

Escobar Syndrome Affecting Two Male Siblings in a Family: A Rare Case Report

Dr. Uday C. Rajput¹, Dr. Srikanth Kulkarni¹, Dr. S.S Wagh²

¹Assistant Professor, Department Of Pediatrics, Govt. Medical College, Miraj- 416410, Maharashtra.

²Professor, Department Of Pediatrics, Govt. Medical College, Miraj- 416410, Maharashtra.

*Corresponding Author:

Name: Dr. Uday C Rajput

Email: drudayrajput@gmail.com

Abstract: Escobar syndrome also known as non lethal type of multiple pterygium syndrome, is characterised by webbing (pterygium) of neck, axilla and extremities, fixed contracture of multiple joints (arthrogryposis) and with normal intelligence. Pterygium syndromes are heterogenous group of disorders with sporadic, autosomal recessive (most common) and autosomal dominant inheritance pattern. We report two male siblings born of consanguineous marriage with Escobar syndrome.

Keywords: Escobar syndrome, multiple pterygium syndrome, arthrogryposis

INTRODUCTION

Multiple pterygium syndrome comprises a group of multiple congenital anomaly disorders characterised by pterygium of neck, axilla, popliteal fossa, elbow and digits and arthrogryposis multiplexa congenital i.e. multiple fixed joint contractures. The multiple pterygium syndromes are phenotypically and genetically heterogeneous disorders divided into prenatally lethal and nonlethal (Escobar syndrome) types. Mode of inheritance in Escobar syndrome is most commonly by autosomal recessive pattern, though other modes of inheritance has been described. It was first described in 1902 by J. A. Boussiere [1]. In Pondicherry later on Victor Escobar and his associates compiled the various clinical manifestations and the disease was termed as Escobar syndrome in 1982[2].

Only 3 case reports have been published from India till date. Proper diagnosis of disease is important because of its genetic inheritance and disease can be prevented by genetic counselling.

CASE REPORT

4 year old male child was referred to paediatric department for limb deformities and facial dysmorphism. Child was 2nd issue of III degree consanguineous marriage born of uneventful pregnancy with no neonatal complications.

Anthropometric assessment showed following details: height- 97 cms(10th percentile), weight- 13.5

kg(5th -10th centile) and head circumference 48.5 cms(50th percentile). On general physical examination child had characteristic facies- Sad, emotionless face, congenital B/L ptosis, low posterior & posterior-lateral hairline downward slanting eyes, low set ears, depressed nasal bridge, high arched palate, and epicanthic folds. Child's intelligence was normal.

Pterygium involving Axilla, Neck, Popliteal fossa and elbow joint with multiple joint contractures in the form of B/L knee flexion, fixed flexion deformity of hip, rocker bottom feet, camptodactyly, clinodactyly were predominant signs. In addition child also had scoliosis and undescended testis. Systemic examination doesn't reveal any significant abnormality.

On investigation, radiography was suggestive of rocker bottom feet with vertical talus, flexion contracture of fingers, mild scoliosis and fusion of cervical vertebra. Liver, kidney, heart and hematological work up were normal. Karyotyping was normal.

Child's clinical features were consistent with Escobar syndrome. On analyzing family history younger sibling also had similar clinical features with ptosis and joint contractures. Pterygium in this child was not prominent. Parents and elder sister were normal.

Pedigree chart

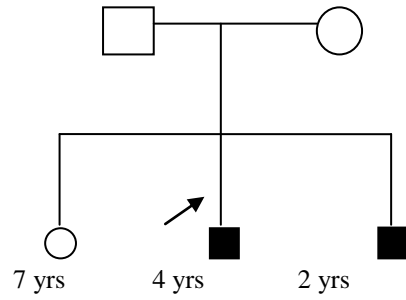


Fig. 1: B/l ptosis in a case of Escobar syndrome



Fig. 2A, 2B, 2C: Pterygium of axilla, neck (with low hairline) and elbow



Fig. 3A, 3B: Multiple joint contractures with rocker bottom foot and camptodactyly



Fig. 4: Cryptorchidism



Fig. 5: Younger sibling with ptosis and rocker bottom foot

DISCUSSION

The clinical & laboratory features of MPS have most often been described in literature under the diagnosis of arthrogryposis multiplex congenita, Bonnevie-Ullrich syndrome & more recently Multiple Pterygium syndrome (Escobar syndrome OMIM 26500).

