Case Report

A new syndrome with overlapping features of Townes-brocks syndrome and single median maxillary central incisor syndrome

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A 14-month-old boy with overlapping features of Townes-Brocks syndrome (TBS) and single median maxillary incisor syndrome (SMMCIS) is being reported with brief review of the above syndromes and possible differential diagnosis.

Key words: Microcephaly, single median maxillary central incisor syndrome, Townes-Brocks syndrome

Introduction

Townes-Brocks syndrome (TBS) (OMIM # 107480) is an autosomal dominant disorder with incomplete penetrance and variable expression characterized by imperforate anus, ear anomalies, thumb and renal malformations.[1] Single median maxillary central incisor is specifically seen in association with SMMCI syndrome (SMMCIS) (OMIM # 147250), which is characterized by SMMCI, congenital nasal obstruction, midline facial malformations including holoprosencephaly, short stature, and microcephaly.[2] We report a rare association of TBS with SMMCI in a 14-month-old male child. This association to our knowledge has not been reported previously in literature.

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Case Report

A 14-month-old male child presented with acute diarrhea for 3 days. The child was born as second child to non-consanguineously wed parents by spontaneous vaginal delivery following an uneventful antenatal period with a birth weight of 2.5 kg. He was noted to have imperforate anus at birth for which a corrective surgery was done in the first week of life. He was exclusively breast-fed for 6 months and immunized for age. Child was noted to have mild global developmental delay. The Social Quotient according to Vineland social maturity scale (VSMS) was 60%. Physical examination revealed dysmorphic facial features in the form of microcephaly, dysplastic ears [Figure 1], hypoteleroism, absence of superior labial frenulum, and single median maxillary central incisor [Figure 2]. The child also had bilateral pre-axial polydactyly. Anthropometry revealed height, weight, and head circumference less than 3rd centile for age and sex. Systemic examinations were within normal limits. In view of dysmorphic features, the child was investigated for other associated anomalies. Screening audiometry was found to be normal. Ultrasound abdomen revealed numerous cysts in both renal cortices measuring 2 to 5 mm in size; however, renal function tests were normal. Computerized tomography of brain revealed no abnormalities. Electrocardiogram and Echocardiography were normal. Chest and skeletal radiographs were ordered to rule out any bony abnormalities but found to be normal. There were no similar complaints in the family and examination of the elder sibling and parents were

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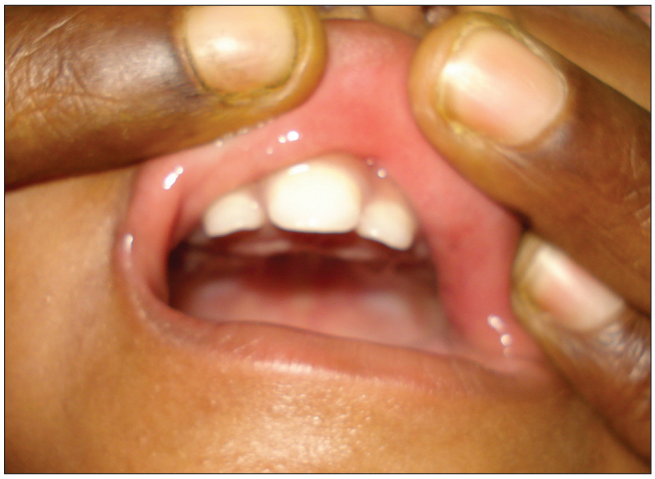

Figure 1: Overfolding of superior helix of ear

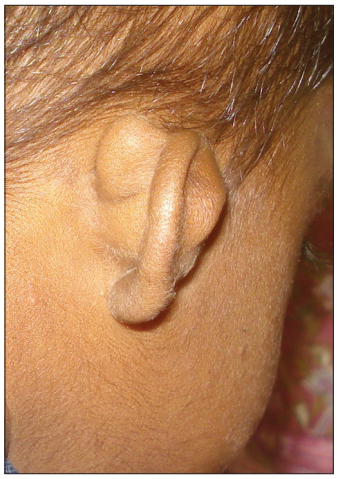

Figure 2: Solitary median maxillary central incisor

normal including ultrasonography of abdomen. Genetic study could not be done due to limitation of resources and expertise in this part of the world.

Discussion

TBS was first described by Townes and Brocks in the year 1972. The gene associated with this disorder has been found to be *SALL* 1 gene mapped to chromosome 16q12.1.[1] The diagnostic criterion of this disorder includes two or more of the following: Anorectal malformation, radial anomalies, ear malformations, and family history of similar abnormalities.[1] The reported renal anomalies in this syndrome include bilateral hypoplastic, dysplastic, or polycystic kidneys, renal agenesis, posterior urethral valves, vesicoureteric reflex, and meatal stenosis. Intelligence is usually preserved in most of the cases, but 10% of cases can sustain mental retardation.[3] It was previously known as R-E-A-R syndrome (Renal, ear, anal, and radial anomalies).[1]

Solitary median maxillary central incisor syndrome (SMMCI) is a complex disorder consisting of multiple midline defects of development of unknown etiology. Missense mutation in the *SHH* gene (I111F) at 7q36 may be associated with SMMCI.[4] It can occur as an isolated condition or in association with serious anomalies like holoprosencephaly. Subtle facial dysmorphic features include a flat nasal bridge and tip; a single, midline, upper incisor; a bifid uvula; absent nasal bones and nasal septum; and congenital nasal pyriform aperture stenosis.[2]

Table 1: Comparative features of townes-brocks syndrome, Single median maxillary incisor syndrome and the reported case

Abnormality	TBS	SMMCIS	Case
Ear anomaly	+		+
Hearing loss	±		
Polydactyly	+		+
Imperforate anus	+		+
Genito-renal	+		+
Cardiac anomaly	±	+	
Dev delay and MR	±	+	+
Dysmorphic face		+	+
Holoprosencephaly		+	
Nasal stenosis		+	
SMMCI		+	+
Microcephaly		+	+
Short stature		+	+
Hypoteleorism		+	+

± -- (Incidence is <10%); TBS = Townes-brocks syndrome; SMMCIS = Single median maxillary incisor syndrome

The reported case had features overlapping both TBS and SMMCIS. The comparative details of individual features are given in Table 1.

The clinical findings described in our report share features of both TBS and SMMCIS. To the best of our knowledge, this association has never been reported earlier. Both *SALL* 1 gene and SHH play important roles during embryonic development, especially in vertebrate organogenesis, limb formation, and neural tube development.[3,5]

The expression of *SALL* gene depends upon several signal transduction pathways including SHH.[6] Since the gene involved in SMMCI is *SHH*, there can be a theoretical possibility of a single mutation in either *SALL*

or *SHH* gene leading to the development of a combined phenotypic expression of both syndromes.

Though VACTERL association was considered as one of the differential diagnosis, it was ruled out as they typically do not have dysmorphic features, growth retardation, and microcephaly.[7] Other closely related differential diagnoses that were considered include oro-facial digital syndrome, Meckel-Gruber syndrome, and hemi facial microsomia. However, our case did not fit into any one of these syndromes.

Conclusion

The case report indicates the possibility of a new syndrome with overlapping features of TBS and SMMCI, since the genes involved in the pathogenesis of both these syndromes are inter-related. Similar reports in future with genetic studies specifically looking at *SALL* 1 and *SHH* gene can help in understanding this new syndrome in a better manner.

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