"Bead to death," Fibromuscular Dysplasia Presenting as A Rapidly Enlarging Right Anterior Axillary Mass

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CONFLICTS OF INTEREST: None

Abstract

Fibromuscular dysplasia (FMD) is a rare non-inflammatory, non-atherosclerotic arterial disease characterized by abnormal cellular proliferation and distorted architecture. It commonly affects the renal and extracranial carotid and vertebral arteries, but nearly all arterial beds may be affected, and multivessel involvement is common. We report a rare case of a 31-year-old Filipino female who presented with a rapidly enlarging right anterior axillary mass. Initial consideration was a bleeding soft tissue sarcoma as seen on chest CT scan, while whole abdominal CT scan with IV contrast revealed incidental findings of multiple aneurysms in the superior mesenteric artery, both renal arteries and right common iliac artery, suggestive of fibromuscular dysplasia. Further vascular imaging studies showed a looped left internal carotid, and a tortuous left brachial artery with beading pattern.

INTRODUCTION

Fibromuscular dysplasia (FMD) is a non-inflammatory, non-atherosclerotic arterial disease that is characterized by abnormal cellular proliferation and distorted architecture of the arterial wall. FMD primarily manifests as beaded (multifocal) or focal lesions in medium or small-sized arteries, though the clinical phenotype of FMD has recently been expanded to include arterial dissection, aneurysm, and tortuosity.[1,2] It commonly affects the renal and extracranial carotid and vertebral arteries, but nearly all arterial beds may be affected, and multivessel involvement is common. Approximately 80–90% of patients with FMD are women.[2,3] Though less common, men also develop FMD and may have a more aggressive course with a higher frequency of aneurysms and dissections.[3]

The exact prevalence of FMD is unknown, hence a US registry was created. A review of eight studies between 1963 and 2011 showed a mean prevalence of 3.3% among healthy transplant donors.[3] There are no prevalence studies established worldwide and in Asia.[4-6] Locally, there is only one published case report by Delos Reyes, et. al., of a 26-year-old female who presented with multiple aneurysms and arteriovenous malformation.[7]

CASE

This is a 31-year-old Filipino female, who came in due to a rapidly enlarging right anterior axillary mass of two weeks. She had no previous comorbid conditions and did not smoke. She has no family history of any connective tissue diseases, heart disease, or any autoimmune diseases.

On initial assessment, the patient was normotensive, tachycardic, afebrile and not in cardiorespiratory distress. She was weak-looking and pale. She has good carotid pulses with no bruit. The right upper extremity was cold to touch, with absent pulses in the right brachial and radial arteries, cyanosis with a capillary refill time of more than 2 seconds and absent sensation and motor strength in the right upper extremity. There was also a large, soft, tender mass on the right anterolateral axillary area measuring 12 cm x 12 cm with bleeding ulcerations

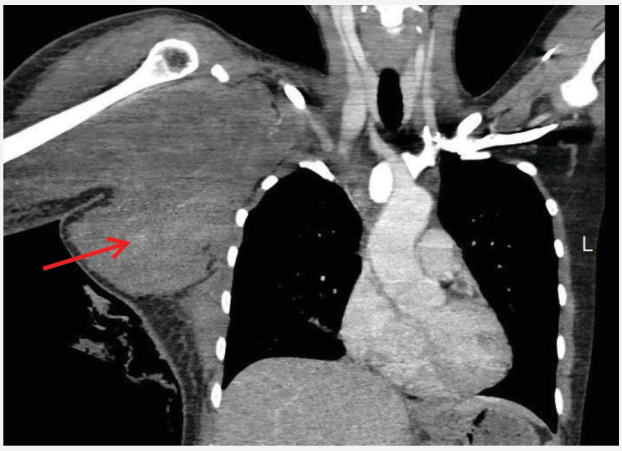

Figure 1. Chest CT scan with IV contrast showing an extrathoracic soft tissue sarcoma on the right posterolateral chest wall (red arrow).

