Escobar (Multiple pterygium) syndrome – Report of a rare genetic disorder

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Abstract

Pterygium syndromes are a heterogeneous group of syndromes with sporadic, autosomal recessive or autosomal dominant inheritance. Multiple pterygium syndrome is a rare, autosomal recessive inherited disorder manifested by two types - lethal and the non-lethal type. Escobar syndrome is the name given to the non-lethal type. The characteristic features of this syndrome are congenital arthrogryposis, pterygia and spine deformities. In this case report we present a seven year old Indian boy with characteristic facial and radiographic features suggestive of this syndrome. Patient's syndromic features, intra oral findings, and management are also discussed.

Key words: Autosomal recessive, Escobar, multiple pterygium syndrome, sporadic

Introduction

Escobar syndrome or the multiple pterygium syndrome (MIM 609339) is an autosomal recessive condition characterized by excessive webbing (pterygia), congenital contractures (arthrogryposis) and spine deformities.[1] The synonyms of this rare syndrome are arthrogryposis multiplex congenita, Bonnevie - Ulrich Syndrome, pterygium syndrome and more recently as multiple pterygium syndrome.[1,2] The most distinguishing characteristic feature of this syndrome is the presence of multiple pterygia or cutaneous contractures but with normal intelligence. The first case was described by Bussiere from Pondicherry in the year 1902[3]. However, it was named as multiple pterygium syndrome by Gorlin *et al* in 1976.[4] Six years later in 1982 it was named as Escobar Syndrome after Escobar who along with his associates prepared an extensive report on this disease in 1978[3]. The etiology of this syndrome is unknown. However it has been suggested that mutations within the gamma subunit of CHRNG gene of Acetyl Choline receptor (AChR) is responsible for the muscle contractures seen in this disorder.[5]

Extensive review of Indexed literature revealed very few case reports on this disorder[1-24] [Table 1]. To the best of author's knowledge till date only four cases are documented from India. One case is from Vellore (Tamilnadu, India) and three cases from Pondicherry. Therefore, the aim of this article is to present the fifth case of Escobar syndrome a very rare genetic disorder from Karnataka, India.

Case report

A 7-year-old male patient reported to the Department of Pedodontics and Preventive Dentistry complaining of decayed teeth present in right and left upper and lower back tooth region from the past one month. Patient was born to non-consanguineous parents. There was no family history of congenital anomalies and he was the only child in his family. Physical examination revealed head circumference of 45cm (50th percentile), height 101 cm (below 3rd percentile) indicative of a short stature and weight of 12 kgs (below 3rd percentile) [Figure 1, a, b]. He showed an awkward gait with a marked one side limping. His mental intelligence was normal. Scalp hairs were thick with anterior and posterior low hairline. Other facial features included were anteverted nostrils, small posteriorly rotated ears, and accessory auricular tags with respect to left ear, long philtrum and thin lips. Eyes showed mild ptosis, hypertelorism, anti-mongoloid slant of palpebral fissures and median epicanthal folds [Figure 1, c,d,e].

Patient's neck was short with webbing and torticollis (wry neck) was present to right side. Webbing was also observed at the auxiliary region [Figure 2, a,b]. Features noticed with hands and feet were the presence of a simian's crease on the left hand, camptodactyly of thumbs, cutaneous syndactyly and rocker bottom feet [Figure 2, c,d]. Radiograph of the spine revealed anterior wedging of C3, elongated spinous process of C4 and fusion of C2 and C3 vertebrae [Figure 3].

On intraoral examination high arched palate, multiple carious teeth in relation to 54,53,52,51,61,62,63,64,65,75,74,84 and 85 were observed [figure 4, a,b,c]. 75 and 85 were grossly destructed. Deep dentinal caries involving pulp was present in 54, 64, 65 and dentinal caries was seen in 53, 52, 51, 61, 62, 63, 74 and 84. Patient also exhibited limited mouth opening, microstomia and mandibular retrognathism [Figure 1, c.d].

Complete blood examination report and hearing test was found to be normal. Examination of the cardiovascular system revealed no abnormal findings. Pediatrician was consulted, and finally based on the clinical, radiological findings the case was diagnosed as Escobar syndrome. At present, patient is undergoing physiotherapy for improvement of muscle tonicity.

