**INTRODUCTION**

Congenital constriction ring (CCR) (OMIM-217100) is a rare and heterogeneous condition which results in loss of limbs/digits.\(^1\) It is presented as an annular defect which ranges from circumferential groove in upper skin to the amputation of limb. It may occur with cranio-facial disturbances like face clefts, orbital defects, and anencephaly.\(^1,2\) However, CCR occurring with intellectual disability (ID) is very rare. Symbrachydactyly is another limb deficiency sequence characterized by brachymesophalangy, syndactyly and hypoplasia of hand.\(^2,3\) Symbrachydactyly has a non-syndromic occurrence while its involvement with ID is highly unusual.

Here, we present two sporadic subjects with CCR or symbrachydactyly, and with associated ID.

**CASE REPORT**

**Case 1:** An 18-year female subject was recruited from the urban locality of upper Punjab. Parental consanguinity was denied and there was no family history of any hereditary/congenital malformation. Reportedly, pregnancy events had been unremarkable and there was no history of any maternal exposure or risk factor. The subject was fourth of five siblings. She had a standing height of 145 cm and weighted 67 kg.

The physical examination showed bilateral CCR affecting the fingers, asymmetrically (Figures 1A and B).

In the right hand, digits 3-4-5 were replaced by a stubby mass. Roentgenograms revealed five metacarpals and the remnants of the proximal phalanx of digits 3-4-5. The index finger, though normal, demonstrated a compensatory ulnar splaying. In the left hand, digits 2-3-4 were amputated near the palm while the 5th finger was short and camptodactylous. The thumbs were unremarkable while there was crowding of carpals. Radii and ulnae exhibited no signs of shortening and sized 24 cm and 26.5 cm, respectively. The malformation was classified as CCR type 4, according to the scheme proposed by Patterson.\(^4\) The subject had flat and stubby feet with abnormal gait. Roentgenographic examination suggested metatarsus adductus (Figure 1C).

Additionally, the subject had mild ID (classified as per scheme of American Psychiatric Association).\(^5\) Reportedly, the developmental landmarks and speech had been slow. She learned toileting late and rarely had drooling and enuresis. She had some concept of money and was consistent with routine activities. There were no symptoms of psychosis and aggression. There was a normal onset of puberty. She had squint in the left eye and mild obesity. There were no oro-facial symptoms except hypodontia and abnormally arranged teeth. Hair and nails were normal.

**Case 2:** A 13-year male subject was recruited from North Khyber Pakhtunkhwa. His parents were first cousins and he was sixth of 10 siblings (Figure 1D). Paternal and maternal ages at the time of the subject's birth were 37 and 29 years, respectively. The family denied any history of maternal exposure or drug intake during that pregnancy.

The subject had unilateral symbrachydactyly of the right hand resulting in loss of fingers 2-3-4 (Figure 1E). There was an adducted thumb and rudimentary fingers 4 - 5. The extension/flexion movements at the wrist...
appeared normal. According to the Blauth and Gekeler scheme, this condition was classified as 'monodactylous hand' (type III). The left hand was unremarkable. Additionally, the subject had profound ID (classified as per scheme of American Psychiatric Association). He had no concept of money, food and clothes, showed no sense of social responsibility, and was completely dependent on his parents for self-care and toileting. He had weak lower limbs and was unable to walk without support. He had drooling and speech/hearing impairments. The behavioural problems like attention deficiency, aggression and hyperactivity were also evident.

**DISCUSSION**

Here, we report two independent subjects with congenital limb amputation associated with ID, which is a very rare and remarkable presentation. The first individual presented with CCR and ID. As differential diagnosis, we considered Adams-Oliver syndrome (AOS) (OMIM-100300), which is characterised by cutis aplasia and transverse limb defects. However, mental retardation and squint eye are not part of AOS. There is also some overlap of clinical symptoms with Cohen syndrome (OMIM-216550), which in addition to mental retardation, poor dentition, eye abnormalities, and truncal obesity, has other cardinal features like microcephaly, micrognathia, narrow and high-arched palate, infantile hypotonia, and short stature. Further, mental retardation, mild obesity and eye defects are also features of Bardet-Biedl syndrome (OMIM-209900), which additionally exhibits polydactyl, abnormalities of genitalia and kidneys, and impaired speech, among several other complications. Nonetheless, the frequent occurrence of CCR with neurological symptoms has been argued to have common etiology. For instance, Chen and Gonzalez recruited six subjects with CCR and among the neurocutaneous manifestations they observed microcephaly, mental impairment, hypertonia, micro-ophthalmia, and psychomotor deficiencies. Yamanouchi et al. reported a child with CCR and congenital perisylvian syndrome (pseudobulbar palsy, bilateral perisylvian polymicrogyria, epilepsy, mental retardation).

For the phenotypic condition in our second subject, we considered Poland syndrome and Moebius syndrome. Poland syndrome (OMIM-173800) is a well characterised disorder, hallmarks of which are symbrachydactyly/limb deficiency and ipsilateral pectoral hypoplasia. The rare association of Poland syndrome with mental retardation, microcephaly, cerebral atrophy and psychosocial retardation, have also been reported. Moebius syndrome (OMIM-157900) is another rare abnormality presenting with symbrachydactyly/limb deficiency associated with facial paralysis and the inability to move eyes. The affected subjects additionally have chest wall abnormalities, difficulty in breathing and/or in swallowing and strabismus. Rarely however, Moebius syndrome has also been shown to be associated with ID.

Congenital limb defects put a great impact on the lives of the affected subjects and are a matter of tremendous shock for a pregnant couple discovering the situation in their child. Fortunately, a large number of limb anomalies can be correctly detected prenatally through Doppler/3D ultrasound. Hence, there is a dire need for prenatal diagnosis and genetic counselling for helping the
parents in families at risk, and in making an informed decision for the status of pregnancy. The families could be counselled regarding the hereditary conditions resulting in limb defects, maternal factors like diabetes mellitus, vasculature disruptions and intrauterine infection, and pharmaceutical factors involving exposure of drugs like thalidomide and teratogens.

In conclusion, the cases presented here exhibit a unique and rare combination of congenital limb deficiency and ID, which are not reported in the regional/local medical literature. Further studies are warranted in order to characterise the malformations observed in the recruited subjects on molecular genetic bases.

REFERENCES


