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Original article

Spinal imaging contributes to the diagnosis of Marfan syndrome

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ABSTRACT

The diagnosis of Marfan syndrome (MFS) is defined by a combination of major and minor criteria, related to the different systems involved, according to the Ghent nosology of the spine. Spinal imaging can detect both skeletal (including scoliosis and spondylolisthesis) and neurological involvement (i.e. dural ectasia). The aim of the present study was to assess the interest of screening the rachis by conventional radiography CR and complementary imaging (computed tomography [CT] or magnetic resonance imaging [MRI]) in patients suspected of MFS, and to modelise the most relevant imaging procedure to diagnose MFS.
Methods: Evaluation of the sensitivity and specificity of CR of the lumbosacral spine versus sectional imaging for the detection of dural ectasia (DE) in a subgroup of 92 patients suspected of MFS. Retrospective analysis of the contribution of CR to the diagnosis of MFS in 1992 patients referred to our clinic.
Results: DE was detected by CR in 12 of the 92 patients (13%) and was always confirmed by CT or MRI. Complementary imaging alone detected 33 DE (35.9%). All patients with DE detected by CR were diagnosed with MFS. Among the 1992 patients, 591 were confirmed MFS; 117 patients had DE detected by CR (19,8%) while 12 (2,0%) were detected by complementary imaging. In MFS patients, 98 (16.6%) had significant scoliosis and 14 (2.4%) had spondylolisthesis. The positive predictive value of DE detected by CR for the diagnosis of MFS was 92.9% (95% IC: 86.8–96.4), and the negative predictive value was 74.6% (95% IC: 72.6–76.5). We conclude that spinal imaging is useful for the diagnosis of MFS.

1. Introduction

Marfan syndrome (MFS) is an inherited autosomal dominant disorder of the connective tissue with an estimated incidence of 1/5000 live births [1]. MFS is characterized by a broad range of clinical manifestations involving skeletal, ocular, cardiovascular, integument, pulmonary and central nervous systems (Table 1). The diagnosis is mainly clinical and is currently defined by a combination of major and minor criteria related to the different systems potentially affected according to the Ghent nosology [2]. Cardiovascular involvement in the form of aortic aneurysm or dissecting aorta is the most serious life-threatening aspect of the syndrome. Aortic dissection can be prevented by timely cardiovascular surgery, thus enforcing that an early diagnosis is essential in MFS.

For major skeletal involvement, four signs must be present including scoliosis or spondylolisthesis. For neurological involvement, the presence of dural ectasia (DE) is required, for it is the only major sign of MFS in this system. Exploration of the spine is sometimes needed to complete the diagnosis of MFS. Furthermore, DE may cause back or rectal pain, headache, and even sensory neurologic deficit and/or weakness of lower limb. DE may also be associated with herniation of the nerve root sleeves. Perineural and meningocele cysts can also occur [3–6].

According to the Ghent criteria, DE is defined as a widening of the dural sac on computed tomography (CT) or magnetic resonance imaging (MRI). Even if CT and MRI are very sensitive and specific diagnostic tools, conventional radiography is widely available

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Table 1
Ghent diagnostic nosology.

System	Major criterion	Involvement
Skeletal	At least 4 of the following features: Pectus carinatum Pectus excavatum requiring surgery ULSR <0.86 or span:height >1.05 Wrist and thumb signs Scoliosis >20° or spondylolisthesis Reduced elbow extension (<170°) Pes planus Protrusio acetabulae	2 of the major features, or 1 major feature and 2 of the following: Pectus excavatum Joint hypermobility High palate with dental Crowding Characteristic face
Ocular	Lens dislocation (ectopia lentis)	Flat cornea Increased axial length of globe (causing myopia) Hypoplastic iris or ciliary muscle (causing decreased miosis)
Cardiovascular	Dilatation of the aortic root Dissection of the ascending aorta	Mitral valve prolapse Dilatation of the pulmonary artery, below age 40 Calcified mitral annulus, below age 40 Other dilatation or dissection of the aorta
Pulmonary	None	Spontaneous pneumothorax Apical blebs
Skin/Integument	None	Striae atrophicae Recurrent or incisional hernia
Dura	Lumbosacral dural ectasia	None
Genetic findings	Parent, child or sibling meets these criteria independently Fibrillin 1 mutation known to cause Marfan syndrome Inheritance of DNA marker haplotype linked to Marfan syndrome in the family	None

