Frank's Painful Flank

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Meet Frank

- A nine-year-old boy presents with pain and erythema in the lateral right flank
- He is the product of an uncomplicated pregnancy, full-term, normal spontaneous delivery
- His past health is unremarkable, except that he had chickenpox when he was one-year-old
- There is no history of recent exposure to individuals with an infectious disease
- On examination, there is an erythematous rash on his right flank. Papules can be seen in some of the erythematous areas
- The rest of the examination is normal

What is your diagnosis?

a) Chickenpox
b) Herpes simplex
c) Herpes zoster
d) Molluscum contagiosum
e) Lichen striatus

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See page 2 for the answer to last month's case

Here is the answer to last month's case

Meet Ronald

Ronald, a 24-year-old new patient presents to the clinic. His medical files are not readily available. On examination, he is tall with a thin stature and long limbs. Pectus carinatum and kyphoscoliosis is noted. He also has a long surgical scar on his sternum.

A genetic condition is suspected. He is asked to perform a simple manoeuvre, demonstrated in the adjacent image.

What is your diagnosis?

a) Alien hand syndrome (anarchic hand)
b) Subclavian steal syndrome
c) Peutz-Jeghers syndrome
d) Marfan syndrome
e) von Hippel-Lindau syndrome

Answer: D

The patient displays positive thumb (Steinberg) sign: the thumb projects beyond the ulnar border of the clenched hand. This is a demonstration of arachnodactyly.

Marfan syndrome (MFS) **(answer d)** is one of the most common single gene mutation disorders encountered in clinical practice. It has a prevalence of approximately 1 to 10,000 in the general population. MFS is inherited in an autosomal dominant fashion. Approximately three-quarter of cases have a positive family history; the rest represent spontaneous mutation.

There is a defect of the gene FBN1 (chromosome 15) encoding for the fibrillin protein. More than 500 different mutations of the fibrillin gene have been described. Impaired fibrillin production leads to abnormal microfibrils, which are essential in the the formation of the elastin and connective tissue matrix in the body. Interestingly, mutations in the transforming growth factor-β receptor signalling

Table 1: Brief Summary of Ghent Criteria 1:

Major diagnostic features include:

a) First degree relative
b) Presence of FBN1 mutation
c) Inheritance of FBN1 haplotype, known to be associated with equivocally diagnosed Marfan syndrome in the family
d) In family members, major involvement in one organ system and minor involvement of a secondary organ system suffice for diagnosis
e) In the absence of positive family/genetic studies, the involvement of two different major organ systems, as well as minor involvement of a third organ system qualifies for the diagnosis

Table 2: Highlights of Major and Minor Organ System Involvement

a) Musculoskeletal findings: dolichostenomelia (limbs disproportionately long compared to the trunk), arachnodactyly changes (positive thumb/Steinberg and Walker's (wrist) sign), pectus excavatum or carinatum, scoliosis/lordosis, joint hypermobility, and typical facies
b) CV abnormalities: aortic root dilatation, aortic dissection, mitral valve prolapse and valvular insufficiency
c) Ocular findings: ectopia lentis, cataract, myopia, retinal detachment
d) CNS: Dural ectasia (*i.e.* enlargement of dural sac and spinal cord canal leading to lower back pain)
e) The pulmonary and integumentary systems represent minor criteria. Complications include pneumothorax, striae distensae, and recurrent hernia

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pathway may also produce similar Marfanoid features.

This single gene mutation results in a protean manifestation of clinical findings involving the musculoskeletal, cardiac, and ocular systems. Clinical implications are enormous. Patients are easily identified by their tall and thin stature, long arm span, and spider like fingers, often associated with scoliosis.

The diagnosis of MFS is based on family history, molecular studies, and six organ systems (Ghent criteria). However, the classification system remains imperfect. Furthermore, because molecular studies are not readily available, an inaccurate diagnosis of the gene defect may occur, and complete understanding of the condition remains elusive.

It should be noted that other disorders can produce the appearance of MFS; therefore, genetic testing is of paramount importance. These conditions include Ehlers-Danlos syndrome, Loeys-Dietz syndrome (transforming growth factor β1 gene mutation), homocystinuria, multiple endocrine neoplasia, as well as congenital contractural arachnodactyly (Beals syndrome).

The management of MFS requires a multidisciplinary approach with the family physician overseeing the suggestions and recommendations of a clinical geneticist, cardiologist, ophthalmologist, orthopaedic, maxillofacial, and cardiovascular surgeons. Psychological and social work support are also essential.

General health care and advice for MFS include moderate restriction of physical activity, endocarditis prophylaxis, and cardiac monitoring for aortic root dilatation, which includes regular echocardiography as well as β-blocker therapy. Patients should be advised that there is a 50% risk of transmission to offspring. Pregnancy can place a severe strain on the health of the patient. CVD is the most common cause of death. Progressive aortic dilatation will lead to aortic dissection if untreated. Dysrythmias, valvular insufficiency, and regurgitation may also cause significant morbidity.

Despite all these challenges, the average life span of a patient with MFS often exceeds six decades. This is a laudatory testimony to the efforts of early diagnosis, patient education, lifestyle changes, medical advances, and improved surgical care of affected patients.

As an interesting aside, famous persons with MFS/MFS features include Abraham Lincoln, the greatest Olympic swimmer of all time: (Michael Phelps), composers/ musicians Niccolò Paganini and Sergei Rachmaninoff, Charles de Gaulle, and the infamous Osama bin Laden.

References

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