A complete blood count (CBC) showed anemia with a hemoglobin of 68 g/dL, and blood was transfused. To evaluate the right anterior axillary mass, a chest CT scan with IV contrast was done, which showed an extrathoracic soft tissue sarcoma on the right posterolateral chest wall with extension to the right upper arm. Tumoral bleed was considered (see Figure 1). The patient was referred initially to an oncologic surgeon for evaluation and co-management.

The working impression at that time was soft tissue mass probably sarcoma, and acute limb ischemia of the right upper extremity probably due to compression of the right axillary artery. A whole abdominal CT scan with IV contrast was also done for malignancy work-up, which showed multiple abdominal dilatations in the following areas: superior mesenteric artery with thrombus formation, both renal arteries, right common iliac artery findings suggestive of fibromuscular dysplasia.

From her chest CT scan, initial consideration of a bleeding soft tissue sarcoma was made, while her whole abdominal CT scan with IV contrast showed incidental findings of multiple aneurysms in the superior mesenteric artery, both renal arteries and right common iliac artery, suggestive of fibromuscular dysplasia. A carotid duplex scan showed looping of the left ICA and left upper extremity duplex scan showed a severely tortuous left proximal brachial artery with beading pattern.

Due to the findings of multiple aneurysms suggestive of fibromuscular dysplasia, the patient was referred for co-management to the Cardiology–Vascular Medicine and Rheumatology services for evaluation of a possible vasculitis. Beta-blocker was started for blood pressure and heart rate control. Due to the bleeding, anticoagulation was contraindicated. ANA was negative.

Imaging of the peripheral arteries was done to search for other vascular anomalies. The carotid duplex scan showed a smooth intimal lining and a looped left ICA (Figure 2A-C). The arterial duplex scan of the bilateral upper extremities showed a smooth blood vessel intima with absent signals in the right distal brachial, ulnar and radial arteries; tortuosity and beading appearance of the left proximal brachial artery (Figure 3A-C).

Due to the sudden onset of symptoms, absence of intimal thickening or stenosis of the arterial beds, and lack of constitutional symptoms, vasculitis was unlikely. The revised working impression was fibromuscular dysplasia due to the presence of a beading appearance in the bilateral renal arteries and left brachial artery, left ICA tortuosity, and multiple aneurysms seen in the right common iliac and superior mesenteric arteries. The patient was then referred to vascular surgery and orthopedic surgery services, for surgical exploration of the right anterior axillary mass with possible amputation contemplated after the patient was stabilized and anemia corrected prior to surgery.

During wound exploration, upon entering the axillary space, there was an approximately 700-800 cc hematoma with a point of rupture at the proximal axillary artery. Hematoma evacuation was done. Vascular reconstruction was contemplated, however the axillary artery and its branches were noted to be extremely friable, easily avulsed even with vascular clamps. Instead, the axillary artery was ligated. Amputation of the right upper extremity was contemplated; however, due to the massive blood loss and the easy friability of the blood vessels, the surgeons opted to correct anemia prior to amputation. Histopathology of the ruptured axillary artery showed fragments of artery with surrounding blood clots and organizing hematoma and fibrofatty tissues showing organizing hematoma and fat necrosis (Figure 4).

On the first post-operative day, there was recurrence of epigastric pain which suddenly became diffuse, severe and progressive. Our impression was mesenteric ischemia probably secondary to acute thromboembolism. Patient underwent abdominal CT aortogram which showed new findings of celiac trunk saccular aneurysm with mural thrombus formation and tiny intimal flap to consider minimal dissection. Superior mesenteric artery also showed thrombus formation. Both renal arteries, right common iliac artery were suggestive of fibromuscular dysplasia with superimposed arteritis (see Figure 5). Pain medications and trial of steroids were given. However, the patient had sudden hypotension and decrease in sensorium, and eventually succumbed.

