Scoliotic curve patterns in patients with Marfan syndrome

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Abstract

Purpose Cases of “non-idiopathic” scoliosis are deemed atypical. These require a comprehensive work-up in order to choose the best treatment (and to determine an extent of fusion if needed). Marfan syndrome (MFS) is a genetic disease often marked with the presence of scoliosis, which is poorly described in the literature. Knowing that the clinical diagnosis of MFS is not always obvious, we investigated how atypical the scoliosis associated with MFS was when compared with that of adolescent idiopathic scoliosis (AIS).

Methods In our series, we included 30 patients diagnosed with MFS. Each patient was proposed to undergo a plain radiographic examination of the spine. Scoliotic patients were classified according to the Scoliosis Research Society (SRS) curve pattern classification. Curve patterns with a very low rate of occurrence in historic control were defined as “atypical”.

Results A total of 19 patients were defined as scoliotic. In 9 cases, the curve pattern was atypical. In the other 10, the curve pattern was typical, but a fine analysis revealed some atypical features in the position of the apex and end vertebrae.

Conclusions Scoliosis associated with MFS was found to be atypical in all cases. This supports the idea that an atypical

curve pattern should be considered as an argument in favour of a non-idiopathic aetiology and, therefore, an appropriate work-up should be performed before deciding treatment.

Keywords Scoliosis · Marfan syndrome · Radiographic analysis · Atypical features

Introduction

Marfan syndrome (MFS) is a genetic disease with autosomal dominant inheritance [1]. The disease is often marked with the presence of a scoliosis [2–4]. Surprisingly, curve patterns of scoliosis associated with MFS have been very poorly described in the literature, although it is well known that its natural history is quite different from that of adolescent idiopathic scoliosis (AIS), with or without surgery [5–7].

In order to better understand the scoliosis associated with MFS, our aim was to perform a radiographic analysis of the deformity using the classical SRS definitions [8] and to determine whether curve patterns of scoliosis associated with MFS are different from those observed in AIS and, thereby, how atypical the scoliosis associated with MFS was when compared with AIS.

Materials and methods

Data collection

The period of inclusion spanned between August 2004 and 2006. Each patient attending our institution (at the clinic of orthopaedic surgery, paediatric orthopaedic surgery, ophthalmology, heart surgery, vascular surgery, cardiology or

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genetics) was considered for inclusion. Criterion for inclusion was a diagnosis of MFS according to the Ghent criteria [9]. Criteria for exclusion were an age under 4 years, a standard radiographic examination of the spine made less than 1 year before, a pregnancy or suspicion of pregnancy in women and patient's refusal (or parental refusal in minor patients) to be included in the study. Of the patients, 57 were considered as being possibly affected with MFS. Of these, 14 refused to be included in the series (in 12 cases, they had moved far from the area of our institution, and, in 2 cases, they did not want to hear about their disease for some psychological reasons) and 3 were found to be dead when we tried to contact them. Of the remaining 40 who accepted to be included in the series, 5 did not meet the criterion for inclusion (i.e. according to the Ghent criteria [9], the diagnosis of MFS was not certain), and 3 were excluded because of a standard radiographic examination of the spine passed less than 1 year before. No patient had to be excluded because of pregnancy or suspicion of pregnancy. Eventually, 32 patients were included in our series, each of whom was proposed to pass a radiographic examination of the spine (Standardized AP view).

The threshold of the Cobb angle used to define a scoliosis was arbitrarily fixed at 10° . The evaluation of the AP radiographs focused on both the overall curve pattern and specific curve features (end vertebrae, levels, apex and magnitude). Curves were classified according to their apical vertebra or apical disc space, as defined by the Scoliosis Research Society (SRS). Thoracic curves have an apex between T2 and T11, whereas thoraco-lumbar curves have an apex at T12, the T12-L1 disc or L1. Lumbar curves have an apex at or below the L1–L2 disc space. An upper thoracic curve was defined based on the presence of a curve between T1 and T6 with T1 tilt. According to the SRS, there are 21 different curve patterns, each having a specific frequency of occurrence [10]. Each curve in our series was classified according to this 21-cluster SRS classification.

