CASE REPORT

Marfan syndrome presenting with headache and coincidental ophthalmic artery aneurysm

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SUMMARY

A 24-year-old Ugandan woman was referred for a neurology opinion after complaining of a year long history of right-sided retro-orbital stabbing pain. Brain imaging revealed a coincidental 3 mm left ophthalmic artery aneurysm. Marfanoid habitus was noted; after further investigations she was diagnosed with mild aortic root dilatation, subtle lens dislocation and Marfan syndrome. Her symptoms were secondary to temporomandibular joint dysfunction, an under-recognised complication of Marfan syndrome. Her ophthalmic artery aneurysm is likely to be a coincidental finding.

BACKGROUND

This case highlights some of the difficulties of diagnosing individuals with Marfan syndrome. Some clinical signs such as an elongated arm span and joint hypermobility are non-specific and are found in varying prevalence in the general population for different ethnic groups.

Intracranial aneurysm, historically reported as a feature of Marfan syndrome, is in fact likely to be of similar prevalence to that seen in the general population. Large case series have not identified an increased prevalence of intracranial aneurysm or rate of rupture in Marfan syndrome.

New diagnostic criteria for Marfan syndrome emphasise the importance of detailed cardiac, genetic and ophthalmological investigations for patients where Marfan syndrome is suspected.

CASE PRESENTATION

A 24-year-old Ugandan woman was referred for a neurology opinion after complaining of a year long history of right-sided retro-orbital stabbing pain. The neurological examination was normal. The patient also had a Marfanoid habitus and was referred for a genetics opinion as to whether she could have Marfan syndrome.

Further evaluation identified that she was the oldest of three children of unrelated Ugandan parents. Her mother was 163 cm and her father was 196 cm tall. There was no known family history of ectopia lentis, aortic root dilatation or unexplained sudden death.

The clinical examination was remarkable for two of the major skeletal features of Marfan syndrome: a positive wrist (Walker) and thumb (Steinberg) sign and pes planus. The patient had an arm-span to height ratio of 1.1, well above the normal value seen in the Caucasian population, but at the high end of normal for those of Afro-Caribbean descent

(normal <1.1).¹ Her upper to lower segment ratio was 0.92 which is probably reduced, no ethnically matched data are currently available. The patient also had some of the minor criteria for skeletal involvement: a high arched palate, joint hypermobility and some of the characteristic facial features with dolichocephaly and malar hypoplasia.

INVESTIGATIONS

An ophthalmology assessment and investigations including an erythrocyte sedimentation rate, C reactive protein, MRI of the brain were normal; however, MR angiogram revealed an incidental 3 mm ophthalmic artery aneurysm (figure 1).

The patient was referred for an echocardiogram. She was noted to have a mildly dilated aortic root at the sinuses of valsalva (3.8 cm). Sequencing of *Fibrillin1* identified a mutation in exon 36 (c.4567C>T, p.Arg1523X). This mutation has been previously reported in association with classic Marfan syndrome² and has been reported in two other Marfan patients (<http://www.umd.be/FBN1/>). A second ophthalmology assessment noted a subtle unilateral lens subluxation. The patient therefore met the modified Ghent criteria for a diagnosis of Marfan syndrome.³

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for Marfan syndrome includes multiple hereditary disorders of connective tissue (HDCT). Symptoms related to joint laxity, including temporomandibular joint (TMJ) dysfunction, are commonly seen in patients with Ehlers-Danlos syndrome hypermobility type/joint hypermobility syndrome.

Marfan syndrome is rare with an estimated population prevalence of 1:10 000. Joint hypermobility is seen in 10% of the general population and up to 40% of school age children. While Marfan syndrome has autosomal-dominant inheritance, in a quarter of affected individuals the mutation occurs

Figure 1 A 3 mm ophthalmic artery aneurysm.

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de novo with no family history. In this situation, mutation testing may be particularly important.

HDCTs associated with intracranial aneurysm include pseudoxanthoma elasticum (MIM#264800), Loeys Dietz syndrome (MIM#609192) and vascular Ehlers-Danlos syndrome (MIM#130050).

Case reports of Marfan patients with cerebrovascular disease have led to debate as to whether there is an increased incidence of intracerebral and carotid vascular pathology outside the aortic root in these patients. A retrospective case series reported neurovascular complications secondary to cardiac emboli from prosthetic heart valves and that these were more common in older Marfan patients.⁴ There was no observed increase in the prevalence of symptomatic or asymptomatic intracranial aneurysm compared to the general population in two large case series using postmortem and neurosurgery audit data.^{4 5 6}

TREATMENT

A trial of medical treatment (angiotensin II receptor antagonists) for aortic root disease in Marfan syndrome patients was extremely promising,⁶ numerous clinical trials (including one in the UK) are ongoing (AIMS study ISRCTN90011794).

OUTCOME AND FOLLOW-UP

Cascade screening for family members, cardiac and ophthalmological surveillance was recommended.

DISCUSSION

The patient's symptoms were compatible with TMJ dysfunction. This has been reported in a single retrospective questionnaire-based study to affect up to 52% of patients with Marfan syndrome.⁷

Learning points

- ▶ Assessment for Marfan syndrome requires multisystem assessment according to the revised Ghent criteria.
- ▶ Temporomandibular joint dysfunction is reported in up to 50% of patients with Marfan, but is an under-recognised feature.
- ▶ Asymptomatic intracranial aneurysm is a relatively common coincidental finding in the general population and not thought to be a specific association of Marfan syndrome.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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