DISCUSSION

This 31-year-old Filipino, female, with no known comorbidities or any familial history of connective tissue diseases, initially came in for a right anterior axillary mass and was treated as a case of soft tissue mass to consider sarcoma, acute limb ischemia, and anemia secondary to tumoral bleed. Surveillance imaging with a whole abdominal contrast CT scan revealed

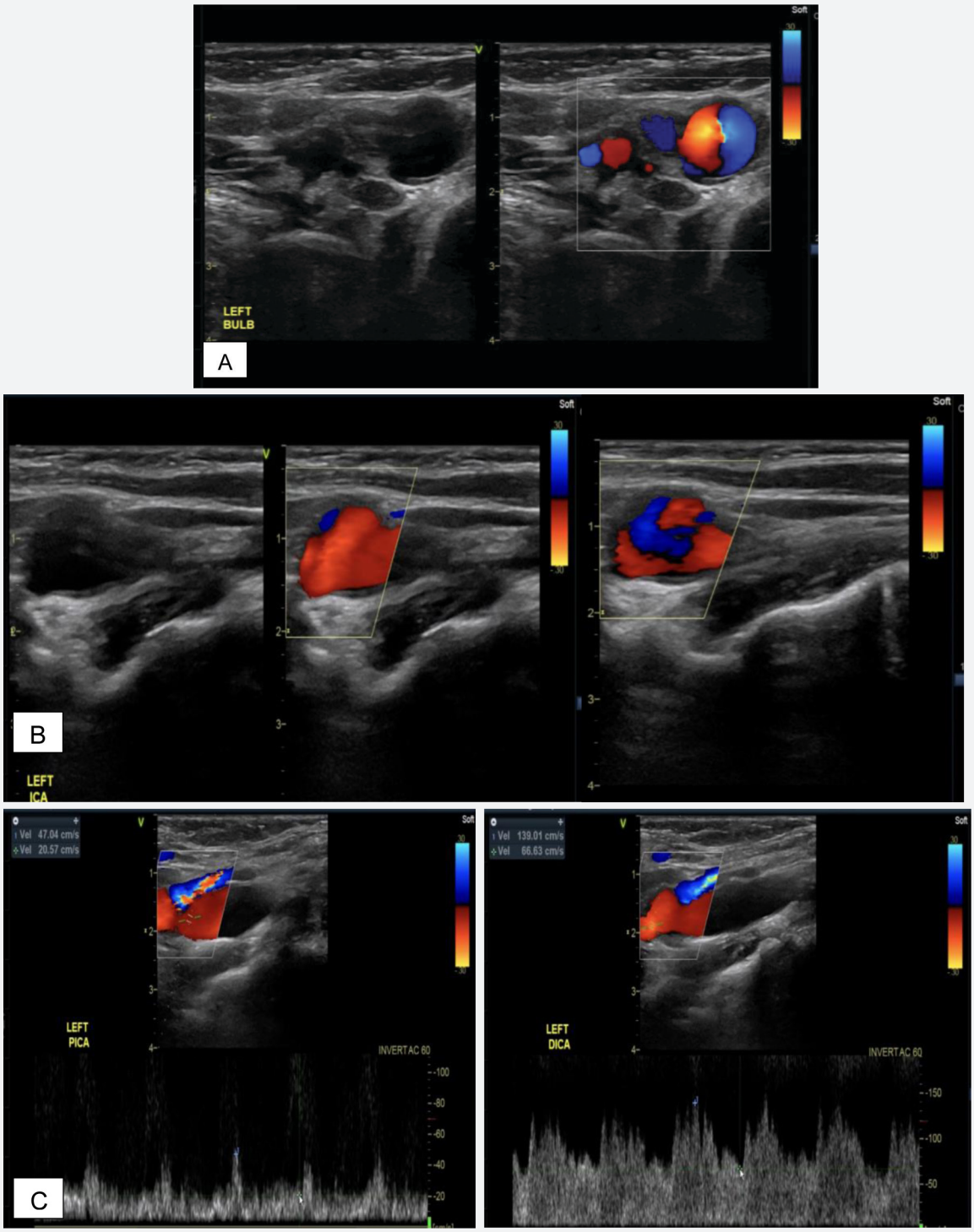

Figure 2A-C. Carotid duplex scan of the left internal carotid artery. **A.** Short axis view **B**. Long axis view **C.** Doppler study showed an increase in the peak systolic velocity from the proximal going to the distal ICA due to looping.

