Intellectual disability in boys: mark the face!

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DESCRIPTION
A 5-year-old boy presented with developmental delay noted during infancy and behavioural problems for the past 2 years. He was noticed to be hyperactive and aggressive. He frequently hit his peers in school, showed bizarre habits such as smelling of undergarments, chewing of shirt collar and was self-absorbed. There was no history of seizures, encephalopathy, progressive neuromotor impairment, self-mutilation, abnormal body odour, skin rash or coarse facial features. He was born at full term to non-consanguineous parents by vaginal delivery and weighed 3.5 kg at birth. Postnatal period and family history was unremarkable. On examination, his developmental age was 4 years in motor sector and 2 years in language/social sector. He was alert, interested in surroundings, responded to simple commands, indicated toilet needs but could not sit at one place. He had a prominent forehead and upper lip, macro-orchidism, large ears and constant drooling (figure 1A,B). Rest of the systemic examination was unremarkable. A clinical diagnosis of fragile X syndrome was considered and confirmed by the presence of expanded CGG repeats (>200, full mutation range) on the FMR1 gene by PCR.

Fragile X or marker X mental retardation syndrome is characterised by moderate to severe intellectual disability, behaviour abnormalities, macro-orchidism (63%–95%) and a distinct facial profile consisting of high-arched palate (94%), long and/or narrow face (83%), macrocephaly (81%), prominent jaw (80%) and prominent ears (72%–78%) in men.1 Prominent ears is considered one of the hallmark clinical signs in patients with fragile X. Other physical features include long palpebral fissures, closely placed eyes, epicanthic folds, strabismus, broad nose and philtrum and flat nasal bridge which evolve with increasing age. Phenotype in women with fragile X is more variable and depends on the X-linked inactivation pattern. Nearly all (99%) cases are associated with unstable, trinucleotide CGG expansions (typically >200 triplets) in FMR1 gene resulting in hypermethylation, suppression of FMR1 transcription and reduced protein levels in the brain.2 The condition is hereditary, and a full family history is mandatory. Mothers are carriers, either of premutation or full mutation. Epilepsy, hyperactivity and autism spectrum disorder are important comorbidities in children with fragile X besides intellectual disability.3

Learning points
- Fragile X or marker X mental retardation syndrome is an important cause of moderate to severe intellectual disability.
- Distinct facial features such as high-arched palate, long and/or narrow face, macrocephaly, prominent jaw and ears make identification easy in the outpatient clinics.
- Epilepsy, hyperactivity and autism spectrum disorder are important comorbidities in children which need multidisciplinary care.

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