Freeman-Sheldon Syndrome—Prenatal and Postnatal Diagnosis

Sridevi S. Hegde, Mitesh S. Shetty and B.S. Rama Murthy

Department of Medical Genetics, Manipal Hospital Bangalore and 1 Srinivasa Ultrasound Scanning Centre, Bangalore, India

ABSTRACT

A six-day-old girl, born to normal non-consanguineous parents presented with mask like facies with a small mouth giving a ‘whistling’ appearance. Other dysmorphic features include deep set eyes, broad nasal bridge, long philtrum and ‘H’ shaped cutaneous dimple on the chin. There was congenital windmill vane hand position and severe talipes equinovarus deformity. The above features are characteristic of Freeman-Sheldon syndrome also known as Whistling Face syndrome. Ultrasound scanning during 8th month of the pregnancy showed the fetus to have facial abnormality and bilateral clenched hand and talipes with extension contractures of knees. Provisional diagnosis of FSS was made which was confirmed after the birth. Thus all cases of Arthrogryposis during prenatal scan should be carefully looked for the facial abnormality in the fetus.

[Indian J Pediatr 2010; 77 (2) : 196-197] E-mail:sridevi.hegde@manipalhealth.com

Key words: Freeman-Sheldon syndrome; Whistling face syndrome; Arthrogryposis; MYH3 Gene

Freeman-Sheldon syndrome (FSS) is a rare autosomal dominant genetic disorder with facial and joint abnormalities. It was first described as craniocarpotarsal dystrophy by Freeman and Sheldon in 1938.1 Burian et al. (1963) rediscovered the entity and called it the ‘Whistling Face Syndrome’.2 Bamshad et al. (1996) suggested that FSS should be considered a form of distal arthrogryposis with facial abnormality and referred as distal arthrogryposis type 2A (DA2A).3 Most cases are sporadic but affected siblings of unaffected parents suggest autosomal recessive inheritance also. Toydemir et al. (2006) showed mutations in the embryonic myosin heavy chain (MYH3) gene at 17p-13.1-pter causing FSS.4 Vimercati et al. (2006) reported the first case of prenatal diagnosis in a fetus with FSS.5

REPORT OF CASE

A six-day-old female baby was referred with dysmorphic features for genetic evaluation. She is the second child of normal non-consanguineous parents. Mother had undergone ultrasound scan in the last trimester for polyhydramnios. Following bilateral fetal abnormalities of micro-ophthalmia, clenched hand and talipes with extension contractures of knees were observed. A soft tissue ridge extending from one cheek to the other cheek across the chin was noted by the sonologist (Fig.1). This was discussed with us at the genetics department. A preliminary diagnosis of FSS was made on the basis of above mentioned features. There is no family history of congenital malformation. She was born at full term by caesarian section. On day six, weight of the child was 2200g (<5th centile), the height was 42cm (<5th centile) and head circumference measurement was 33.4cm (<25th centile). She had mask like facies with small puckered mouth giving a ‘whistling’ appearance. She had small mouth which could not be opened fully. Eyes were deep set with hypertelorism and micro-ophthalmia. Nose was small with broad nasal bridge and hypoplastic alae nasi. Ears

Correspondence and Reprint requests : Dr Sridevi S. Hegde, Head and Consultant Clinical Geneticist, Department Of Medical Genetics, Manipal Hospital, Old Airport road, Bangalore-560017, India.

[DOI-10.1007/s12098-009-0227-6]
[Received June 27, 2008; Accepted October 15, 2008]
were malformed and posteriorly rotated. Neck was short with lax skin over the nape. She had long philtrum with ‘H’ shaped dimpling of chin. There was congenital windmill vane hand position, bilateral ulnar deviation and contracture of fingers 2-5 at the metacarpophalangeal joints with adduction of thumbs. There was limited abduction of hip with bilateral severe club foot (Fig.2). Chromosome analysis was normal.

Fig. 2. Six day old baby showing hypoplastic alae nasi, long philtrum, ‘H’ shaped dimpling of chin, small mouth giving whistling appearance, congenital windmill vane hand position and bilateral severe club foot.

DISCUSSION

In the present case, there is contracture of the distal joints of hands and feet like camptodactyly and club foot plus facial dysmorphism thus meeting the diagnostic criteria of classical FSS. Hence the provisional diagnosis made during prenatal period was confirmed after the birth. There is no family history of similar disorders and normal non-consanguineous parents with normal older sibling suggest sporadic case due to mutation only in the proband. Zampino et al. (1996) suggested that it would be more appropriate to speak about the Freeman-Sheldon spectrum rather than syndrome because of the different pathogenetic mechanisms (muscular, skeletal, and neurologic), the wide range of clinical manifestations, and the genetic heterogeneity. This syndrome should be differentiated from other arthrogryposis syndrome, Schwartz-Jampel syndrome and Trismus-pseudo camptodactyly syndrome.

The prognosis or natural history in these children is feeding difficulties, vomiting and dysphagia leading to failure to thrive. Most of the features are secondary to increased muscle tone. There may be early mortality due to aspiration. Intelligence and life expectancy is normal in majority who survive with modest motor and speech delays in childhood. Dental crowding and oral hygiene secondary to small mouth can be a problem. There is postnatal growth deficiency. Anesthetic complications are relatively common therefore need to carefully evaluate before surgery. Genetic counseling was given to the parents explaining the nature, the prognosis and the management of this syndrome. Recurrence risk in the future offspring is probably slightly higher than the population risk. Prenatal diagnosis is possible in the subsequent pregnancy by level II ultrasound scan. Facial and limb abnormality of FSS can be detected in the second trimester anomaly scan and standard chart for fetal lip width prepared by Vimercati et al can be used. Thus all cases of arthrogryposis during prenatal scan should be carefully looked for the facial abnormality in the fetus.

Acknowledgment: We thank Dr Jagadish Chinnappa, Manipal Hospital, Bangalore for referring the patient to Department of Medical Genetics.

Contributions: Dr Sridevi Hegde was involved in the clinical evaluation of patient and correction of the manuscript. Dr Mitesh Shetty was involved in literature review and drafting of the manuscript. Dr B. S. Rama Murthy was involved in the ultrasound scanning of the fetus and provided the ultrasound pictures.

Conflict of Interest: None.

Role of Funding Source: None.

REFERENCES