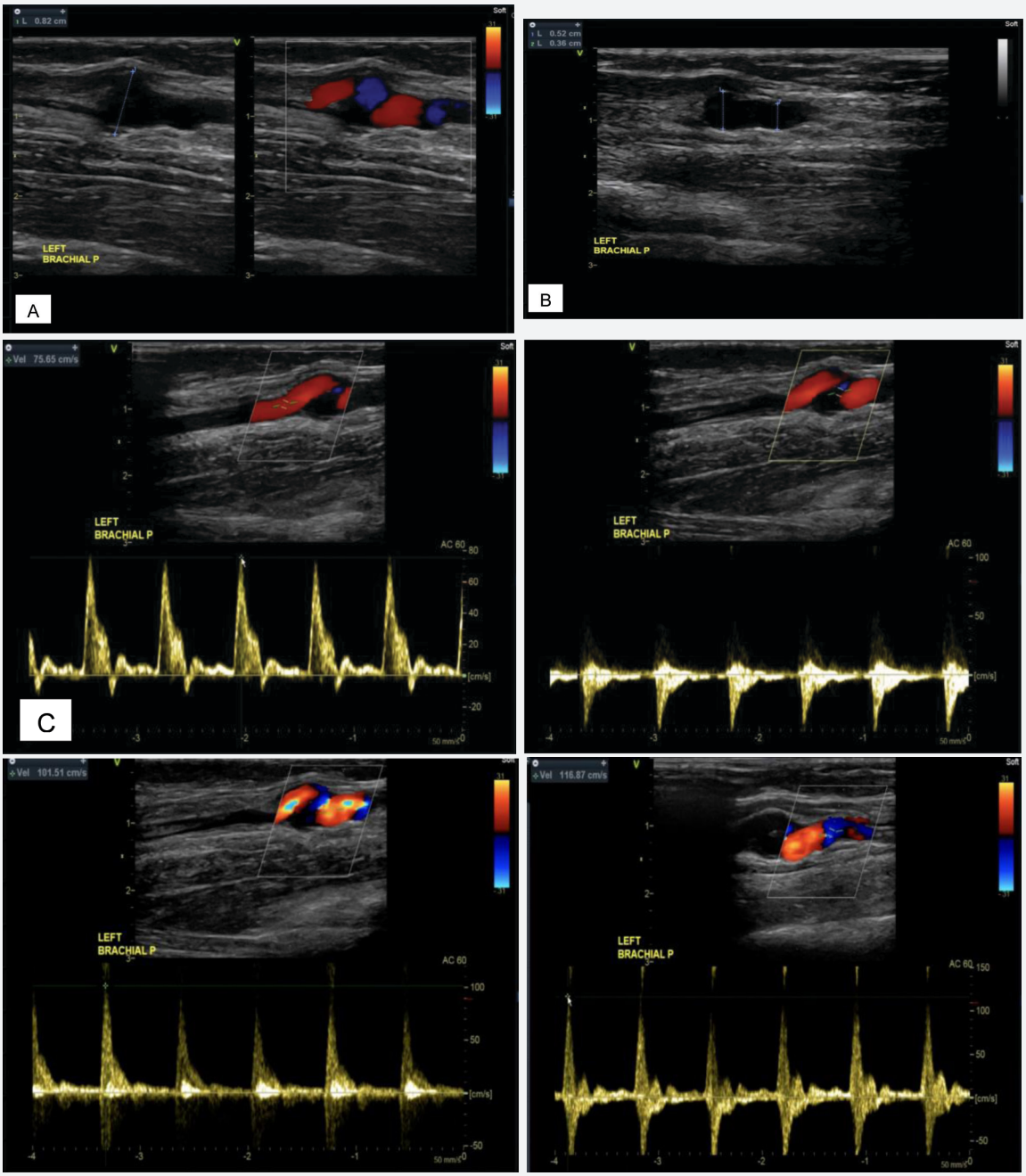

Figure 3A-C. Arterial duplex scan of the left upper extremity. **A.** Long axis view at the level of the proximal brachial artery, there is note of focal dilation but no areas of stenosis, plaque or intimal thickening. **B.** The dilated segment is followed by some widening and narrowing of the arterial segments. **C.** The color flow study of the left brachial artery in the dilated segment showed a delineation between the red and blue color. The blue color indicates a retrograde flow of blood while the red color indicates a forward flow of blood. As the blood flows forward, notice