LEGIUS SYNDROME IN A 16 YEAR OLD CHILD

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ABSTRACT
A 16 yr old male child was presented in paediatric intensive care unit in status epilepticus with generalized tonic clonic seizures (GTCS) type of seizures and postictal left sided hemiplegia. We diagnosed the case of Legius syndrome (LS) based on multiple café au lait spots (CALMS) total seven in number of varying sizes all more than 15mm along with frecklings in the axillary region, macrocephaly, with subnormal IQ level, learning disabilities and recurrent seizures since early childhood. Family history was significant for the presence of multiple café-au-lait spots in the mother and maternal grand-father. The family was thoroughly examined for other features, but no signs suggestive of the Legius syndrome were found in them.

BACKGROUND
Legius syndrome is autosomal dominant disorder and caused by mutations in the sprouty related, EVH1 domain containing protein 1(SPRED-1) gene. Clinical manifestations include multiple cafe-au-lait spots, axillary/inguinal freckling and a degree of macrocephaly. Learning disabilities, developmental delay and attention deficit hyperactivity disorder (ADHD) are also known. Without the non-pigmentary signs of neurofibromatosis type 1 (NF1). It is a rare disorder (fewer than 200 individuals with a confirmed diagnosis), and it is difficult to differentiate from NF1 in early childhood (1). This is important in terms of prognosis and monitoring. We describe such a case in a 16 year old boy.

CASE
A 16 yr old boy was admitted to paediatric intensive care unit in status epilepticus (GTCS type) and loss of consciousness for 5 hours, with post ictal weakness in left upper and left lower limb. Initially child was stabilized with antiepileptics. Patient had past history of seizures from early childhood and was on antiepileptic therapy with partial control. He was evaluated and labelled with mental retardation with subnormal IQ and poor scholastic performance. Perinatal and birth history were not significant. Developmental milestones were normal except learning disability was present. His head circumference measured at 99.2th centile. On objective examination he was noted to have more than seven café-au-lait spots of varying sizes >15 mm in diameter over the back and trunk (Fig). In examination of central nervous system patient was conscious, oriented to time place and person, memory intact, intelligence quotient subnormal, insight present, difficulty in speech with all cranial nerves intact except seventh cranial nerve which revealed right sided upper motor neuron type facial nerve palsy. In motor There was flaccid paralysis of left upper and lower limb with normal muscle mass with decreased tone and power 0/5 power while right upper and lower limb motor examination normal. All superficial and deep tendon reflexes were normal except in right upper and lower limb with abnormal coordination of movements of both upper and lower limb in right side with abnormal gait, were sensory system was preserved. Basic blood and urine analysis showed no positive findings. Radiological investigation as MRI (magnetic resonance imaging) brain had signs of hypoxic ischemic encephalopathy showing large area of altered signal and partial restricted diffusion in right cerebral hemisphere likely a post epilepticus insult – one likely possibility of Neurofibromatosis type 1 was ruled out due to absence of neurofibromas or lisch nodules. Thus further genetic evaluation was advised (SPRED 1 mutation) for definite diagnosis.
DISCUSSION
Legius syndrome or NF1-like syndrome is a rare, autosomal dominant genetic skin pigmentation disorder. The clinical presentation of Legius syndrome is similar to that of NF1, characterized by multiple CALMs with or without axillary or inguinal freckling. Other NF1-associated features such as Lisch nodules, neurofibromas, NF1-specific bone lesions, optic pathway gliomas, and malignant peripheral nerve sheath tumors are absent. Additional clinical features have been reported in Legius syndrome: pectus excavatum or carinatum and unilateral postaxial polydactyly (2-5). Learning disabilities and behavioral problems are also possible manifestations of the disease (6). The syndrome was first described in 2007 by Brems et al (7) who identified that a heterozygous mutation in SPRED1 gene was responsible for this mild NF phenotype. Several SPRED1 variants, including sequence based changes and large deletions/duplications, have been linked to Legius syndrome (8,9) (Table).

CONCLUSION
It is a rare disorder and hard to distinguish it from NF1. Paediatricians must be aware of LS in all children with CALMs. The presentation in this case LS can be present with recurrent seizures with post ictal hemiplegia, learning disability, sub normal IQ level and macrocephaly. Recognition of the condition is important, to avoid the stress related to a NF1 diagnosis, but also for early cognitive and behavioural therapy.

REFERENCES

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