For management of multiple carious teeth, full mouth rehabilitation was planned. In the upper arch, pulp therapy was performed with 54, 64 and 65 followed by stainless steel crown [Figure 5, b]. Composite restorations were done with respect to the maxillary anterior teeth (53,52,51,61,62,63) [Figure 5, a]. In the lower arch, extraction was carried out with respect to 81 for preshedding mobility, and 75 and 85 as they were grossly decayed. Glass ionomer restorations were done on 74 and 84 followed by space maintainer.

Discussion

Escobar syndrome is a very rare autosomal recessive genetic disorder introduced first by Victor Escobar in 1978.[3] According to him the most consistent malformations present in this disorder are: 1. pterygia of the neck (100%), antecubital (90%), popliteal areas (90%), 2. syndactyly (74%) and camptodactyly (84%) of fingers, 3. numerous joint flexion contractures (74%) and 4. foot deformities (74%). Other occasional features mentioned in the literature which were not present in our case are umbilical hernia (26%), inguinal hernia (26%) and congenital hip dislocation (21%).[3]

The exact etiology of this syndrome is not known till date. However, a study done by Hofmann *et al*[5] suggested that CHRNG gene of AChR subunits could be responsible for the arthrogryposis multiplex congenita (multiple congenital contractures) observed in this syndrome. This receptor has 5 subunits - 2 alpha, 1 beta, 1 delta and 1 gamma/epsilon unit. The gamma subunit is replaced by the epsilon in later fetal or perinatal life. Absence of gamma subunit in fetal life causes reduced fetal movement which is responsible for the contractures.

Most of times, the mode of inheritance is usually autosomal recessive and rarely autosomal dominant.[13,17] Sporadic inheritance has also been suggested in few cases.[1,7,9] The pattern of inheritance in the present case appears to be sporadic as the family history revealed no such occurrence in other family members.

The oral manifestations recorded in our patient were microstomia, mandibular retrognathism, high arched palate, limited mouth opening and multiple carious teeth. Among these microstomia and high arched palate have been reported in most of the case reports.[7,8] Mandibular retrognathism and limited mouth opening have also been reported and treated using mandibular distraction method in a case report by Parashar et al in 2006.[8] Sub mucosal cleft has been reported in one case report.[9] Conductive deafness was said to be a consistent part of this syndrome according to Thompson *et al*[4] where he presented 11 cases on multiple pterygium syndrome. Out of the 11 cases this feature was said to be present in four cases, unknown in two cases and absent in the remaining 5 cases.[4] This feature was absent in the present case as the hearing tests done were found to be normal.

The first case of Escobar syndrome reported in India was a five year old girl from Vellore who had features similar to our patient except for a few which were absent uvula, ulceration of the lower eyelids, conjunctival hyperplasia and pterygia of popliteal region.[10] Our patient also showed the presence of accessory auricular tags with respect to his left ear. This feature could be a part of the syndrome but it has not been reported in any other case report published previously.

The differential diagnosis for this syndrome considered is popliteal pterygium syndrome and antecubital pterygium syndrome. In the former, pterygia of the neck, antecubital area and axilla are not present but it includes cleft lip, lip pits, syngnathia and ankyloblepharon. The latter includes bilateral antecubital webbing and absent long head of triceps.[1] Both these syndromes are inherited in autosomal dominant manner.

There is no specific treatment for this syndrome. Rather treatment involves multidisciplinary management including services of Physician, Orthopedic surgeon, Physiotherapist and Plastic surgeon for management of limb deformities. The long term complications include hearing loss and infertility in males. At present, genetic counseling and in utero detection where ever possible remains the mainstay of treatment. According to Barros *et al*[11] Escobar syndrome can be diagnosed prenatally during the 23rd week of pregnancy by using two dimensional ultrasound scan. This is of great importance in enabling the parents to understand the severe malformations, and making it possible for them to receive appropriate counseling. Additional longitudinal studies are however required to determine life expectancy, further medical problems, complications and outcome of surgical and therapeutic intervention.

Dental considerations

These patients can be treated in usual manner as like normal patients. However, general anesthesia should be contraindicated as they have a risk of developing malignant hyperthermia which could be life threatening. In addition to this, more patience and behavior modification is required for these patients as they could not keep their mouth open for long time because of their reduced muscle strength and movement. Treatment should be carried out in short appointments.