“Typical” versus “atypical” curve pattern

In order to compare curve patterns in our scoliotic patients with idiopathic patterns, we used the concept developed by Spiegel et al. [11], namely that of “typical” curve pattern, based on historic control. These authors assumed that “atypical” refers to patterns seen with a low frequency in the idiopathic population. They have arbitrarily defined “typical” versus “atypical” based on a review of selected articles (Bunch, cited by Spiegel et al. [11], Coonrad et al. [10], Moe and Kettleson [12], Ponseti and Friedman [13]). They defined “atypical” curve patterns as follows: left thoracic, left thoracic/right lumbar, left thoracic/right thoracolumbar, right (King 5) and left double thoracic, right

thoracic (King 4), and right and left triple and quadruple curve patterns. These all had a frequency of less than 2.5% in the series by Coonrad et al. (combined total of 11.6% of 2,000 cases) [10]. According to Spiegel et al. [11] “Typical” patterns would therefore include the King 1, King 2, King 3, right thoracic/left thoracolumbar, thoracolumbar and lumbar patterns.

“Atypical” features in typical curve pattern

In addition, and using the same historic series (Bunch, cited by Spiegel et al. [11], Coonrad et al. [10], Moe and Kettleson [12], Ponseti and Friedman [13]), Spiegel et al. [11] developed the concept of “atypical” end vertebrae and “atypical” apex in “typical” curve patterns. In these “typical” curve patterns, the “typical” ordered pair of end vertebrae are as follows: right thoracic (T5 and T12), right thoracic/left lumbar [King 1 (T6 and T11/T11 and L3), King 2 (T5 and T11/T11 and L3)], right thoracic/left thoracolumbar (T5 and T10/T10 and L3), thoracolumbar (T9 and L3), and lumbar (T12 and L4). In the same way, the “typical” apices were as follows: right thoracic (T9), right thoracic/left lumbar [King 1 (T8/L2), King 2 (T9/L2)], right thoracic/left thoracolumbar (T7/L1), left thoracolumbar (T12), and left lumbar (L2). Any end vertebra or apex that would not match these previously defined positions would therefore be considered as an “atypical” feature in typical curve pattern.

“Typical” versus “atypical” curve patterns in scoliosis associated with MFS

Our MFS patients affected with a scoliosis were separated into two different groups. The first group consisted of patients with “atypical” curve patterns, the second of patients with “typical” curve patterns. In each SRS type [10], the frequency of occurrence among our scoliotic MFS population was recorded.

“Atypical” features in typical curve patterns in scoliosis associated with MFS

In the group of patients demonstrating typical curve patterns, in each curve, the position of the apex and end vertebrae were compared with the theoretical “typical” position of the apex and end vertebrae as previously defined. The distance d was defined as the distance (expressed as an amount of vertebrae) separating the index vertebra and the theoretical position of this vertebra, as previously defined. As a convention, d was recorded as a positive value when the index vertebra was more caudad than its theoretical position, and as a negative value when the index vertebra was more cephalad than its theoretical

Table 1 Ghent criteria*Skeletal system*

A major skeletal criterion is assigned when at least four of the following are present:

Pectus carinatum

Pectus excavatum requiring surgery

Upper to lower segment ratio <0.86 or span/height >1.05

Wrist and thumb signs: both signs should be present to diagnose Arachnodactily according to the Ghent criteria

Scoliosis $>20^\circ$ or spondylolithesis

Reduced elbow extension ($<170^\circ$)

Pes planus

Protrusio acetabulae

Involvement of the skeletal system is diagnosed when two of the major features, or one major feature and two of the following are present:

Pectus excavatum of mild severity

Joint hypermobility

High palate with dental crowding

Characteristic face (Dolicocephaly, Malar hypoplasia, Enophthalmos, Retrognathia, Down-slanting palpebral fissures)

Cardiovascular system

Major

Aortic root dilation

Dissection of the ascending aorta

Involvement

Mitral valve prolapse

Dilation of the pulmonary artery

Calcified mitral annulus in individuals <40 years of age

Other dilation or dissection of the aorta

Ocular system

Major

Lens dislocation (Ectopia lentis)

Involvement

Flat cornea

Increased axial length of globe (Causing myopia)

Hypoplastic iris or ciliary muscle (Causing decreased miosis)

