Respiratory Dysfunction in Patients with Marfan Syndrome

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Marfan syndrome (MS) is inherited in an autosomal dominant way. MS is characterized by a high degree of penetration and expression of the pathological gene. Fibrillin, the gene product is a protein that acts in the composing of elastic fiber. Therefore, MS syndrome is a multisystem disorder that affects connective tissue. The aim of this paper is to evaluate the frequency of occurrence of factors influencing abnormalities in respiratory tract functioning. The study encompassed 45 patients with MS syndrome ranging in age from 2 to 54. Both clinical examination and morphological measurements were performed in each case. The following anthropometrical measurements were performed: cephalometric and measurements of the chest. All measurements were standardized as mean values for healthy population. Based on the measurements recorded, the following indexes were evaluated: width/length index of the head, morphological index of the face, and index of chest flattening. The occurrence of chest deformities was also evaluated. The study indicate that several factors can result in pulmonary disease in patients with Marfan’s syndrome.

Key words: anthropometrical measurements, elastic fiber, marfanoid habitus, respiratory dysfunction

INTRODUCTION

Marfan syndrome (MS) is a disorder of the connective tissue inherited in an autosomal dominant pattern. Up to 30% of cases result from a spontaneous new mutation. MS is caused by mutations in the gene fibrillin-1. Mutations in this gene causes overgrowth of the long bones of the body, resulting in the tall stature.
and long limbs seen in Marfan patients. Other characteristic features in skeletal system in MS (described as marfanoid habitus) are as follows: dolichostenomely, dolichocephaly, arachnodactyly, joint laxity, scoliosis, chest deformities - pectus excavatum or pectus carinatum, high arched palate and crowded teeth. Fibrillin-1 also plays an important role as the scaffolding for elastic tissue in the body. Disruption of such scaffolding (by mutations in fibrillin-1) which results in changes in elastic tissues, particularly in the aorta, eye, and skin, also has an impact on the lung tissue (1-3).

The aim of this paper was to evaluate the frequency of occurrence of factors influencing abnormalities in respiratory tract functioning.

MATERIAL AND METHODS

The study encompassed 45 patients with Marfan’s syndrome ranging in age from 2 to 54 years. The family history focused on MS was checked in all cases. The diagnosis was established based on the presence of symptoms in 3 systems (skeletal system, cardiovascular system, and the organ of vision) with a negative family history, or in minimum 2 systems with a positive family history, according to the criteria of Lee and Ramirez (4). The following anthropometrical measurements, including head measurements were performed: height of the body (b-v), the length (g-op), width (eu-eu) and occipital width (ms-ms) of the head, the largest width of the face (zy-zy), the width of the mandible (go-go), the morphological length of the face (n-gn), the length of the nose (n-sn), the width of the nose (al-al). The following anthropometrical measurements of the chest were considered: chest circumference, fibular (xi-ths) and transversal (thl-thl) chest dimensions. Based on the measurements recorded, the following indices were evaluated: width/length index of the head [(eu-eu)/(g-op)] x 100, morphological index of the face [(n-gn)/(zy-zy)]x100 (go-go)/(zy-zy) and index of chest flattening (xi-ths/thl-thl)x100, all of which were classified according to Saller, Lundborg-Linders and Garson-Saller scales (5). All measurements were compared against the standard mean values for healthy population.

RESULTS

Clinical and anthropometrical examinations showed the typical features of marfanoid phenotype in the examined group of patients. A number of marfanoid habitus symptoms, such as bone overgrowth and concomitant skeletal malformations, such as chest deformities and scoliosis, have an impact on vital and total lung capacity (1, 6). The skeletal abnormalities characteristic of MS, which can result in restrictive respiratory dysfunction, were present. The B-v (Basis – vertex) measurement confirmed that 78% of patients exceed +1SD of the narrow physiological norm and 10% of the patients exceed +3SD. Scoliosis was observed in 40% of the examined patients. The analysis of chest circumference showed a decrease in its value when compared with healthy population (60% of pts exceeded -1SD). Pectus excavatum was observed in 30% patients. The decrease of transversal chest dimension below -1SD was observed in 40% of patients. The
decrease of fibular chest dimension was recorded in 52% patients (-1SD) and -3SD was observed in 10% of patients. According to the classification of chest flattening, more than 68% of patients showed the typical parameters of flat or very flat chest. Patients with significant chest deformities have been excluded from this evaluation in order not to skew the results.

Of the 30% of patients with chest deformities who underwent surgical procedures (according to Ravitsch’s and Nuss’ methods), the majority of patients were between 10 and 13 years of age. Two patients underwent the procedure after puberty. Two patients had a surgery twice and in one case the procedure was combined with cardiosurgery.

Based on the performed anthropometrical measurements, head circumference value was recorded within -0.5SD and dolichocephaly was observed in 30% of patients. Morphological index of the face indicating face narrowing was observed in 63%. High arched palate was seen in 80%. It should be emphasized that increases of the morphological length of the face (n-gn) and of the length of the nose (n-sn), and a decrease of the length of the head (g-op) were observed. The decrease of anthropometrical parameters of head was also observed regarding the width of the head (eu-eu), the width of the face (zy-zy), and the width of the mandible (go-go).

In 80% of patients recurring infections of the respiratory tract occurred in childhood. Emphysema or pneumothorax was noted in 15%. Approximately 80% of patients reported symptoms, such as easy fatigability, dyspnea upon exertion and chest pain. In 8% of the examined group of patients allergy and/or asthma occurred.

DISCUSSION

The above results confirmed the existence of an association between the features of marfanoid habitus and the pathology of the respiratory tract. Long bones overgrowth, scoliosis, and chest deformities (pectus excavatum) all influence the vital lung capacity, which can lead to respiratory tract diseases (especially restrictive respiratory dysfunction). Despite the unfavorable impact of the deformation of the pectus excavatum on the functioning of the organs in the chest region, a widely disputed matter, much research indicates that this very serious form of deformation is accompanied by cardiorespiratory dysfunction, including dyspnea with mild exertion, decreased endurance, front chest pain, and tachycardia (1, 6-8). Therefore, surgical repair is recommended to improve pulmonary and cardiac functions as well as for cosmetic reasons. This requires an individualized approach to timing and type of repair. Precise radiological assessment parameters delineating the limits of norm and pathology have not as yet been defined (9). Due to genetic considerations and the tendency of the deformation to recurrence, it is recommended to delay surgery until the patient
reaches skeletal maturity (6, 10). At the same time, however, it is suggested that the chest deformation and the cardiovascular abnormalities can be cured by surgery (11).

The relationship between cephalometric parameters (in particular maxillary and mandibular retrognathia, long face and highly arched palate) and high nasal airway resistance (NAR), suggests the potential role of craniofacial structure in the pathogenesis of obstructive sleep apnea (OSA) in patients with MS and necessitates further investigation (12-14).

Respiratory failure in MS could also be connected with the dysfunction of muscle weakness as a result of myopathy or the weakness of the lung tissue which is caused by fibrillin abnormalities. It seems that elastin degradation plays an important role in the pathogenesis of some pulmonary diseases. In patients with MS, a rapid rise of airway pressure can be induced even by minor exertions. For example, a coughing attack can cause the laceration of the connective tissue in the airway, resulting in mediastinal and epidural emphysema (1-3, 15, 16). The relationship between anthropometrical measurements and clinical symptoms of respiratory abnormalities suggests that further studies should be carried out in MS patients

REFERENCES


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