Table 1 : Reported cases of Escobar syndrome in the literature

Author	*Year*	*No. of cases*	*Type of inheritance*	*Associated features along with the syndrome*
Escobar et al[2]	*1978*	*20*		
Penchaszadeh [9]	*1981*	*2*	*Sporadic*	
Thompson et al[4]	*1987*	*11*	*5-Autosomal Recessive, 6-sporadic*	
Hennekam [12]	*1993*	*1*		*Lingua cochlearis*
Goh et al[1]	*1994*	*1*	*Sporadic*	
Spranger et al[13]	*1995*	*2*	*Autosomal Recessive*	
DiGennaro et al[14]	*1996*	*2*		*Scoliosis*
Ozkinay et al[7]	*1997*	*1*	*Sporadic*	*Optic atrophy*

Capilupi et al1[5]	*1998*	*1*		*Bony lesions below ptetygia*
Hayashi et al[16]	*1998*	*1*	*Sporadic*	*Horse shoe shaped kidney*
Aslan et al[17]	*2000*	*3*	*Autosomal Recessive*	*Hypoplasia of nose, oral cavity, vocal cords and tongue*
Madhuri et al[10]	*2001*	*1*	*Autosomal Recessive*	
Holtmann et al[18]	*2001*	*1*		*Bilateral periventricular nodular heterotopias, mental retardation*
Brink et al1[9]	*2003*	*1*		
Dodson et al[20]	*2005*	*1*		*Thoracic kyphoscoliosis, severe restrictive lung disease*
Parashar et al[8]	*2006*	*1*	*Sporadic*	*Respiratory obstruction*
Prontera et al[21]	*2006*	*1*		
Chen [22]	*2007*	*1*		*Omphalocele*
Giray et al[23]	*2009*	*1*	*Autosomal Recessive*	*Polydactyly, horse shoe shaped kidney*
Amalnath et al[3]	*2011*	*3*	*Autosomal Recessive*	-
Ezirmik et al[24]	*2012*	*1*	*Autosomal Recessive*	*Congenital patellar syndrome*
Present case	*2013*	*1*	*Sporadic*	*Accessory ear tags*

