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Case Report

Marfan's Syndrome: A Case Report from the Mother and Child Centre of Chantal Biya's Foundation

Syndrome de Marfan : à propos d'un cas au Centre Mère et Enfant de la Fondation Chantal Biya

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ABSTRACT

Marfan's syndrome comprises disorders caused by an inherited genetic defect of the connective tissue. It manifests itself mainly by cardiovascular, ophthalmic, and musculoskeletal disorders. We report the case of a toddler aged 2 years 10 months brought to consultation for a thoracic deformity noted since birth. She presented with a multitude of progressively evolving signs. Marfan's syndrome was diagnosed based on significant dilatation of the ascending aorta, amblyopia with bilateral lens ectopia, and a systemic score of 11/20. Marfan's syndrome may be diagnosed without genetic testing. The major signs should be warning signs that would initiate a multidisciplinary approach for early diagnosis.

RÉSUMÉ

Le syndrome de Marfan est un ensemble de troubles causés par une anomalie génétique héréditaire du tissu conjonctif qui se manifeste principalement par des atteintes cardiovasculaires, ophtalmiques et musculo-squelettiques. Nous rapportons le cas d'une fillette de 2ans et 10 mois amenés en consultation pour une déformation thoracique constatée depuis la naissance. Elle présentait une multitude de signes évoluant progressivement. Le diagnostic de syndrome de Marfan a été posé devant dilatation importante de l'aorte ascendante, une amblyopie sur ectopie cristallinienne bilatérale et un score systémique de 11 sur 20 regroupé dans le score révisé de Ghent. Il existe des possibilités de diagnostic de syndrome de Marfan sans tests génétiques. Les signes majeurs devraient être des signes d'alerte qui initieraient une approche multidisciplinaire pour un diagnostic précoce.

INTRODUCTION

Marfan's syndrome is a group of rare disorders caused by an autosomal dominant genetic defect in connective tissue. The commonest genetic defect is an abnormality in the *FBN1* gene on chromosome 15, which codes for fibrillin. Its prevalence worldwide varies from 1 in 5000 to 2–3 in 10,000 living persons (1).

The clinical expression is variable; the disease can present as a severe and progressive multi-systemic disorder that mainly affects the cardiovascular, ocular, and musculoskeletal systems. The diagnosis is based on a combination of clinical and paraclinical elements, combined in the revised Ghent score. Patient prognosis depends on the type of cardiovascular involvement. We report the case of a girl aged 02 years 10 months who was diagnosed using a multidisciplinary approach.

CASE PRESENTATION

A toddler aged 2 years 10 months was brought to the clinic by her mother with a thoracic deformity found at birth. It was not painful and did not limit physical activity. This was her seventh medical consultation since birth for the same complaint. She was born at term from a non-consanguineous couple. She has no history of malformations in her pedigree. On physical examination, she had a height of 102 cm (height-for-age >3 Z score), dysmorphism (associating an elongated face, pectus carinatum [Fig 1.b], thoracolumbar scoliosis, dolichostenomelia [i.e. wingspan/height ratio = 1.06], arachnodactyly, a positive wrist sign, positive thumb sign [Fig 1.a], genu valgum, and flat feet [Fig 1.c]). She also had a reducible umbilical hernia. Ophthalmological examination revealed enophthalmos, bilateral convergent

strabismus, and high myopia associated with amblyopia on bilateral crystalline ectopia. Cardiovascular examination was normal. Cardiac ultrasonography showed significant dilatation of the ascending aorta (>3 Z score) without mitral prolapse.

All these elements resulted in a systemic score of 11/20, an element of the revised Ghent criteria for Marfan's syndrome. We diagnosed Marfan's syndrome based on this score, aortic dilatation, and bilateral lens ectopia.

The parents were informed of the diagnosis and limitations of the hospital's technical resources. The management was multidisciplinary. No treatment was provided for the aortic aneurysm and orthopedic anomalies. Corrective lenses were provided for the ophthalmologic anomalies. No play restrictions were imposed on the child. However, the parents were instructed to prevent him from carrying loads and carrying out climbing activities.

DISCUSSION

We report the case of a girl with no relevant family history, who presented with several signs and symptoms common to Marfan's syndrome. Her diagnosis was not made until her seventh visit at the age of 2 years 10 months in our health structure.

