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Larsen Syndrome
Larsen Sendromu

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ABSTRACT
Larsen syndrome is an inherited condition characterized by multiple joint dislocations and typical facial features including depressed nasal bridge with hypertelorism and a prominent forehead. There are only several cases reported since its first report by Larsen in 1950s. The aim of this review is to illustrate the pathogenesis, clinical features, diagnosis, and differential diagnosis of this condition.
Key words: Larsen syndrome, joint dislocation, ultrasonography

ÖZET
Larsen sendromu çoğul eklem dislokasyonları, deprese burun köprüsü, hipertelorizm ve belirgin bir alın ile karakterize tipik yüz özellikleri olan bir kalıtsal durumdur. İlk olarak 1950'li yıllarda bildirilmiş olmasına karşın bildirilmiş olgu sayısı oldukça azdır. Bu yazının amacı, Larsen sendromunun patogenezi, klinik özellikleri, tanı ve ayırıcı tanısı hakkında bilgi vermektir.
Anahtar kelimeler: Larsen sendromu, eklem dislokasyonu, ultrasonografi

Introduction

Larsen syndrome is a rare syndrome with genetic heterogeneity. It has both autosomal dominant and autosomal recessive patterns of inheritance[1]. The filamins which is involved in Larsen syndrome are cytoplasmic proteins that regulate the structure and activity of the cytoskeleton by cross-linking actin into three-dimensional networks, linking the cell membrane to the cytoskeleton and serving as scaffolds on which intracellular signaling and protein trafficking pathways are organized. Several mutations have been identified in the gene encoding filamin B (FLNB gene) in individuals with autosomal dominant Larsen

syndrome[2]. Al-Kaissi et al. noted the presence of the syndrome in three generations of the same family, which is suggestive of inheritance consistent with single-gene autosomal dominance. They also reported that the multiple neonatal deaths in the family might represent the higher expression of the syndrome[2]. This review briefly illustartes the features and diagnosis of Larsen syndrome.

Mode of Inheritance

Latta suggested the following three possibilities to explain the mode of inheritance of the syndrome[3]. These are;

1. The mother's anomaly may have been acquired and unrelated to the syndrome.

2. Larsen's syndrome might be inherited as an autosomal recessive trait, the mother being heterozygous and displaying only minor manifestations.

3. Larsen's syndrome could be a single-gene, dominantly inherited disorder with wide variability in severity. If the disease is inherited as a single-gene, autosomal dominant trait, several other corollaries would follow. In one of these corollaries, the fully expressed gene might result in higher rates of death in utero and during the neonatal period (this could account for the apparent rarity of this syndrome). In the other one, the cases reported in the literature in which neither parent nor siblings were involved might represent new mutations which would then be passed on as a dominant gene.

Clinical Features

Larsen syndrome is characterized by multiple joint dislocations and unusual facies. The most significant facial features are depressed nasal bridge with widely spaced eyes and a prominent forehead. Cleft palate, hydrocephalus, cardiac malformations and abnormalities of spinal segmentation are also described[4]. Further several other features have also been reported.

Spinal Anomalies

There are reports of cervical vertebrae hypoplasia, scoliosis, Khyphosis, wedge vertebrae, spondylolysis, spina bifida oculta in Larsen syndrome [5].

Hands and Feet

Cylindrical fingers, spatulate thumbs, and short metacarpals could be observed in these cases. Feet may have talipes equinovalgus or equinovarus deformity along with short metatarsals[5].

Cardiovascular Anomalies

Thre are reports of aortic dialatation, atrial septal defect, ventricular septal defect, patent ductus arteriosus, mitral valve prolapse and aneurysms of ductus arteriosus in Larsen syndrome[5].

Cartilages

Maldeveloped cartilage of the larynx and the tracheal rings ('flabby cartilage') may cause respiratory difficulty[6].

Craniofacial Anomalies

Marked frontal bossing typically flattened face, depressed nasal bridge; eyes widely set, small mouth, and micrognathia[7].

Oral

Oral features of Larsen syndrome are maxillary prognathism, malocclusion, supernumerary teeth, macroglossia, microdontia, delayed dental development, hypodontia affecting all the permanent canines, second and third molars, maxillary lateral incisors and second premolars; morphological anomalies of the maxillary first premolars and molars; a class 3 skeletal pattern and reduced upper facial height. Cephalometric radiographs showed the skull bones to have an appearance similar to that of osteopetrosis[8,9]. Bilateral cleft lip and palate have also been reported[5].

Lethal Forms

A few lethal forms of Larsen syndrome inherited autosomal recessively have been described in previous reports. One case with diaphragmatic hernia and a few cases with laryngomalacia and apnea were described [5]. At these cases, four different collagen fiber genes were analysed, but no defected molecules could be detected despite the electrophoretic analysis with fibroblast cultures. In two cases, multiple joint dislocations, tracheomalacia and lung hypoplasia led to death by pulmonary failure in a short time have been reported. Abnormal collagen bands were detected at these cases and described as collagen fiber dismaturity [5].

