DOOR Syndrome

MEENAKSHI GIRISH, NILOFER MUJAWAR AND ATUL SALODKAR*

From Department of Pediatrics, NKP Salve Institute of Medical Sciences & Lata Mangeshkar Hospital; and Salodkar Hospital, Dermatology Clinic, Ramdaspeth; Nagpur, India.*

Correspondence to:
Dr Meenakshi Girish,
101, Shubham Enclave, Darda Marg,
Rahate Colony, Nagpur 440 022,
Maharashtra, India.
min_gir@rediffmail.com
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DOOR syndrome is a rare multisystem genetic disorder, consisting of deafness (sensorineural), onychodystrophy, osteodystrophy, and mental retardation. Seizures reported frequently in this condition are often refractory to treatment.

Key words: *Deafness, DOOR syndrome, Onychodystrophy, Osteodystrophy, Mental retardation.*

DOOR syndrome is a rare genetic disorder with fewer than 35 cases reported from all over the world. Its mode of inheritance is presumed to be autosomal recessive. "DOOR" is an acronym that refers to deafness (sensorineural hearing loss), onychodystrophy (small or absent nails on hands and feet), osteodystrophy (small or absent distal phalanges of the hands and feet), and mental retardation [1]. A neurometabolic etiology is postulated though the exact etiology is not known. There are no reports of such a case from India.

CASE REPORT

A 14-month-old boy presented with history of focal clonic seizures since the age of 5 months. The boy was the only child of a consanguineous marriage, born full term by normal vaginal delivery. There was no history of polyhydramnios. His birthweight was 3.5 kg and there were no perinatal or neonatal problems. Developmental retardation maximally affected the motor and language milestones while cognitive and social milestones were minimally delayed . He had no response to verbal or nonverbal sounds. Family history was unremarkable.

On examination, he weighed 6.04 kg (<5th centile), length was 65.5 cm (<5th centile), and head circumference 43.5 cm (<5th centile). There were no distinctive facial features. Dentition was normal. General examination showed characteristic abnormalities of the digits including abnormal thumbs, which were unusually long and had an extra flexion crease bilaterally. Hypoplastic nails with clinodactyly was seen bilaterally on the fifth finger and small deep-set nails were present on all other digits. Similarly, nails were absent in the 2nd through 4th toes, while the 1st and 5th toes had hypoplastic nails bilaterally (***Fig* 1**). Systemic examination including neurologic examination was normal except for deafness. Ophthalmic examination was also normal.

Investigations revealed profound bilateral sensorineural deafness on BAER test. Biochemical workup was within normal limits. Urinary 2-oxoglutaric acid was elevated. Interictal EEG, CSF study and MRI brain, and echocardiogram all were normal. USG abdomen did not show any renal abnormalities. *X*-Ray of wrists and hands showed triphalangeal thumb on both sides with hypoplastic and dysplastic middle and distal phalanx. Distal phalanges of little fingers on both sides were aplastic (***Fig* 2**). The seizures could only be controlled on a combination of valproate and topiramate.

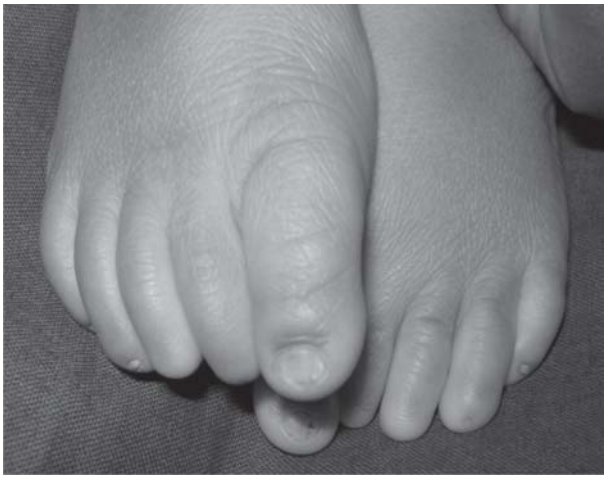

FIG. 1 *Absent nails in 2nd through 4th toes and hypoplastic nails in fifth toe.*

