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Title: Takayasu Arteritis Presenting as Renovascular Hypertension and Renal Failure in a Patient with Factor VII Deficiency

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Abstract

A 23-year-old female patient with FVII deficiency was admitted with severe hypertension and renal failure. Brachial arterial pressures were 230/120 and 220/115 mm/Hg on the right and left arms, respectively. There was no blood pressure difference between the arms. Renal artery Doppler ultrasonography revealed bilateral severe renal artery stenosis (RAS). Contrast-enhanced magnetic resonance imaging (CE-MRI) revealed severe mural irregularities, contrast enhancement in the aorta and its branches, and long-segment stenosis starting in the abdominal aorta and extending into the proximal renal arteries. The diagnosis of Takayasu arteritis (TA) complicated by RAS in a patient with FVII deficiency was established. This is the first case of concomitant TA and factor VII deficiency in the literature. In conclusion, TA complicated with RAS should be kept in mind in the etiology of secondary hypertension, even when there is no blood pressure difference between the arms in patients. CE-MRI is an accurate, sensitive, and safe imaging method for diagnosing vasculitis, even in the early phases of the disease, and should be considered for evaluating the activity and response to treatment in patients with TA.

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Keywords: Takayasu arteritis, factor 7 deficiency, renovascular hypertension, secondary hypertension, magnetic resonance angiography

Introduction

Takayasu arteritis (TA) is granulomatous vasculitis of the aorta and medium-sized arteries. The clinical presentation of patients with TA depends on the involvement of the arterial segment and the severity of the disease. The most common presentation of patients with TA involves the subclavian and renal arteries (1).

Factor VII (FVII) deficiency is a rare coagulation disorder that can be congenital or acquired. Congenital FVII deficiency is inherited in an autosomal recessive manner and has a prevalence of 1/500000 individuals (2). Acquired FVII deficiency is very rare and has been reported to occur due to sepsis, myeloproliferative diseases, and drugs (3,4). The usual clinical presentation is bleeding tendency, ranging from minor to life-threatening events (5). Paradoxically, 3–4% of patients with FVII deficiency present with thrombotic events (6). In this report, we aimed to present the first case of FVII deficiency together with TA complicated by renovascular hypertension and renal failure secondary to renal artery stenosis (RAS).

Case

A 23-year-old female patient with a history of hereditary FVII deficiency presented to a hospital with severe hypertension. The diagnosis of moderate FVII deficiency was established one year ago when she presented with abdominal pain. Her laboratory examination revealed increased prothrombin

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time (26.3 s), international normalized ratio (2.38), and fibrinogen levels (655 mg/dl) and decreased FVII antigen levels (19.3). The patient's medical history included a previous miscarriage six months ago. Tests for antiphospholipid syndrome including lupus anticoagulant and anticardiolipin IgM and IgG and anti-beta glycoprotein were negative. Brachial arterial pressures were 230/120 and 220/115 mm/Hg on the right and left arms, respectively. There were no blood pressures differences between the arms. Arterial pulses were normal in the upper extremities but diminished in the lower extremities. The ankle-brachial index was calculated to be mildly decreased at 80%. Cardiac auscultation revealed a 2/6 apical systolic murmur radiating to the left axilla. Serum creatinine levels were elevated (1.83 mg/dL), indicating renal failure. To exclude pheochromocytoma as a cause of secondary hypertension, 24-h urine metanephrine and normetanephrine levels were measured and were found to be normal. Renal ultrasound (US) revealed normal-sized kidneys. Renal artery color Doppler ultrasonography displayed RAS with increased peak flow velocity in the suprarenal abdominal aorta (510 cm/s), right renal artery (350 cm/s), and left renal artery (320 cm/s). The resistive indexes increased in both renal arteries (0.82). Echocardiography revealed moderate-degree mitral regurgitation with normal left ventricular systolic function. Contrast-enhanced magnetic resonance angiography (MRA) revealed 50% segmental stenosis in the right subclavian artery and 55% stenosis in the left subclavian artery (Figure 1). Long-segment stenosis (nearly 75%) in the abdominal aorta was observed, which extended into the proximal portion of the left renal artery (Figure 2). Additionally, contrast-enhanced magnetic resonance imaging (CE-MRI) displayed severe mural irregularities and contrast enhancement in the descending thoracic aorta, abdominal aorta, and bilateral subclavian and renal arteries, indicating inflammatory processes without thrombosis. These findings were consistent with the diagnosis of type 5 TA based on imaging findings (1). The patient is currently being followed up and has been receiving antihypertensive and immunosuppressive treatments. TA was brought under control in the six-month follow-up with normal acute phase reactant levels and without complaints.