Skin/integument system

Major

None

Involvement

Striae atrophicae

Recurrent or incisional hernia

Pulmonary system

Major

None

Minor

Spontaneous pneumothorax

Apical blebs

Nervous system

Major

Lumbosacral dural ectasia

Table 1 continued

Minor

None

Genetic criteria

Major

Parent, child or sibling meets the criteria independently

FBN1 mutations known to cause MFS

Inheritance of DNA marker haplotype linked to MFS in the family

Minor

None

position. In each curve, three values of d were defined, one for the apical vertebra, one for the upper end vertebra and one for the lower end vertebra, namely d_{apex} , $d_{\text{upper end}}$ and $d_{\text{lower end}}$. In each curve, the mean of absolute values of d_{apex} , $d_{\text{upper end}}$ and $d_{\text{lower end}}$ were assessed. For each of these three mean values, a student's t -test was performed to assess whether these values were significantly different from 0. A student's t -test showing a significant difference from 0 would indicate a position of the index vertebra different from its theoretical position.

Eventually, the rate of curves considered as "typical" but presenting at least one "atypical" position was assessed.

Results

Of the patients with MFS, 30 were included in our series. There were 14 females and 16 males. The mean age was 25.9 years, ranging from 4 to 65 years; 11 were under 16 years. Of all the patients, 19 were defined as scoliotic (Cobb angle over 10°), and 11 were defined as non-scoliotic (Cobb angle under 10°). There were 6 cases of single-curve scoliosis, 9 of double-curve scoliosis and 4 of triple-curve scoliosis. Thus, there were 36 curves with a Cobb angle over 10° in 19 patients.

The distribution of the 19 scoliosis cases in our series according to the SRS curve patterns [10], the frequency of occurrence among our scoliotic MFS population and the frequency of occurrence of the same SRS curve pattern among an AIS population [10] are shown in Table 1. Among the 21 SRS curve patterns defined in the literature [10], only 10 matched with our cases.

"Typical" versus "atypical" curve patterns in scoliosis associated with MFS

In our series, 9 cases (47% cases) were considered as "atypical", as previously defined. Therefore, 10 cases of scoliosis were considered as "typical".

Table 2

Curve pattern	Type reported by Coonrad et al.	Number of cases described by Coonrad et al.	Prevalence reported by Coonrad et al. (%)	Prevalence in (%)	
Right thoracic–left lumbar (CobbT > CobbL)	2AR	353	18.00	4	21.00
Left lumbar	7L	114	5.70	2	11.00
Right thoracic–left lumbar (CobbL > CobbT)	1AL	190	9.50	2	5.00
Right thoracic (King III)	3R	484	24.00	1	5.00
Right thoracic–left thoraco lumbar (CobbT > CobbTL)	2BR	82	4.00	1	21.00
Triple-curve left	3L	19	1.00	4	11.00
Left thoracic (Reverse King IV)	4L	1	0.05	2	5.00
Left thoracic	3L	44	2.20	1	5.00
Left thoracic–right lumbar (CobbT > CobbL)	2A1	24	1.20	1	5.00
Left thoracic–right lumbar (CobbL > CobbT)	1AR	9	0.60	1	5.00
Total		1320		19	

Table 3

Curve pattern	Type reported by Coonrad et al.	Prevalence reported by Coonrad et al. (%)	Typical end vertebrae	Typical apex	Number of cases in our series	End vertebrae in our series	Apex in our series
Right thoracic–left lumbar (CobbT > CobbL)	2AR	18.00	[T5-T11]:[T11-L3]	T9:L2	4	[T5-T11]:[T11-L5] [T7-L1]:[L1-L5] [T2-T11]:[T11-L5] [T9-L2]:[L2-L5]	T8:L1 T10:L3 T7:L3-L4 disc T10-T11 disc; L4
Left lumbar	7L	5.70	[T12-L4]	L2	2	[L1-L5] [T8-L5]	L3 L2
Right thoracic–left lumbar (CobbL > CobbT)	1AL	9.50	[T6-T11]:[T11-L3]		2	[T9-L2]:[L2-L5] [T2-T8]:[T12-L5]	T11:L3 T6-L2
Right thoracic (King III)	3R	24.00	[T5-T12]	T8:L2	1	[T8-T11]	T9-T10 disc
Right thoracic–left thoraco lumbar (CobbT > CobbTL)	2BR	4.00	[T5-T10]:[T10-L3]	T9	1	[T5-T10]:[T10-L3]	T7-T8 disc; T12
Total				T7:L1	10		

“Atypical” features in typical curve patterns in scoliosis associated with MFS

In these 10 “typical” cases, 17 different curves were identified, namely 8 thoracic curves, 8 lumbar curves, and 1 thoracolumbar curve. These 10 patients matched five of the SRS curve patterns, as defined by Coonrad et al. [10]. Their actual apex and end vertebrae and their “theoretical” apex and end vertebrae, as previously defined, are shown in Table 2.