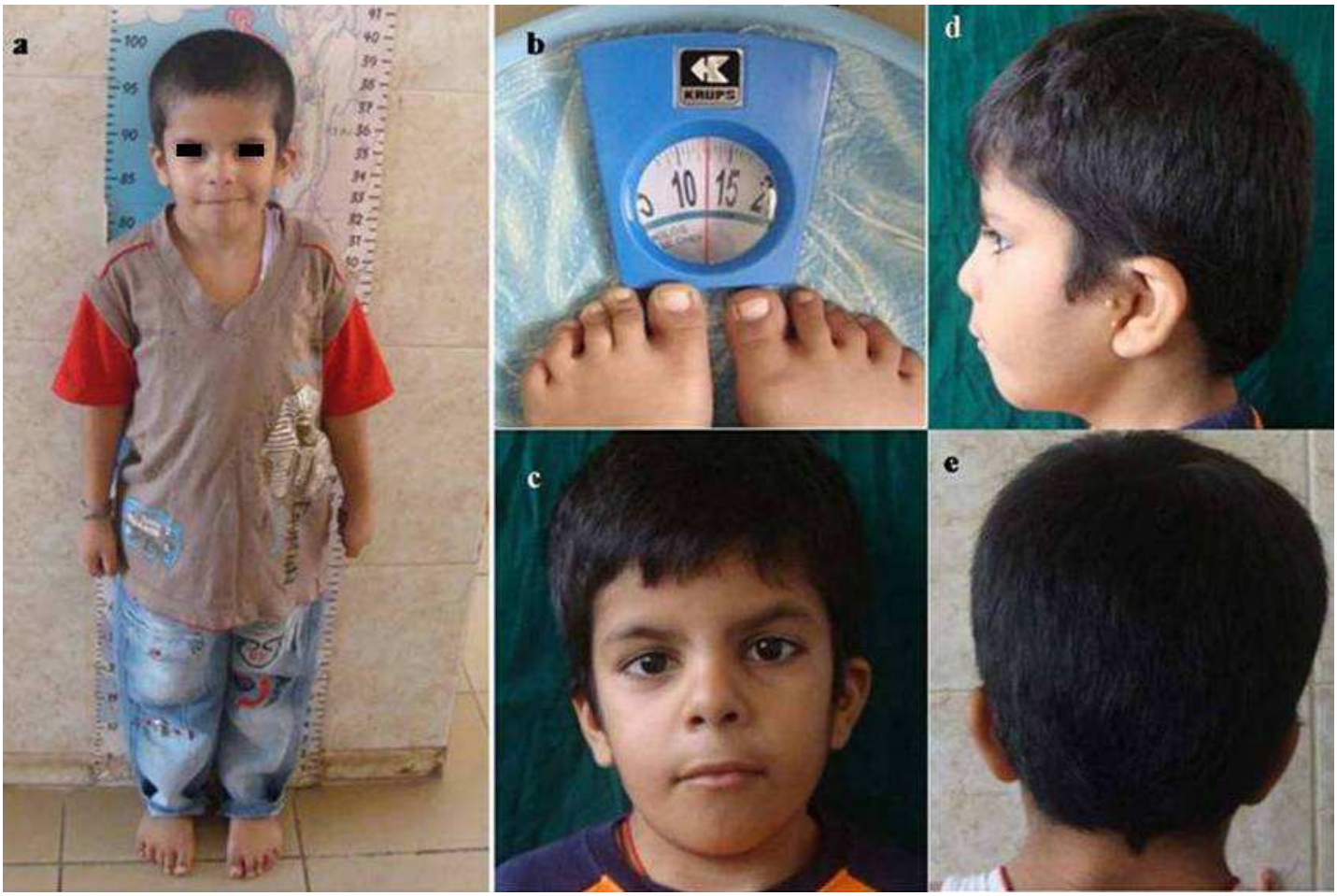

Figure.1 Physical examination showing height (101cms) and weight (12kgs). (c,d,e) - Facial features involving eyes, nose, lips and hair.

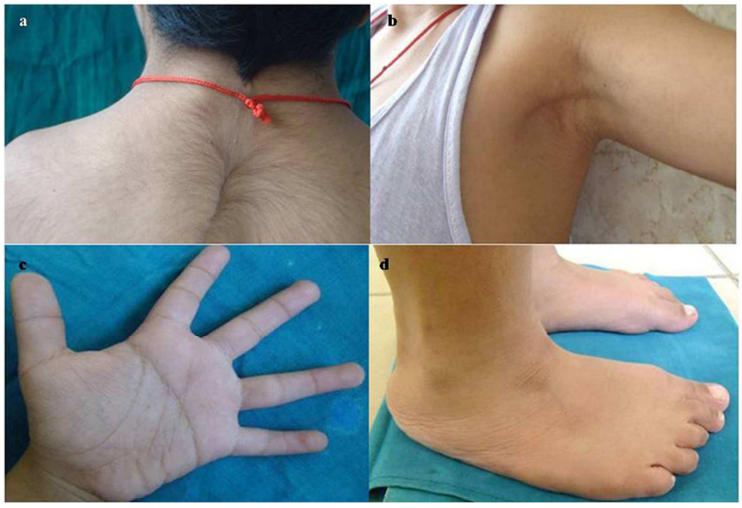

Figure 2: (a,b) - Pterygia (webbing) seen in neck and auxiliary region. (c,d) - Features of hands (simian's crease on left hand) and feet (rocker bottom feet).

