Skeletal Manifestations of Marfan Syndrome

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Marfan syndrome affects multiple organs and systems, many of which are musculoskeletal. The genetic basis of Marfan syndrome is related to chromosome 15 that encodes fibrillin-1 and 2. As with most genetic diseases the nature and location of mutations in the genes are only an approximate guide to the severity of the phenotype unless the same mutation has been seen in other members of the same family or in similar unrelated patients. The estimated prevalence of the syndrome is about 10 cases per 100,000 births.

Diagnosis is made by defining the involvement of multiple systems. The musculoskeletal criteria require at least four phenotypic expressions to be present. These include: pectus excavatum/carinatum, reduced upper to lower body segment ratio or hand span to length ratio of > 1.05, wrist and thumb signs, scoliosis of > 20 degrees or spondylolysthesis, reduced extension of the elbows < 170 degrees (also evident in the fingers, often referred to as spider-like hands due to flexion contractures of the interphalangeal joints), medially displaced medial malleoli, and protrusio acetabuli [1]. The wide variety of mutations affected by different subtypes of collagen abnormalities is responsible for the somewhat diverse phenotype.

It is important to note that although the great majority of patients are diagnosed before the age of 10, few present with four skeletal criteria, developing them later in life [1].

While most characteristic abnormalities of the musculoskeletal system are easily recognized, protrusio acetabuli is often overlooked or non-apparent until clinical symptoms emerge. This review will focus on two of them: spinal manifestations and protrusio acetabuli

Protrusio acetabuli

The medial protrusion of the femoral head due to deepening of the femoral head is common in Marfan syndrome, affecting 31–100% of patients to varying degrees [2]. The clinical manifestations of protrusio acetabuli are hip joint stiffness and progressive limitation in activity related to joint pain, a waddling gait, limited range of motion, flexion contracture, a pelvic tilt with a resulting hyperlordosis of the lumbar spine, and eventual osteoarthritic changes. Locally progressive protrusion can lead to early hip pain and osteoarthritis

The radiographic changes of protrusio acetabuli can be measured and quantified with several measuring methods. One important tool to measure the acetabular position is the teardrop, a radiographic marker on the inferomedial border of the acetabulum just superior to the obturator foramen. Four degrees of change to the teardrop are defined: open, closed, crossed, and reversed. The center-edge-angle, as defined by Wiberg, measures the degree of displacement of the femoral head. Yet another method uses the illioischial line as a marker of protrusion when relating to the medial border of the acetabulum. Today, most authors use a combination of at least two measuring techniques to define protrusion [2].

Treatment of this condition comprises both conservative and surgical methods. Conservative options include mostly physiotherapy by forcible stretching (stress fractures of the femoral neck due to stretching are documented [3]), weight extension on an abduction frame, local heating, and reeducation concerning daily activities. Surgical options are directed at arresting progression, relieving pain, and restoring the function of the hip. The choice of treatment is age and condition related. Older patients with protrusio acetabuli and substantial arthritis can be treated effectively by total hip replacement with bone grafting of the medial acetabular cavity. Results of primary total hip replacement in Marfan syndrome patients are satisfactory and comparable to those in rheumatoid arthritis or normal controls [1].

For a selected group of patients under the age of 40 and with minimal arthritic changes, osteotomy to create a valgus correction of 20–30° reduces the transverse vector of forces acting on the hip joint and results in long-term pain relief and restoration of function, and can delay the need for total hip arthroplasty for a decade or more [4]

The arrest of progression of protrusio acetabuli in skeletally immature patients involves closure of the triradiate physis at the base of the acetabulum (Steel procedure). This now rare procedure should be reserved for children with Marfan syndrome ranging in age from 8 to 10 years who have documented progression of acetabular deepening. Progression of protrusio acetabuli can occur after closure of the triradiate cartilage.

The clinical dilemma of whether to operate and the timing of the operation in a child or adolescent with progressive protrusio acetabuli remains. Most authors believe closure of the triradiate cartilage to be indicated when the cartilage is still open and the protrusio acetabuli appears to be progressing even if the patient has no hip symptoms or limitation of motion [Figure 1].

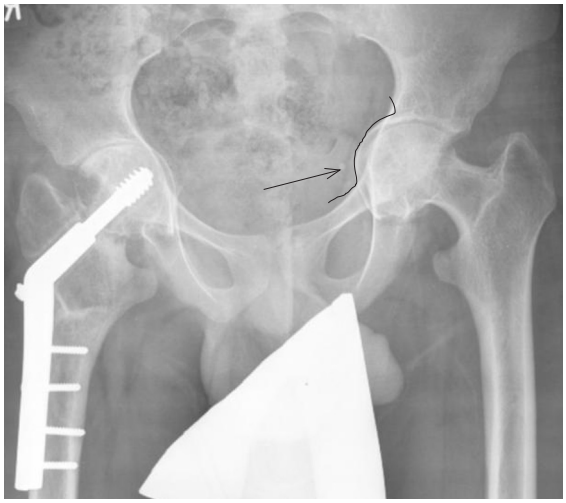

Figure 1. Pelvic X-ray of a young patient treated for a subcapital fracture of the femoral neck of his right hip. Although not defined as a Marfan patient he does have many of the musculoskeletal characteristics of Marfan syndrome. Note the distinct protrusio acetabuli on both sides, more prominent on the left (arrow pointing to the line marking the acetabular border protruding into both columns)