First description of the disease was done by J.A. Bussiere in 1902 from Pondicherry [1], who described a patient with multiple pterygia with resemblance to a cobra (cobra man/l'homme cobra), possibly because of the webbing of neck and microcephaly. This syndrome was fully delineated by Escobar *et al.* in 1978 and got its name as Escobar syndrome in 1982 [2].

Most consistent clinical features of the disease described by Escobar *et al.* [2] are: pterygium of neck(100%), antecubital fossa(90%) and popliteal fossa(90%), camptodactyly (84%) and syndactyly(74%) of fingers, numerous flexion contractures of joints(74%) and foot deformities(74%). Other features included are umbilical hernia, lordosis, vertical talus, cleft lip, cleft palate, furrowed tongue, peculiar spoon shape tongue (lingua cochlearis), ptosis, cryptorchism, small penis, small clitoris, and hypoplastic/absent labia majora [3].

Lethal form of MPS is characterised by multiple pterygium, hydropsfetalis and /or hygroma coli. Usually it is associated with pulmonary

hypoplasia. It can be diagnosed by 2nd trimester ultrasonography and stillbirths are common [4].

Spranger *et al.* [5] reported 2 cases with autosomal recessive multiple pterygium syndrome, type Escobar, who described multiple pterygia, severe contractures, short stature and external genital anomalies are prominent features. A striking feature was severe muscular atrophy.

Rajab *et al.* [6] described 6 Omani children with a multiple congenital anomaly syndrome showing clinical features of Escobar syndrome overlapping with Freeman-Sheldon syndrome as well. Affected individuals manifested arthrogryposis multiplex congenita, multiple pterygia, typical facial appearance, ophthalmologic anomalies and atrophic calf muscles. In addition, the patients presented distinctive features, including furrowed tongue and enlarged corneal nerves that had not previously been described in association with distal arthrogryposis syndromes.

Shalev *et al.* [7] reported a large consanguineous Arab family in which 9 members had some of the typical features of Escobar syndrome. Affected members were unusual in that they lacked pterygia in the lower body, and 8 of 9 had an abnormally widened umbilical area with an umbilical hernia and apparent hypoplasia of the periumbilical skin.

Hoffmann *et al.* [8] found that the first diagnostic sign is that of reduced fetal movement detected by ultrasound or reported by mothers. At birth,

the children come to medical attention because of variable joint contractures, multiple pterygia, and facial dysmorphism with long face, high-arched palate, small mouth, and retrognathism. Respiratory distress is a frequent life-threatening complication.

The mode of inheritance is usually autosomal recessive and rarely autosomal dominant or sporadic. The pattern of inheritance seen in our case report appears to be autosomal recessive, though X-linked cannot be ruled out since all affected were males. Prontera *et al.* [9] reported a 3-year-old girl with classical clinical features of multiple pterygium syndrome with father showing subtle minor signs of the disorder. The authors suggested that this family may either show autosomal dominant inheritance or that the father is a manifesting heterozygote.

Michalk *et al.* [10] and Hoffmann *et al.* [8] describes mutations in the fetal expressed γ subunit (*CHRNA3*) of AChR were found in both lethal MPS and Escobar syndrome.

Hoffmann *et al.* [8] noted that the congenital contractures characteristic of Escobar syndrome may be caused by reduced fetal movements at sensitive times of development. Possible causes of decreased fetal mobility include space constraints such as oligohydramnion, drugs, metabolic conditions, or neuromuscular disorders including myasthenia gravis.

Differential diagnosis of this condition include popliteal pterygium syndrome, antecubital pterygium syndrome and arthrogryposis multiplexa congenital. In popliteal pterygium syndrome, pterygium of neck, axilla and antecubital fossa are absent with contractures are restricted to knee [11]. Antecubital pterygium syndrome reported by Wallis *et al.* [12] had clinical feature of bilateral antecubital webbing, absent long head of triceps and absent skin creases over dorsal surface of distal interphalangeal joint. Both these conditions have autosomal dominant inheritance.