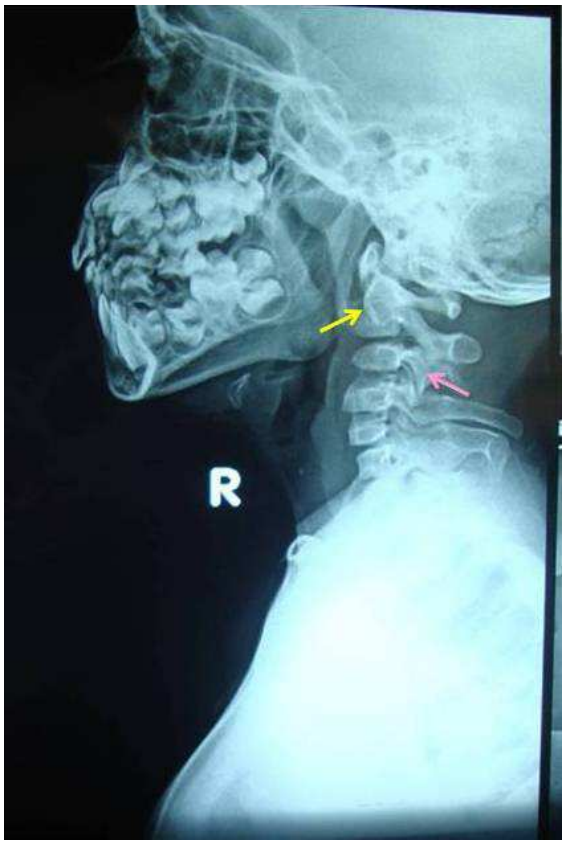

Figure 3: Radiograph of spine showing anterior wedging of C3 (yellow arrow), elongated spinous process of C4 (red arrow) and fusion of C2 and C3 vertebrae.

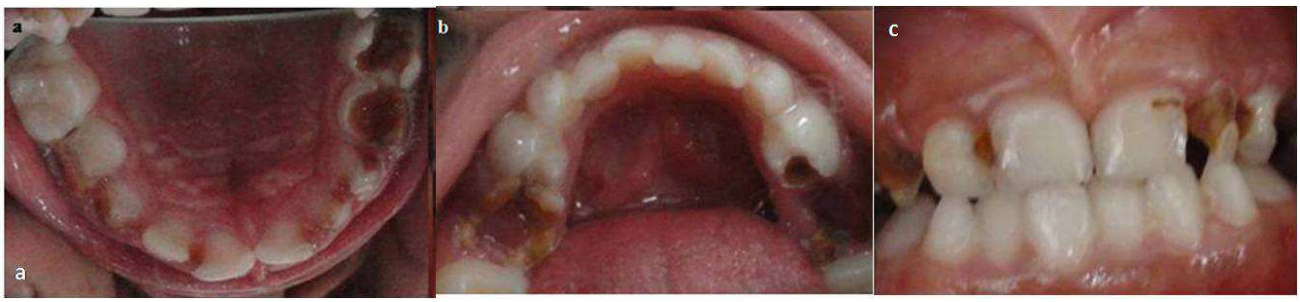

Figure 4: (a,b,c) - Pre operative photographs of the upper and lower arches.