that the color flow is disturbed and becomes turbulent as it passes to the alternating narrowed and dilated segments. The Doppler study showed a forward and reversal waveform pattern.

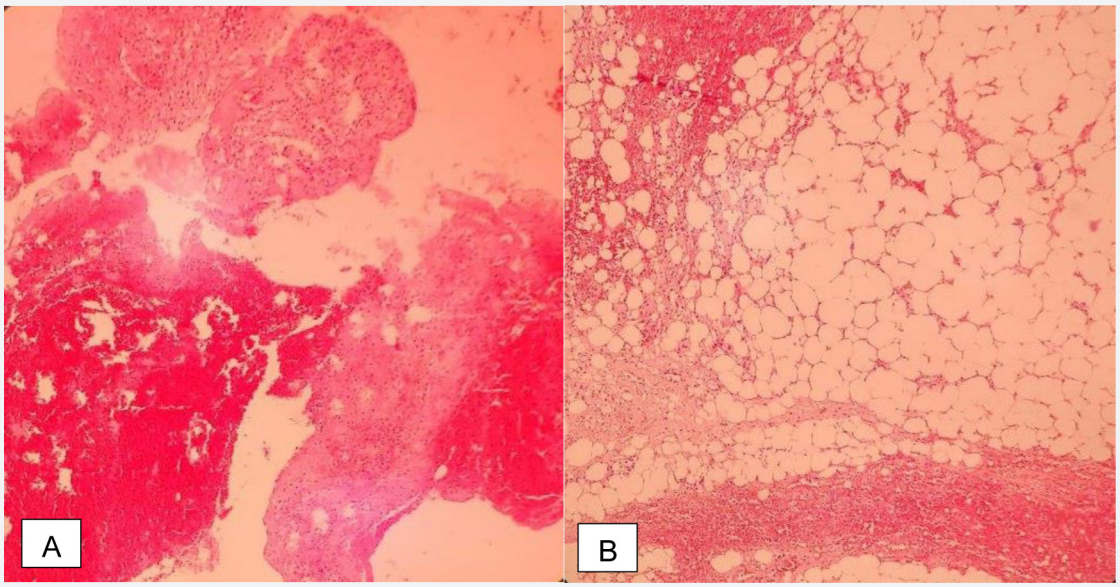

Figure 4A-B. Histopathology of the ruptured axillary artery. **A.** Fragments of artery with surrounding blood clots and organizing hematoma. **B.** Fibrofatty tissues showing organizing hematoma and fat necrosis.

multiple abdominal arterial dilatations in the following areas: superior mesenteric artery, both renal arteries, and right common iliac artery, findings suggestive of fibromuscular dysplasia.

