineous and otherwise healthy parents after an uneventful pregnancy. Physical examination showed a verrucous epidermal nevus extending over left side of neck (Fig 1), axilla and arm (Fig 2), dorsum of hand and anterior surface of thigh, ipsilateral asymmetrical deformity of skull, limb length discrepancy, bilateral genu valgum, ptosis, esotropia, delayed canine eruption, dental hypoplasia, and left side abdominal wall mass (Fig 3 & 4). USG abdomen was suggestive of lipomatous mass of anterior abdominal wall and X Ray Lumbosacral spine showed central beaking of L₂ & L₃ Vertebrae. CT head showed large cerebral volume of left cerebral hemisphere with mild ipsilateral ventriculomegaly with fibrous dysplasia of left frontal bone (Fig 5-8). FNAC from abdominal wall mass showed features of lipoma. The child displayed characteristic features of CLOVES syndrome and could be distinguished from Proteus syndrome by the lack of progressive or distorting bony overgrowth which is cardinal feature of the later in the absence of studies for gene mutations.



Fig.1. Verrucous epidermal nevus extending over left side of neck.



Fig.2. Verrucous epidermal nevus extending over left side of axilla and arm.



Fig.3 Lipomatous mass of anterior abdominal wall



Fig.4. Ptosis, asymmetric Skull deformity

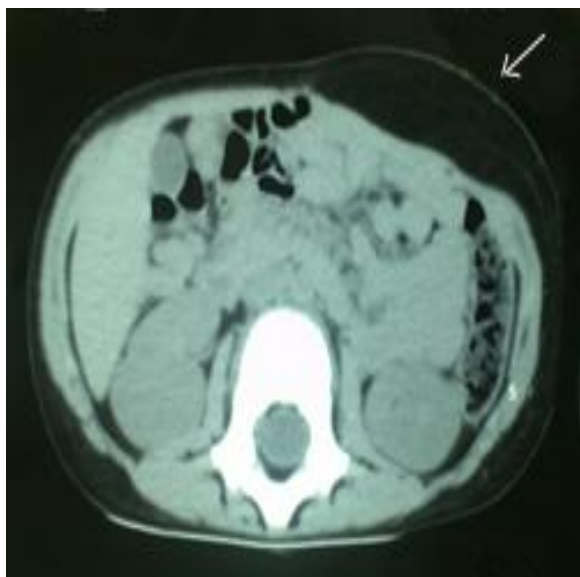


Fig.5. Anterior abdominal wall lipomatous mass

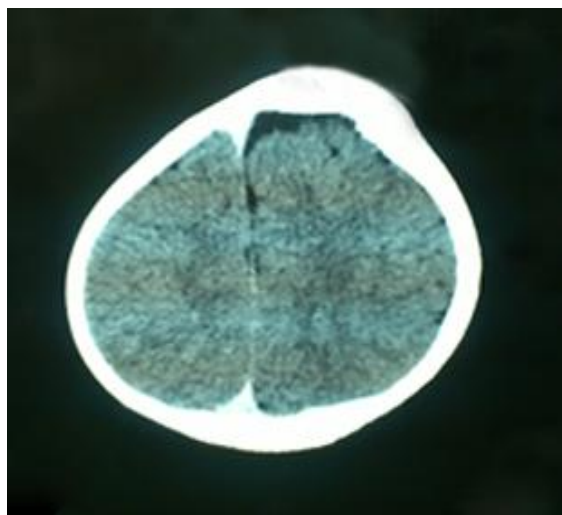


Fig.7. Large cerebral volume of left cerebral hemisphere.