The age of diagnosis varies worldwide and depends on several factors: the phenotype that becomes more apparent with age and the evolution of diagnostic criteria, revised in 2010 by Ghent et al. (2). In a review by Groth et al. conducted in 2015 in Denmark, the average age of diagnosis was 18.3 years for males and 19.9 years for females (3). Diagnosis was made in 10% and 25% of patients at the ages of 1.5 and 6.5 years, respectively (3). In Taiwan, Chiu et al. reported a peak prevalence of 32.3% in patients aged 15–19 years in 2014 (4). The prevalence of Marfan's syndrome in Africa is unknown. Despite the presence of warning signs such as severe myopia and major bone deformities, the diagnosis is always made late. Thus, Ndongo et al. in 2016 reported a case of Marfan's syndrome with aortic dissection—a complication—in a 30 year old Cameroonian adult (5). Atipo-Tsiba et al. reported a case of Marfan's syndrome with decrease in visual acuity in an 8-year old girl in Congo Brazzaville (6).

Of note, an index case requires a family investigation like done in a Nigerian family where after discovering marfan syndrome in the third child of a four siblings family, investigations was done for the other. Diagnosis of Marfan syndrome was made in three members of the nuclear family – the father and his two children(7). In our patient, we did not carry out a complete examination of the other members of the family. we limited ourselves to an interrogation in search of morphological anomalies.

Given the disparity of clinical features, in 2010, Ghent et al revised the criteria for the diagnosis of Marfan's syndrome (Table 1). they put more weight on the cardiovascular manifestations and in which aortic root aneurysm and ectopia lentis are the cardinal clinical features. In the absence of any family history, the presence of these two manifestations is sufficient for the unequivocal diagnosis of MFS. In absence of either of these two, the presence of a bonafide FBN1 mutation or a combination of systemic manifestations is required. Our patient had a score of 11/20.

Our case highlights the value of multidisciplinary management of genetic conditions in our setting. We involved the pediatrician, cardiologist, ophthalmologist, orthopedic surgeon, geneticist, and psychologist in the management of our patient. As of this time she is healthy, she does daily activities and the monitoring of the aortic dilatation is done every 6 months.

CONCLUSION

We report a case of Marfan's syndrome in a female toddler. The relevance lies in possibility of early diagnosis of Marfan's syndrome in the presence of suggestive signs and appropriate use of the revised Ghent score. A multidisciplinary approach for both early diagnosis and optimal management is important.

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Figure 1a: Thumb sign

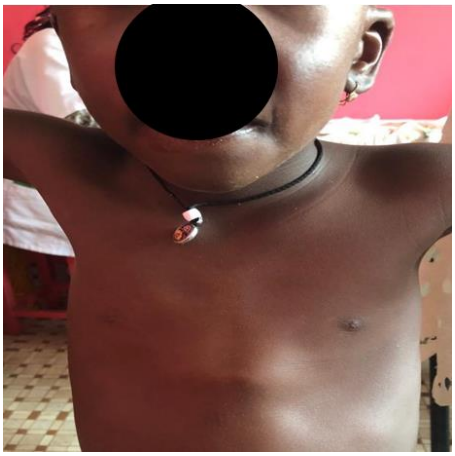

Figure 1b: pectus carinatum

Figure 1c: genu valgum, flat feet

Table 1: Diagnostic Criteria for Marfan's Syndrome
In the absence of a family history of Marfan's syndrome, a diagnosis can be established in four distinct scenarios:
1. Aortic root Z score ≥2 AND ectopia Lentis*
2. Aortic root Z score ≥2 AND a bona fide *FBN1* mutation
3. Aortic root Z score ≥2 AND a systemic score ≥7*
4. Ectopia lentis AND a bona fide *FBN1* mutation known to cause aortic disease
In the presence of a family history of Marfan's syndrome, a diagnosis can be established in the presence of:
1. Ectopia lentis
2. A systemic score ≥7*
3. Aortic root Z score ≥2, if older than 20 yrs or ≥3 if younger than 20 yrs*
* Denotes caveat with features suggestive of an alternative diagnosis that must be excluded with appropriate alternative molecular testing.

Table 2: Systemic score for Marfan's syndrome	
Points	**Features**
3	Wrist AND thumb sign (1 point for wrist OR thumb sign)
2	Pectus carinatum deformity (1 point for pectus excavatum or chest asymmetry)
2	Hindfoot deformity (1 point for plain pes planus)
2	Pneumothorax
2	Dural ectasia
2	Protrusio acetabuli
1	Reduced upper segment/lower segment ratio AND increased arm/height AND no severe scoliosis
1	Scoliosis or thoracolumbar kyphosis
1	Reduced elbow extension
1	3/5 facial features: dolichocephaly, enophthalmos, downslanting palpebral fissures, malar hypoplasia, retrognathia
1	Skin striae
1	1 Myopia > 3 diopters
1	Mitral valve prolapse (all types)
A patient can have a maximum of 20 points. A score ≥7 indicates systemic involvement (2).	