Radiographic Findings

Radiographs reveal under-mineralisation and over-tubulation of the long bones, a bifid calcaneus and advanced bone age in the carpal, or extra carpal bones[7]. Further radiographic changes include dislocations, as previously noted. The distal phalanges are abbreviated. The metacarpals and metatarsals are relatively shortened. Bone age is retarded. When the carpal bones appear, they are irregular. There are from one to four supernumerary carpal bones in 75%. Abnormal segmentation and/or hypoplasia of cervical and thoracic vertebrae are common. This may be associated with marked cervical kyphosis. In some cases, cervical vertebral instability has led to quadriplegia or death. The vertebral bodies may be flattened. A juxtacalcaneal accessory bone is present within the first four years of life in approximately 40%. It coalesces with the calcaneus by 5–8 years of age forming a bifid calcaneus that is evident in lateral view. Additional centers of ossification may be seen at the elbow. The proximal tibial epiphysis is often cone-shaped during development[10].

Diagnosis

For antenatal diagnosis, targeted ultrasound in a fetus at risk for Larsen syndrome should include evaluation of face, which tends to be flat, depressed nasal bridge, cleft palate, hypertelorism and prominent forehead. Joints should be examined for club feet, multiple joint dislocations at elbow, hips, knee and abnormal joint positions. Spinal abnormalities include kyphosis and scoliosis. Occasional findings include hydrocephalus, clinodactyly, supernumerary carpal bones and digits. Ultrasonographic diagnosis of the condition before the end of the second trimester affords the patient the ability to terminate the pregnancy if she desires, and gives the physician the chance to reevaluate the patient and plan for appropriate management[11].

In case of a late diagnosis, a cesarean section may be required to avoid birth trauma, especially from cervical instability. The infant would need multidisciplinary care in the neonatal intensive care unit[12].

Differential Diagnosis

Otopalatodigital syndrome is most often mistaken for Larsen syndrome. In contrast, these patients exhibit a pugilistic facies, hearing loss, paddle-shaped metatarsal bones, no

juxtacalcaneal bone, and no supernumerary carpal bones. Differential diagnosis also includes arthrogryposis, fetal akinesia sequence, monosomy 21, Ehlers-Danlos syndrome, types VII and XI, COFS syndrome, cleft palate, short stature, depressed nasal bridge, and sensorineural hearing loss, spondyloepimetaphyseal dysplasia, Desbuquois syndrome and lethal Larsen-like syndrome[10].

Conclusion

Larsen syndrome requires a multispecialty approach with surgical corrections. Patient counseling is essential to have a psychological support. Sonographic evaluation could play an essential role for the management of this condition.

References

1. Gupta N, Kabra M. Larsen syndrome. Indian Pediatrics. 2008; 45:783-4.
2. Centre for Arab Genomic Studies. Larsen Syndrome, Autosomal Dominant. http://www.cags.org.ae/pdf/150250.pdf. (Accessed: Aug 2012)
3. Habermann ET, Sterling A, Dennis RI, Bronx. Larsen's syndrome: a heritable disorder. J Bone Joint Surg.1976; 58:558-61.
4. Orhan D, Balcı S, Deren O, Ütine EG, Başaran A, Kale G. Prenatally diagnosed lethal type Larsen-like syndrome associated with bifid tongue. Turk J Pediatrics. 2008; 50:395-9.
5. Kulkarni ML, Mohammed Z, Kulkarni PM. Larsen Syndrome- Lethal variety. Indian J Pediatr. 2005; 72:1053-4.
6. Kaya RA, Turkmenoglu O, Cavufioglu H, Dilbaz S, Aydin Y. Cervical pedicle screw fixation in a patient with larsen syndrome: a case report. Turkish Neurosurgery. 2006;16:48-52.
7. Al-Kaissi A, Ammar C, Ghachema MB, Hammoub A, Chehidab FB. Facial features and skeletal abnormalities in Lars en syndrome: a study of three generations of a Tunisian family. Swiss Med Wkly. 2003; 133:625-8.
8. Perçin EF, Gedik R, Develioğlu H, Kunt T. Larsen's syndrome with dental anomalies: report of a case. ASDC J Dent Child. 2002; 69:172-4.
9. Tsang MC, Ling JY, King NM, Chow SK. Oral and craniofacial morphology of a patient with Larsen syndrome. J Craniofac Genet Dev Biol. 1986; 6:357-62.
10. Gorlin RJ, Cohen MM, Hennekam A. Syndromes of Head and Neck,4th Ed. New York, Oxford University Press, 2001.
11. Kulkarni ML, Basha MH, Hegade S, Kumarasamy TA, Kulkarni AM. Antenatal diagnosis of Larsen Syndrome. Indian J Pediatr. 2010; 77:819-20.

12. Tongsong T, Wanapirak C, Pongsatha S, Sudasana J. Prenatal sonographic diagnosis of Larsen syndrome. J Ultrasound Med. 2000; 19:419-21.

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