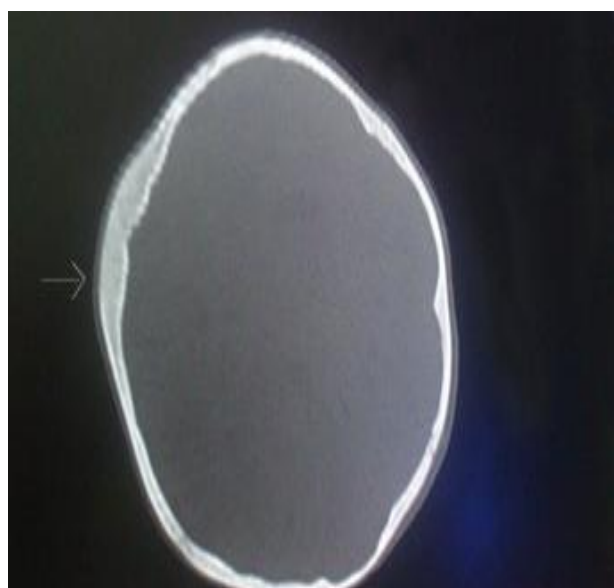


Fig.6. Fibrous dysplasia of left frontal bone

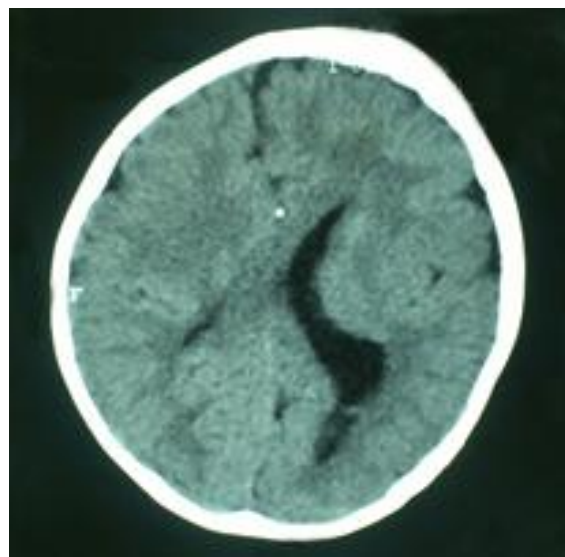


Fig.8. Mild ipsilateral ventriculomegaly

Discussion

The cardinal features of CLOVES syndrome are truncal lipomatous masses, vascular malformations, and cutaneous and acral musculoskeletal anomalies. “CLOVES” is a more precise acronym emphasizing the presence of several common morbid features not included in the “CLOVE,” namely, scoliosis and other skeletal, and spinal anomalies. Patients with CLOVES syndrome are typically born with lipomatous masses of the thoracic and abdominal wall (commonly in the posterolateral chest wall and flank) with variable contiguous extension to the anterior abdominal wall, groin, retroperitoneum, mediastinum, and gluteal area. Slow-flow vascular malformations (including lymphatic malformations and phlebectasia) are common. Other manifestations of the syndrome include musculoskeletal (leg length discrepancy, chondromalacia patellae, dislocated knees, scoliosis, wide hands and feet, furrowed soles, sandal-gap toe, macrodactyly, talipes, windswept hand, hemihypertrophy), neurologic (neural tube defect, tethered cord), cutaneous (capillary malformation, epidermal nevus, multiple small nevi) and other anomalies (such as renal agenesis/hypoplasia). Spinal cord arteriovenous shunts are a rare and heterogeneous group of vascular anomalies.⁵ In CLOVE, the nature of the overgrowth of these conditions is distinct as

overgrowth has been referred to as “ballooning,” meaning gradual increase in volume of the affected soft-tissue whereas in Proteus syndrome, the overgrowth is referred to as “distorting,” and is progressive, far out of proportion to somatic growth and relentless.² Some features of CLOVES such as truncal overgrowth are evident at birth. In contrast, overgrowth in Proteus syndrome is usually minor or absent at birth. Furthermore, vascular anomalies (both slow-flow and fast-flow) are very common in CLOVES and are rare in Proteus syndrome.⁶ Symptoms such as epidermal naevi, hyperlipomatosis and vascular malformations parallel both Proteus syndrome and CLOVE syndrome. IHH is distinguished from both the syndromes by its slow and mild course, without major disfiguration and with isolated overgrowth of extremities.⁴ The suggestions that the management of CLOVES syndrome is mainly supportive’’ is inaccurate and may lead to poor or delayed treatment. Severe scoliosis, large truncal mass, paraspinal high-flow lesions with spinal cord ischemia, lymphatic malformations, cutaneous vesicles, orthopedic problems of the feet and hands and central phlebectasia/thromboembolism are just a few examples of significant morbidities that need active or prophylactic medical interventions. Long-term prognosis is still not clear but appears to be better than in Proteus syndrome.²

References

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