According to Olin, et al., the clinical manifestations of FMD are variable and depend on several factors; most important are the distribution of vascular bed involvement and the type and severity of the vascular lesions (i.e., stenoses of various degrees, arterial dissection, arterial aneurysm).[8] According to the US Registry for FMD, most patients presented with at least one clinical symptom or sign, and only 5.6% of patients were truly asymptomatic, although this high prevalence of symptoms reflects the referral nature of the registry cohort. A detailed table of identified presenting sign and symptoms were provided.[9]

According to Gornik, et al., FMD occurs predominantly in females below the age of 50 years. The female-to-male ratio reported in most studies is 3:1, however, data from the US and French registry supported a 9:1 female preponderance. The median age for FMD is 48 years, though cases have been reported in pediatric as well as geriatric populations. There is no evidence to support racial or ethnic propensity, but Caucasians are more likely to be affected than an African population.[6]

During the patient's admission, fibromuscular dysplasia was entertained due to the imaging findings; however, an inflammatory disease was also considered due to her demographic profile. According to the first consensus on the diagnosis and management of fibromuscular dysplasia, vasculitis is a common mimic of FMD,[5] so the patient was also referred to Rheumatology. An ANA screening test for autoimmune diseases was negative. Other findings that may suggest vasculitis to be unlikely are the absence of intimal thickening on arterial duplex scan, carotid stenosis or occlusion, and the absence of constitutional symptoms, which made the diagnosis of FMD more likely. FMD may also be diagnosed by its "bead and string appearance," which the patient demonstrated both on whole abdominal contrast CT scan and arterial duplex scan of the upper extremities.

According to the first International Consensus on the Diagnosis and Management of Fibromuscular Dysplasia, the histopathological classification of FMD is no longer applicable in modern clinical practice. FMD may result in two types of angiographic appearance: (1) Focal FMD, which may occur in any part of the artery; or (2) Multifocal FMD, alternating areas of stenosis and dilation (the so-called 'string of beads'), which usually occurs in the mid and distal portions of the artery. This classification of FMD does not refer to histology as tissue is rarely available since the advent of endovascular therapy.

FMD most commonly affects the arteries that supply blood to the kidneys (renal arteries) and brain (carotid and vertebral arteries), but it can occur in almost any artery, including those that supply the intestines (mesenteric arteries), the arms (brachial arteries), and the legs (iliac arteries).[2] Nevertheless, it is important that the presence of aneurysms, dissections, or tortuosity in the absence of a focal or multifocal FMD stenotic lesion is not sufficient to establish a diagnosis of FMD. However, if the patient has a focal or multifocal FMD lesion in one vascular bed and a documented aneurysm, dissection, or tortuosity in another vascular bed, the consensus states that the patient be considered to have FMD in the vascular bed with the focal or multifocal lesion, as well as FMD involvement of the vascular bed with aneurysm, dissection, or tortuosity (i.e. multivessel

