Case report / Olgu sunusu

A case report of Marfans Syndrome patient with epilepsy-A Rare concomitance
Epilepsi ile birlikte Marfan Sendromu olgu sunusu- nadir bir birliktelik

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\begin{abstract}

\textbf{Anahtar kelimeler: } Marfan Sendromu, Araknodaktili, Mavi sklera, Epilepsi.
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Marfans Syndrome is a disorder of the connective tissue inherited as an autosomal dominant condition of variable expression and its classical form comprises of skeletal, cardiovascular and ocular abnormalities. It is attributed as a defect in the mutation in the fibrillin gene. The syndrome has a wide range of expression from mild to the severe forms. Sometimes the symptoms are so mild that only few of the symptoms occur. In most cases, the disease progresses with age and symptoms of Marfans Syndrome become noticeable as changes in the connective tissue occur. Most of the reported cases so far are associated with cardiovascular abnormalities. We report a case of Marfans Syndrome associated with epilepsy.

\textbf{Key words: } Marfans Syndrome, Arachnodactyly, Blue sclera, Epilepsy.
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**Introduction:**

Marfans syndrome is a variable autosomal dominant disorder of the connective tissue. It was first described by Marfan in 1896. Approximately 85% of the case are familial with the rest arising as a result of new mutations. Mutations in the FBN1 is associated with a broad spectrum of phenotypes. Marfans syndrome may affect cardiovascular, central nervous system, musculoskeletal, pulmonrny, ocular and integumentary systems. The diagnosis is commonly considered in young patients with tall, thin body habitus, long limbs, arachnodactyly, pectus deformity and scoliosis. Other findings are high arched palate with crowding of teeth. According to Ghents classification 1 major and 4 minor features supports the diagnosis in this case. We report a case of Marfans syndrome with similar features and CNS findings.

**Case report:**

A 14-year-old female patient reported to the department with a complaint of forward placement of teeth. She was aware of the condition following the eruption of the permanent teeth causing severe esthetic discomfort. Patient presented with a history of epileptic seizures that were occasional and transient. The patient was on an ayurvedic medication for the same for epilepsy and had no episodes of seizures since the past one year. She also reported of a history of myopia (near sightedness) which was corrected with spectacles. She was wearing them since young ages.

The patient was well oriented with time, place and was cooperative during the clinical examination. On examination, skeletal findings like tall stature with slender limbs, long narrow face (lepto prosoponic), long narrow head (dolicocephalic), thin body habitus with increased arm span to height ratio, long slender limbs, long fingers and toes (arachnodactyly), deformities of the chest (pectus carinatum), abnormal curvature of the spine (scoliosis), joint hypermobility, flat feet, downward slanting palpebral fissures, malar hypoplasia were observed (Fig. 1a & 1b). Walker sign (wrist) and Steinberg sign (thumb) was positive (Fig 2a & 2b).
Ocular findings under slit lamp examination performed by a qualified ophthalmologist revealed ectopia lentis (subluxation of the lens) that was bilaterally symmetrical and upwards, blue sclera (Fig. 3).

Qualified cardiologist evaluated the patient and an electrocardiography was carried out which revealed no abnormalities. Oral findings were microstomia, incompetent lips, proclination of upper anteriors with high arched palate (Fig. 4).

Orthopantomogram revealed the presence of impacted canine in the maxilla and dilacerated premolar in the mandible (Fig 5). Based on these clinical presentations and opinions from the medical professional a provisional diagnosis of Marfan's syndrome associated with epilepsy was constituted. Oral prophylaxis was carried out and orthodontic treatment was initiated for the correction of malocclusion.