Case reports of Escobar syndrome published in India till date are: Madhuri *et al.* [13] described a 5 yr girl with multiple pterygium syndrome associated with translocation of chromosome 6/7 and Amal Nath *et al.* [14] from Pondicherry reported 3 male patients of Escobar syndrome from same family.

Management option for these patients is multidisciplinary approach involving physician, orthopaedic surgeon, physiotherapists and plastic surgeon. The disease can be prevented by antenatal diagnosis. Many organisations are there for general support to family and social networking websites in the name of Escobar syndrome are created where patients/parents can share their experiences and newer modalities of treatment available for various manifestations of the disease.

Key Message

This crippling disease can be easily diagnosed by its characteristic clinical features without any costly investigations. As there is 25 % chance of affected baby (most commonly autosomal recessive inheritance) to be born in each further pregnancy, which can be prevented by proper genetic counselling.

Contributors

UCR was involved in diagnosis and investigation of the case. SSK and SSW were involved in writing of manuscript of case report.

ACKNOWLEDGMENTS

The authors thank head of the department of paediatrics and the Dean for allowing us to report the case.

REFERENCES

1. Bussiere JA; Developement Abnormal D'un Faisceau Musculaire Acromio-Mastoidien Rudimentaire, Malformation Congenitale Rare, Observe'e A Pondicherry (Indes Orientales). *Annales d'hygiene et de medecine coloniales*, 1902; 5: 686-688.
2. Escobar V, Bixler D, Gleiser S, Weaver DD, Gibbs T; Multiple pterygium syndrome. *American journal of diseases of children*, 1978;132(6): 609-611.
3. Smith DW, Jones KL; *Smith's Recognisable patterns of Human Malformation*, 5th edition, Philadelphia: W.B.saunders; 1997: 306,307.
4. de Die-Smulders CE, Schrandt-Stumpel CT, Fryns JP; The lethal multiple pterygium syndrome: a nosological approach. *Genetic counseling*, 1990;1(1): 13-23.
5. Spranger S, Spranger M, Meinck HM, Tariverdian G; Two sisters with Escobar syndrome. *American journal of medical genetics*. 1995; 57(3): 425-428.
6. Rajab A, Hoffmann K, Ganesh A, Sethu AU, Mundlos S; Escobar variant with pursed mouth, creased tongue, ophthalmologic features, and scoliosis in 6 children from Oman. *American journal of medical genetics Part A*. 2005; 134A(2): 151-157.
7. Shalev SA, Spiegel R, Hall JG; A syndrome characterized by contractures and pterygia of upper body associated with umbilical hernia, short stature, and distinctive face in an Arabic family. *American journal of medical genetics Part A*. 2005;138A(3): 236-240.
8. Hoffmann K, Muller JS, Stricker S, Megarbane A, Rajab A, Lindner TH, et al. Escobar syndrome is a prenatal myasthenia caused by disruption of the acetylcholine receptor fetal gamma subunit. *American journal of human genetics*. 2006; 79(2): 303-312.

9. Prontera P, Sensi A, Merlo L, Garani G, Cocchi G, Calzolari E; Familial occurrence of multiple pterygium syndrome: expression in a heterozygote of the recessive form or variability of the dominant form? American journal of medical genetics Part A. 2006; 140(20): 2227-2230.
10. Michalk A, Stricker S, Becker J, Rupps R, Pantzar T, Miertus J *et al.*; Acetylcholine receptor pathway mutations explain various fetal akinesia deformation sequence disorders. American Journal of Human Genetics. 2008; 82(2):464-76.
11. Escobar V, Weaver D. Popliteal pterygium syndrome: a phenotypic and genetic analysis. Journal of medical genetics. 1978;15(1): 35-42.
12. Wallis CE, Shun-Shin M, Beighton PH; Autosomal dominant antecubital pterygium: syndromic status substantiated. Clinical genetics. 1988; 34(1): 64-69.
13. Madhuri V, Bose A, Danda S, Shivakumar S, Kirubakaran C, Seshadari MS; Chromosomes 6/7 translocation t (6:7) (q15;32) presenting as multiple pterygium syndrome. Indian pediatrics. 2001; 38(2):194-197.
14. Amalnath DS, Subrahmanyam DK, Sridhar S, Dutta TK; Escobar syndrome in three male patients of same family. Indian journal of human genetics. 2011;17(1): 22-25.