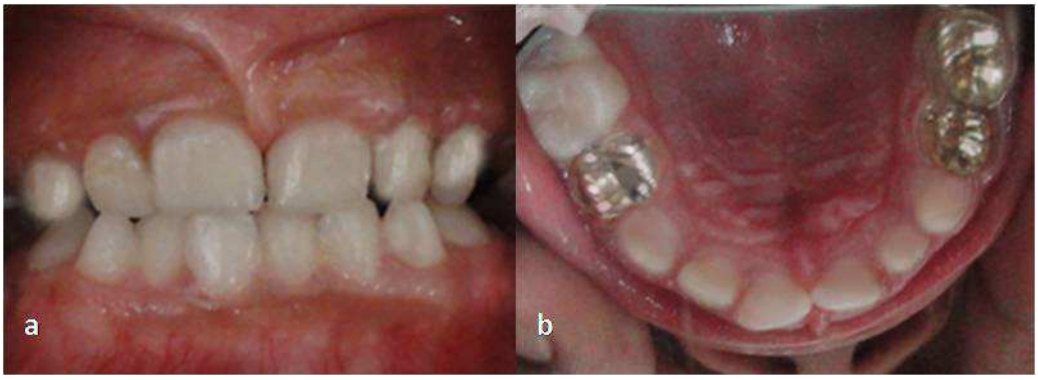

Figure 5: (a,b) - post operative photographs

References

1. Goh A, Lim KW, Rajalingam V. Multiple pterygium syndrome (Escobar syndrome) - A Case report. Singapore Med J. 1994; 35(2): 208-10
2. Escobar V, Bixler D, Bleiser S, Weaver DD, Gibbs T. Multiple pterygium syndrome. Am J Dis Child. 1978; 132(6): 609-11
3. Amalnath DS, Subrahmanyam DK, Sridhar S, Dutta TK. Escobar syndrome in three male patients of same family**.** Indian J Hum Genet. 2011 Jan-Apr; 17(1): 22–25.
4. Thompson EM, Donnai D, Baraitser M, Hall CM, Pembrey ME, Fixsen J. Multiple pterygium syndrome: evolution of the phenotype. J Med Genet. 1987 Dec; 24(12): 733-49.
5. Hoffman 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 unit. Am J Med Genet. 2006; 79(2): 303–12.
6. Cox PM, Brueton LA, Bjelogrlic P, Pomroy P, Sewry CA. Diversity of neuromuscular pathology in lethal multiple pterygium syndrome. Pediatr Dev Pathol. 2003 Jan-Feb; 6(1): 59-68
7. Ozkinay FF, Ozkinay C, Akin A, Azarsiz S,Gunduz C. Multiple pterygium symdrome. Indian J Pediatr 1997; 64: 113-6.
8. Parashar SY, Anderson PJ, David DJ. An unusual complication of mandibular distraction. Int J Paediatr Dent. 2006 Jan; 16(1) :55-8.
9. Penchaszadeh VB, Salszberg B. Multiple pterygium symdrome. J Med Genet. 1981; 18: 451-55.
10. Madhuri V, Bose A, Danda S, Shivakumar S, Kirubakaran C, Seshadri MS. Chromosomes 6/7 translocation t(6:7) (q15-q32) presenting as multiple pterygium symdrome. Indian Pediatr 2001; 38: 194-7.
11. Barros FS, Araujo Júnior E, Rolo LC, Nardozza LM. Prenatal Diagnosis of Lethal Multiple Pterygium Syndrome Using Two-and Three-Dimensional Ultrasonography. J Clin Imaging Sci. 2012; 2: 65.
12. Hennekam RC. Lingua cochlearis in multiple pterygium syndrome. Am J Med Genet. 1993 Oct 1; 47(5): 761.
13. Spranger S, Spranger M, Meinck HM, Tariverdian G. Two sisters with Escobar syndrome. Am J Med Genet. 1995 Jul 3; 57(3): 425-8.
14. Di Gennaro GL, Greggi T, Parisini P. Scoliosis in Escobar syndrome (multiple pterygium syndrome). Description of two cases. Chir Organi Mov. 1996 Jul-Sep; 81(3): 317-23.
15. Capilupi B, Olappi G, Cornaglia A, Novati GP. The multiple pterygium syndrome or Escobar syndrome: a case report. Pediatr Med Chir. 1998 Jul-Aug; 20(4): 295-8.
16. Hayashi M, Maruki K, Maruki K. A case of multiple pterygium syndrome (Escobar) with horseshoe kidney. No To Hattatsu. 1998 Jan; 30(1): 61-4.
17. Aslan Y, Erduran E, Kutlu N. Autosomal recessive multiple pterygium syndrome: a new varialt? Am J Med Genet. 2000 Jul 31; 93(3): 194-7.
18. Holtmann M, Woermann FG, Boenigk HE. Multiple pterygium syndrome, bilateral periventricular nodular heterotopia and epileptic seizures--a syndrome?
    Neuropediatrics. 2001 Oct; 32(5): 264-6.
19. Brink DS, Luisiri A, Grange DK.Case report: lethal multiple pterygium syndrome. Pediatr Pathol Mol Med. 2003 Nov-Dec; 22(6): 461-70.
20. Dodson CC, Boachie-Adjei O. Escobar syndrome (multiple pterygium syndrome) associated with thoracic kyphoscoliosis, lordoscoliosis, and severe restrictive lung disease: a case report. HSSJ. 2005 Sep; 1(1): 35-9.
21. Prontera P, Vogt J, McKeown C, Sensi A. Familial multiple pterygium syndrome (MPS) is not associated with CHRNG gene mutation. Am J Med Genet. 2007 May 15; 143: 1129.
22. Chen CP. Lethal multiple pterygium syndrome associated with omphalocele. Genet Couns. 2007; 18(4): 451-3.
23. Giray O, Bora E, Ercal D. Multiple pterygium syndrome with horseshoe kidney and polydactyly: a further case. Clin Dysmorphol. 2009 Apr; 18(2): 120-1.
24. Ezirmik N, Yildiz K, Can CE. Escobar syNdrome mimicking congenital patellar syndrome. Eur J Med 2012; 44:117-21.