Spinal manifestations of Marfan syndrome

Spinal deformity is one of the most common skeletal manifestations of Marfan syndrome, with dural ectasia being a major criterion for the diagnosis of the syndrome. Other spinal abnormalities include anatomical variations of the lumbosacral spine, scoliosis, spondylolisthesis and cervical spine deformities.

Dural ectasia

Dural ectasia is defined as widening of the dural sac or spinal root sleeves, usually associated with bony erosions of the posterior vertebral body. It is most prevalent in the most quadal part of the spine and might be the cause of low back pain in a Marfan patient, although it is asymptomatic in most cases [5]. The radiographic sign for the diagnosis of dural ectasia is posterior vertebral scalloping seen on plain X-ray, but it is usually diagnosed on computed tomography or magnetic resonance imaging. Dural ectasia rarely indicates surgical treatment but may compromise surgery for other conditions such as scoliosis [6].

Scoliosis

Scoliosis is the most common symptomatic manifestation of Marfan syndrome in the skeletal system. The prevalence of scoliosis in the Marfan population is reported to be as high as 50–70% [7]. Scoliosis is defined as a spinal curvature in the coronal plane greater than 10°. Scoliosis in Marfan syndrome has some unique features differentiating it from idiopathic scoliosis. Idiopathic scoliosis is by far more prevalent during adolescence, whereas in Marfan patients the age at onset of scoliosis is younger than in the general population and can occur in infants and young children. Idiopathic scoliosis is gender selective and is much more common in females. Marfan scoliosis is found in a similar proportion in both sexes. Back pain is more common in patients with Marfan syndrome who also suffer from scoliosis than in other scoliosis patients.

There is no typical curve type in Marfan scoliosis patients but a trend towards a higher rate of double and triple major curves was found. The direction of the curve (right thoracic) is similar to the idiopathic scoliosis curve [8]. The sagital alignment of the spine in idiopathic scoliosis is usually hypokyphotic. In some Marfan scoliosis patients the alignment is hyperkyphotic [9]. Significant curve progression is more prevalent in Marfan scoliosis [8].Conservative treatment using braces of different designs for lower grade curves (< 45°) is effective in preventing curve progression in idiopathic patients but tends to be less effective in Marfan scoliosis patients [10]. In the past Marfan syndrome patients were not considered candidates for spinal deformity surgery because of an unacceptable rate of cardiac and pulmonary complications; however, medical and surgical solutions from other disciplines have made this surgery common practice. Surgical treatment of Marfan scoliosis might be more complicated because of the younger age of patients and anatomic variations. Since patients with Marfan syndrome, particularly those who also have dural ectasia, have smaller pedicles and thinner lamina, the use of pedicle screws and sub-laminar hooks for posterior spine fusion is less beneficial than in the idiopathic scoliosis population. Computed tomography or magnetic resonance imaging is thus recommended as routine practice prior to deformity corrective surgery in Marfan patients [11,12].

Spondylolisthesis

Spondylolisthesis is the displacement of a vertebra in relation to the vertebrae below. Several case reports have been published describing severe spondylolisthesis in Marfan patients. Analysis of the Marfan lumbar spine found a slightly higher prevalence of spondylolisthesis in this group of patients. The degree of displacement, however, was significantly higher than in the general population, and together with a significant degree of scoliosis presents as a complex spinal deformity [8].

Cervical spine

The ligament laxity found in Marfan syndrome raises concerns about possible cervical spine hypermobility and vulnerability to injury. Indeed, several case reports and small case series have described cervical hypermobility or instability and severe cervical spine injury following minor trauma in Marfan patients. A prospective analysis found a higher prevalence of focal cervical kyphosis and increased atlanto-axial translation. The preadolescent Marfan population had a greater range of motion than either the adolescent or adult population. The Marfan population was found to have an increased radiographic prevalence of basilar impression. No increase in the rate of cervical stenosis was found. Neck pain frequency did not differ significantly from that of age-matched controls [13]. Although no evidence of a higher rate of cervical spine injury was found, and most of the radiographic findings were asymptomatic, Marfan patients are advised not to engage in contact sports and other activities condusive to cervical spine injury

In summary, the musculoskeletal manifestations of Marfan syndrome are diverse and include the entire skeleton in various degrees, as would be expected in a condition in which the pathology lies at the very basis of the building blocks of connective tissue and bone. Treatment options are directed at the symptomatology and vary according to the severity of symptoms presented by patients.

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