Informed consent was obtained from this patient for presenting this case.

Discussion

We presented the case of a patient with concomitant FVII deficiency and TA complicated with RAS in a young female. TA is a chronic granulomatous inflammatory disease that affects medium- to large-sized arteries such as the aorta and its main branches. TA is most commonly seen in women of

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reproductive age. The incidence of the disease is 1.2–2.6 cases/million every year and is more commonly seen in Asia. Its clinical picture varies from nonspecific findings to characteristic features such as diminished or absent pulse, claudication, blood pressure difference between the arms, hypertension, or neurologic findings, depending on the involvement of the arterial segment. Inflammation of the affected artery segments leads to segmental stenosis, occlusion, dilatation, and progressive aneurysm formation in a progressive manner. The disease involves subclavian arteries, common carotid arteries, and, less commonly, renal arteries (1). Renal arteries are involved in 35% of cases and may lead to resistant hypertension and renal dysfunction (7).

As an investigation for secondary hypertension, the patient underwent CE-MRA. CE-MRA revealed 50% stenosis in the right subclavian artery and 55% stenosis in the left subclavian artery, with long-segment severe stenosis in the abdominal aorta extending into the proximal portion of the bilateral renal artery. Mural irregularities and thickening with significant contrast enhancement in the vascular walls were observed on performing CE-MRI, with black blood T1-weighted sequence strongly suggesting vasculitis. Although digital subtraction angiography (DSA) is still the gold standard for diagnosing vascular pathologies such as stenosis, occlusions, and aneurysms in the chronic phase of TA, CE-MRI is more sensitive in the early phases of TA (1). MRI is a non-invasive reliable imaging modality that demonstrates various aspects of vasculitis, such as vessel wall thickening, irregularities with mural edema, and increased mural vascularity (8). Typical findings of TA in the acute phase are vessel wall thickening, irregularities with mural edema, and increased mural vascularity (9). Thus, MRA is increasingly used in current clinical practice for diagnosing vasculitis such as TA, and it is more accurate, more sensitive, and safer than DSA in this context (10). Furthermore, in a recent study, it has been suggested that MRA can be used to evaluate the activity and response to treatment in patients with TA (9).

FVII deficiency is a rare coagulation disease in which patients usually present with bleeding in clinical practice (5). Paradoxically, FVII deficiency can induce spontaneous or trauma-induced arterial or venous thrombotic events (3). In the literature, only 20 cases of FVII deficiency-induced thrombotic events have been published. Most of the patients had venous thromboses induced by surgery or trauma (3). Factor deficiencies and mutations that may cause thrombosis may exist with an additional cause of thrombosis with a completely different mechanism such as vasculitis. The pathophysiological mechanisms of the association between FVII deficiency and inflammatory

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vascular process are yet to be elucidated. One possible explanation is that severe FVII deficiency can cause spontaneous intramural microhemorrhages in large arteries due to shear stress. Vasculitis, aneurysms, and fibrosis can develop in the same segments of the arterial tree in the healing phase. To conclude, we presented the first case of concomitant TA and FVII deficiency. TA with RAS should be kept in mind as an etiologic factor for secondary hypertension, even if there is no blood pressure difference between the arms. CE-MRI is an accurate, sensitive, and reliable imaging method for diagnosing vasculitis, even in the early phases of the disease, and may be useful for evaluating the activity and response to treatment in patients with TA.

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Figure legends.

Figure 1. Reformatted coronal thoracic MRA images demonstrating the stenotic segment of the bilateral subclavian artery (arrows).

Figure 2. Reformatted coronal abdominal MRA images demonstrating the stenotic segment of the left renal artery and abdominal aorta (arrows).

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