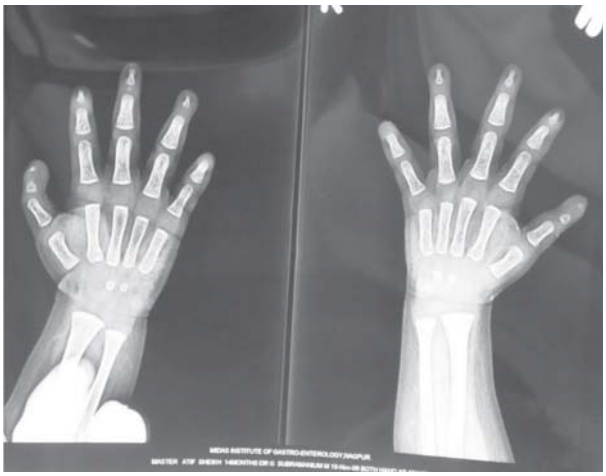

FIG. 2 *Triphalangeal thumb and hypoplastic distal phalanx in other fingers.*

DISCUSSION

Characteristic hand and nail malformations, with sensorineural deafness confirmed on BAER, and retardation suggested the diagnosis on clinical grounds. Due to paucity of cases and heterogeneity of the characteristic manifestations in DOOR syndrome, a tentative classification was proposed in 2000 [2] based on presence or absence of 2, oxoglutaric aciduria. The syndrome was divided into types I and II, with type I (elevated urinary 2-oxoglutaric acid) following a progressive neurologic course and early mortality and type II having a milder clinical course. Sensorineural deafness, onychodystrophy, osteodystrophy and developmental delay were reported in all published cases. Other features described are craniofacial abnormalities, especially coarse facies (78%). Only 67% reported abnormal findings in neuroimaging studies. Peripheral neuropathy and defects in other systems like cardiac (17%), renal (17%) and ophthalmic (29%) have also been reported [3]. Our patient did not have any of these additional features. Radiological evidence of distal phalangeal hypoplasia in toes and fingers and triphalangeal thumbs were the diagnostic features found in all reported cases. Seizure disorders from infancy are reported (87%) as a prominent clinical manifestation [3]. Seizures described are generalized tonic clonic, myoclonic, suspected absence and partial [4-6]. Seizures begin within the first year of life, may have a progressive nature and for the most part they are poorly controlled with medications [7-9]. Episodes of status epilepticus are common. Descriptions of EEG findings in published cases are variable but commonly show high amplitude slow activity and spike/sharp waves.

Prognostic markers have not been clearly defined. 32% have been documented to have early mortality, before 2 years of age with status epilepticus as the most common cause of death. After 4 years, deaths due to this syndrome have not been reported and the mortality is reported to be the same as that of general poulation. The differential diagnosis includes Coffin Siris syndrome (no deafness), Zimmerman Laband syndrome (hepatosplenomegaly present but mental retardation and deafness are not universal), fetal hydantoin syndrome, and fetal alcohol syndrome [3].

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Numb Chin Syndrome in Acute Lymphoblastic Leukemia

JASMIN PANSY, HERWIG LACKNER, MARTIN BENESCH AND CHRISTIAN URBAN

From Division of Pediatric Hematology and Oncology, Department of Pediatrics and Adolescent Medicine, Medical University of Graz, Austria.

Correspondence to:
Dr Jasmin Pansy, Division of Pediatric Hematology and Oncology, Department of Pediatrics and Adolescent Medicine,
Medical University of Graz,
Auenbruggerplatz 30, A-8036 Graz, Austria. jasmin.pansy@medunigraz.at
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Numb chin syndrome is a sensory neuropathy of the inferior alveolar branch of the trigeminal nerve, characterized by unilateral numbness of the chin, the lower lip and the buccal and gingival mucosa. We report a girl with acute lymphoblastic leukemia of B-cell type who initially presented with numb chin syndrome resulting from skull base infiltration.

Key words: *B-ALL, Complications, Cranial nerve involvement, Numb chin syndrome*.

Numb chin syndrome (NCS) is a sensory neuropathy of the inferior alveolar nerve, a branch of the trigeminal nerve. In adults, NCS may be associated with malignancies of breast, lung and prostate [1]. It has also been described in Non-Hodgkin lymphoma and Burkitt lymphoma. Numb chin syndrome is uncommonly reported in children [2-5]. We report this syndrome as one of the initial symptoms of acute lymphoblastic leukemia in a child.

CASE REPORT

A 9-year-old girl presented with a two week history of increasing fatigue, fever, night sweat and weight loss. Physical examination revealed firm and painless right-sided fronto-parietal swellings. There was no lymphadenopathy or hepatosplenomegaly. The girl also reported unilateral hypoesthesia of the left chin, the lower lip, and the gingival and buccal mucosa for one month. There were no other neurological symptoms. MRI of the head showed multiple bone lesions with contrast-enhancement of the extra- and intracranial soft tissue at different locations (frontal, right temporo-parietal, left sphenoid and left mastoid). Complete blood count was within normal limits, but LDH (2315 U/L) and uric acid (16.9 mg/dL) were highly elevated. Typical Burkitt blasts were seen in the blood smear and the bone marrow was completely replaced by blasts. Cerebrospinal fluid showed no evidence of leukemic cells. The patient was treated according to the prospective multicenter trial B-NHL BFM 04 with