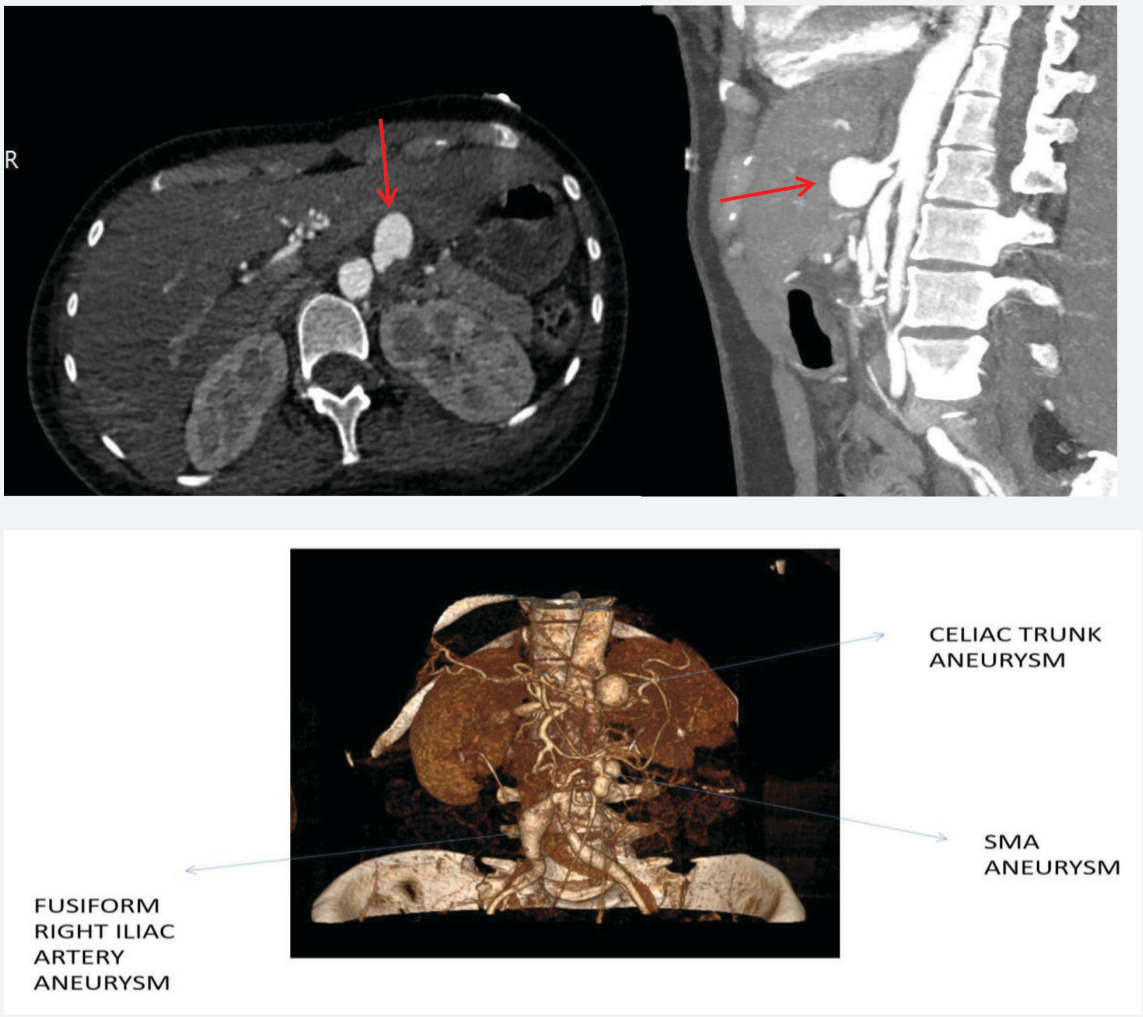

Figure 5A-B. CT Aortogram **A.** There is a new finding of saccular outpouching seen in the celiac trunk (as pointed by the red arrow) approximately measuring 1.7x 1.7cm (W x AP) with mural thrombus formation and tiny intimal flap noted. **B.** 3D Reconstruction.

FMD).[6] In many patients, FMD is found in more than one artery. However, there is no local data regarding age, sex predilection or arterial predilection of this condition.

There are also no current clinical guidelines for medical therapy in patients with FMD, due to the small population and the wide scope of symptoms that these patients may present with. There are conflicting reports regarding the benefit of antiplatelet therapy for FMD; however, these may be started for certain patients since it may present with prothrombotic events and sudden rupture of aneurysms and dissections. Other treatment modalities address control of hypertension and heart rate to decrease the incidence of aneurysmal rupture.

The number of patients with FMD is small, therefore adequate prognostication is difficult. A case series is recommended for this purpose. Also, comparative sensitivity and specificity studies of different imaging modalities may help delineate the degree of accuracy of each imaging modality.

CONCLUSION

Fibromuscular dysplasia is a rare disorder that presents with a wide myriad of signs and symptoms depending on the arterial bed affected. Differential diagnosis includes mimickers of FMD, such as vasculitis. Imaging patterns with the aortogram and arterial duplex scans showed the pathognomonic sign of the beads and string pattern, confirming the diagnosis of FMD. There are no current guidelines for the treatment of FMD making treatment and prognostication of patients difficult. Adaptation of a similar registry of patients with FMD similar to the US registry for close follow-up and prognostication is recommended.

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