From Dean JC. Marfan syndrome: clinical diagnosis and management. Eur J Hum Genet. 2007;15:724–33.
ULSR: upper:lower segment ratio.
Having one of the features listed constitutes a major criterion or system involvement for all systems except the skeletal system, where more than one feature is needed.

and is usually performed during the initial evaluation of patients referred for suspicion of MFS.

The main objective of this study was to assess the interest of spine screening by conventional radiography and complementary imaging in a population of patients suspected of MFS.

Secondary objectives were to modelise the imaging procedure for MFS diagnosis and to evaluate the relationship between DE and scoliosis.

2. Methods

2.1. Multidisciplinary Marfan consultation

All patients referred to our multidisciplinary consultation are evaluated by geneticists, rheumatologists or pediatricians (depending on the patient's age), cardiologists, and ophthalmologists. Systematic slit-lamp examination and cardiac ultrasonography are also performed. In our practice, conventional radiography of the spine is performed in all patients to search for spondylolisthesis, scoliosis and DE. Diagnosis of MFS is in accordance to the Ghent criteria. All patients are included in a dedicated database.

2.2. Detection of scoliosis and spondylolisthesis

Scoliosis is an abnormal lateral curvature of the spine and must be greater than 20° to be a major skeletal sign in Ghent criteria. Spondylolisthesis is a forward slippage of a vertebrae due to a fracture of the posterior bone arch; osteopenie and fibrillin's abnormalities are probably involved in this process.

2.3. Detection of DE by conventional radiography

All patients underwent standard anteroposterior and lateral radiographs of the lumbosacral spine from L1 to S1. All conventional radiographs were read by one experienced radiologist (JPP) using criteria defined by Ahn et al. [7]. DE was diagnosed when at least one of the following signs was present: vertebral scalloping at L5 $\geq$5.5 mm, interpedicular distances at L4 $\geq$ 38 mm, and/or sagittal diameter at S1 $\geq$18 mm. The posterior vertebral scalloping sign appears on a lateral radiograph of the spine as an exaggeration of the normal concavity of the posterior surface of one or more vertebral bodies.

2.4. Detection of DE by CT or MRI

Patients with dilated aortic root and for which a precise measurement was required underwent a 16-multidetector row computed tomography with ECG gating (Philips MX 8000 IDT) to evaluate the entire aorta [8].

Raw data from the thoraco-abdomino-pelvic helical acquisition of the patients was used to perform specific reconstructions of the spine using dedicated filters. Multiplanar axial, coronal and sagittal reconstructions of the lumbosacral spine from L1 to S1 were then obtained on a workstation (Extended Brilliance, Philips). In other patients, the lumbosacral spine was evaluated using MRI. All examinations consisted of axial and sagittal T2-weighted and sagittal T1-weighted sequences of the lumbosacral spine from L1 to S1.

All CT or MRI examinations were read by the same experienced radiologist. The diagnosis of DE was made if one major criterion or two minor criteria were present as defined by Ahn et al. [9]. Major criteria were (1) a sagittal width of the dural sac at or below S1 greater than the width of the dural sac above L4; or (2) the presence of anterior meningocele. Minor criteria included (1) a nerve root sleeve at L5 > 6.5 mm in diameter and (2) scalloping at S1 > 3.5 mm.

Anterior sacral meningocele is defined as herniation of a dural sac through a defect in the anterior surface of the sacrum, or when the sacral meninges are herniating anteriorly into the pelvis through a widened foramen. Herniation of a nerve root sleeve