Considering all of the 17 curves originating from the 10 scoliotic patients previously defined as “typical” in our series, the mean absolute value of d_{apex} was 1.18. The mean absolute value of $d_{\text{upper end}}$ was 1.9, and the mean absolute value of $d_{\text{lower end}}$ was 1.5. The student’s *t*-test showed that

these three mean values were significantly different from 0. Therefore, there was a significant shift of the apical vertebra, and the two end vertebrae relative to their theoretical position.

All of these 17 curves (considered as “typical”) presented at least one “atypical” position of either the apical or the end vertebrae (Table 3).

Discussion

MFS is a genetic disease with autosomal dominant inheritance [1]. The prevalence of the disease is about 0.01% in the general population [14]. It is, most of the time, due to a mutation of the FBN1 gene that codes for an extracellular

Fig. 1 Reverse King IV (SRS 4L)

matrix protein called Fibrillin [15]. The clinical expression of the disease affects several systems of the body (skeleton, heart and vessels, eyes, skin, dura and pleura) [1]. One of the most striking symptoms of the disease is scoliosis, which may affect more than 50% of patients with MFS [2, 4]. Surprisingly, very few series available in the literature describe the curve pattern of the scoliosis associated with MFS. To date, only three series have been published [2–4]. It has been shown that the natural history of the scoliosis associated with MFS is unique and does not resemble that in AIS; it is often more severe [2] in MFS patients, and the King's guidelines used to determine the extent of the arthrodesis in AIS [16, 17] does not fit the scoliosis associated with MFS [5–7].

A subset of patients with both juvenile and adolescent “idiopathic” scoliosis may have an underlying condition that may cause the scoliosis. Most of the time, it is a mild and poorly expressed neurologic abnormality such as Syringomyelia [11], but it can also be a genetic pathology such as MFS. Despite the fact that the diagnosis of MFS is based on a clinical score [9], the disease is not obvious at physical examination in a large subset of patients. In these

patients, the diagnosis is possible only if criteria are carefully investigated [14]. Cases of “non-idiopathic” scoliosis are deemed “atypical”. Nevertheless, none of the previously published series investigating MFS scoliosis [2–4] focused on the typical versus atypical curve patterns in such patients. The aim of our work was to assess how atypical the scoliosis associated with MFS was, when compared with that of AIS. In our series, in almost half of the cases (47%), the curve pattern was found to be obviously “atypical”, such as left thoracic, triple curve or even reverse King IV (Fig. 1), which are very uncommon in AIS. The number of patients was low, and the interpretation of our results should take into account this small sample size. Nevertheless, MFS is a rare condition, and our series was as large as was possible at our institution. The curve pattern was found to be “typical” in 53% of cases, not obviously different from the one observed in AIS. But a closer look at the position of the apical and end vertebrae, using the method previously described by Spiegel et al. [11] in patients with Chiari I malformation, demonstrated that even in “typical” curve patterns, all of the curves demonstrated some “atypical” features, namely a shift of the apical and/or the end vertebrae. Thus, 47% of cases were atypical, and all of the patients that demonstrated a typical curve pattern (53%) also demonstrated some degree of atypicity. No studies reported in the literature have investigated this feature. Even the large series published by Sponseller et al. [2] did not focus on how atypical the scoliosis in MFS was. We based our comparison method on that developed by Spiegel et al. [11], which investigated how atypical the scoliosis associated with Chiari I malformation was. The basic idea is the same and our work strongly supports the idea that an atypical curve pattern or a typical curve pattern demonstrating some degree of atypicity should be considered as an argument in favour of a non-idiopathic aetiology. Therefore, an appropriate work-up should be performed before deciding any treatment. This work-up would include a MRI of the spine to assess the presence of a syrinx and/or a Chiari I malformation, as suggested by Spiegel et al. [11], but also a clinical assessment of the Ghent criteria [9] in order to look for MFS, knowing that the diagnosis of MFS is not obvious in all cases.

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