Discussion:
Marfan's syndrome (MFS) is a variable autosomal dominant disorder of the connective tissue. It was first discovered by Antonie Marfan (French pediatrician) in the year 1896 as dolicostenomelia which means long limbs. It was first seen in a 5-year-old patient, later it was referred as MFS. It is caused due to mutation in the FBN1 gene located on chromosome 15, band q15-q23 which codes for the connective tissue fibrillin. The incidence is 1 in 9800 births and 27% of cases occur due to new mutations. Mutations in FBN1 gene have been associated with a broad spectrum of phenotypes. More than 135 new mutations have been identified in the FBN1 gene. Neonatal MFS constitutes 14% of the total cases. The presentation in adults and adolescents is well known. Fibrillin-1 forms an important component of microfibrillin. It is a glycoprotein synthesized as a precursor that is processed and secured in the extracellular matrix (ECM). It polymerises to form microfibrillin and helps to stabilize the latent transforming growth factor-β binding protein (LTBPs) in the ECM. LTBPs hold the TGF-β in inactive stage. A failure of interaction between fibrillin-1 and LTBPs may result in excess of TGF-β signaling. Most Fibrillin-1 mutations are a missence, suggesting a dominant negative effect on the microfibrillar assembly. Fibrillin-1 is essential for the formation of extracellular matrix and maintenance of elastin fibres. Elastin fibres are found in the aorta, ligaments and ciliary zones of the eyes and these areas are the most affected.
Abnormalities in protein synthesis causes a myriad of distinct clinical problems of which the musculoskeletal, cardiac and ocular problems predominate. There is a striking intrafamilial and individual variability in the clinical manifestations of MFS, variability that is suggestive of some phenotype and genotype correlation. The severe end of the clinical contiguum is defined as a rapidly progressive form that is present at birth and is associated with functional impairment and death in early childhood. Diagnosis is further complicated by the age dependency of symptoms and signs, which leads to a changing clinical picture in younger patients who are suspected with the disorder but do not fulfill the clinical diagnostic criteria should be offered repeated clinical evaluations. The diagnosis of MFS was based on the Berlin classification (1986) and was later revised as the Ghent classification in 1996. The presence of 2 major features and 1 minor feature or the presence of 1 major and 4 minor features supports the diagnosis of MFS because of the presence of ectopia lentis and musculoskeletal abnormalities. This case report satisfies the criteria required to support the diagnosis of MFS. Rare instance of neurological findings such as epilepsy have been reported. On rare events association of mental retardation and lumbosacral meningocele has also been reported. Vascular abnormalities can be a cause of cerebral and spinal ischaemia/haemorrhage events involving the brain/spinal cord are estimated in 10-20% of the patients in MFS. Since there is the risk of the offsprings inheriting the genetic predisposition to the disorder parents should be counseled well in advance. New method of diagnosis can include investigation of mutation analysis (FBN1 gene). As of 1995, the life expectancy of those affected with the syndrome has increased to 72 years, up from 48 years in 1972, which is attributed to the new surgical techniques, improved diagnosis and newer techniques of medical treatment. Advancement of research in MFS holds support of further improvements in the future.

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<thead>
<tr>
<th>System Affected</th>
<th>Major Criteria</th>
<th>Minor Criteria</th>
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<tbody>
<tr>
<td>Cardiovascular system</td>
<td>Dilatation of the ascending aorta, with or without aortic regurgitation, involving at least the sinuses of Valsalva Dissection of the descending aorta</td>
<td>Dilatation or dissection of the descending thoracic or abdominal aorta before 50 years of age Dilatation of a main pulmonary artery before 40 years of age Mitral valve prolapse with or without mitral valve regurgitation Calcification of the mitral annulus before 40 years of age</td>
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<tr>
<td>Musculoskeletal system</td>
<td>Scoliosis with a curvature greater than 20° or spondylolisthesis Pectus carinatum Pectus excavatum requiring surgery Acetabular protrusion Reduced upper-to-lower segment ratio, or arm span-to-height ratio greater than 1.05 Wrist and thumb signs Reduced extension of the elbow (_170°) Medial displacement of the medial malleolus causing pes planus</td>
<td>Pectus excavatum of moderate severity Joint hypermobility Highly arched palate with crowding of teeth Abnormal facial appearance (dolichocephaly, malar hypoplasia, enophthalmos, retrognathism, down-slanting palpebral fissures)</td>
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<tr>
<td>Central nervous system</td>
<td>Lumbar sacral dural ectasia at CT or MR imaging</td>
<td>None</td>
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<td>Pulmonary system</td>
<td>None</td>
<td>Spontaneous pneumothorax Apical blebs</td>
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<tr>
<td>Ocular system</td>
<td>Ectopia lentis</td>
<td>Abnormal flat cornea Increased axial length of the globe Hypoplastic iris or hypoplastic ciliary muscle causing decreased miosis</td>
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<tr>
<td>Integumentary system</td>
<td>None</td>
<td>Striae atrophicae Recurrent or incisional hernia</td>
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