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SHORT REPORT

A Rare Case of Thromboembolism in a 21-year Old Female with Elevated Factor VIII

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In this article we present the history of a previously healthy female adolescent, who was seen at our hospital with abdominal pain. This was the result of a large floating thrombus in the aorta. Widespread embolism occurred, which lead to the loss of a limb and a left hemicolectomy. Although our patient is a smoker, used oral contraceptives and was found to have a heterozygote mutation at the factor V Leiden gene, the most important factor contributing to her thrombophilia is thought to be her significantly elevated factor VIII. We stress an aggressive diagnostic and therapeutic approach in young patients with unknown embolism in order to avoid the grave consequences of delay.

Keywords: Spontaneous aortic thrombus; Young patients; Factor VIII; Peripheral embolism.

Introduction

We report of a young female, who spontaneously developed a aortic floating thrombus and subsequent peripheral embolism, leading to leg amputation and a hemicolectomy. Spontaneous thrombus formation in the aorta is rare. Because of the dramatic effects resulting from embolism we stress that aggressive diagnostic and therapeutic measures are necessary to avoid grave morbidity.

Case Report

A 21-year old, previously healthy woman presented at our Emergency Department with lower abdominal pain. She used an oral contraceptive (OC) and was a sigarette smoker. Shortly afterwards, she developed an ischaemic left leg with loss of sensation and foot pulses. The acute onset suggested peripheral embolism. A selective angiogram showed occlusion of all crural arteries at ankle level in an otherwise normal vascular system. To detect the source, a magnetic resonance angiogram (MRA) was made, showing infarction in the right kidney, occlusion of the left profound femoral artery, progressive occlusion in the left lower leg, and a floating mass in the abdominal aorta. (Figs. 1 and 2) She underwent an acute aortotomy at which a thrombus was removed and a selective thromboembolectomy of all crural vessels. Inspection of the intestine showed embolism in sidebranches of the inferior mesenteric artery resulting in ischaemia, for which a left hemicolectomy was necessary. Because of poor reperfusion of the leg, a second exploration was done at which already newly formed thrombi were extracted. Prompt thrombolysis with urokinase injected directly in all crural vessels was performed in order to resolve any residual thrombus. The patient recovered in the ICU where she received heparin (APTT: ca. 70 sec.), epidural and systemic vasodilative drugs. In spite of this aggressive therapy reocclusion occurred, most likely caused by a no-reflow phenomenon. Finally, a through-knee amputation was performed. Recovery of the hemicolectomy was uneventful. Life-long warfarin was prescribed.

Histological examination of the leg and left colon showed intravascular thrombus, but no obstruction

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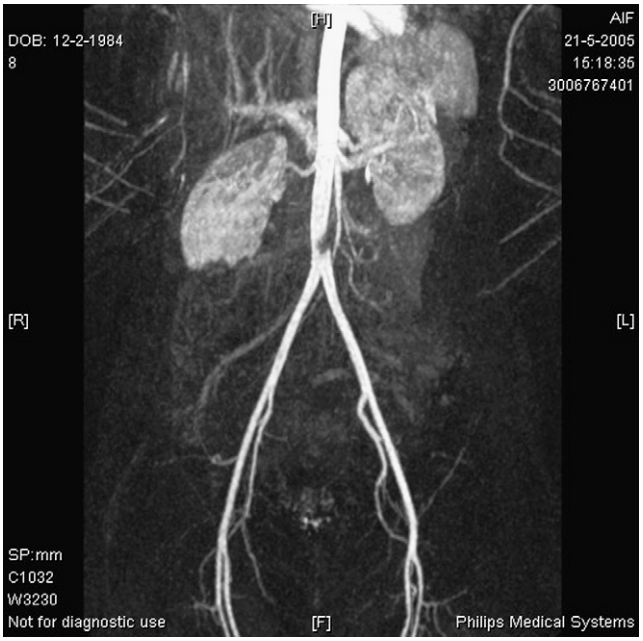

Fig. 1. Preoperative MRA, showing infarction in the caudal section of the right kidney and a large thrombus in the abdominal aorta.

otherwise or signs of vasculitis. Aortic wall samples and thrombus showed no abnormalities. No thrombus was found at trans-oesophageal echocardiography (TEE). EKG was normal. Heparin induced trombosis was excluded because the patient had never beenexposed to heparin before. Anticardiolipin, cholesterol and antithrombin levels were normal. Hypercoagulability screening revealed a heterozygote mutation at the factor V Leiden (fVL)gene. Proteines S and C could not be determined reliably because of warfarin administration.Testing for paroxysmal nocturnal haemoglobinuria was negative. However, an elevated factor VIII (fVIII) serum level (315%; normal: 70−150%) was found.

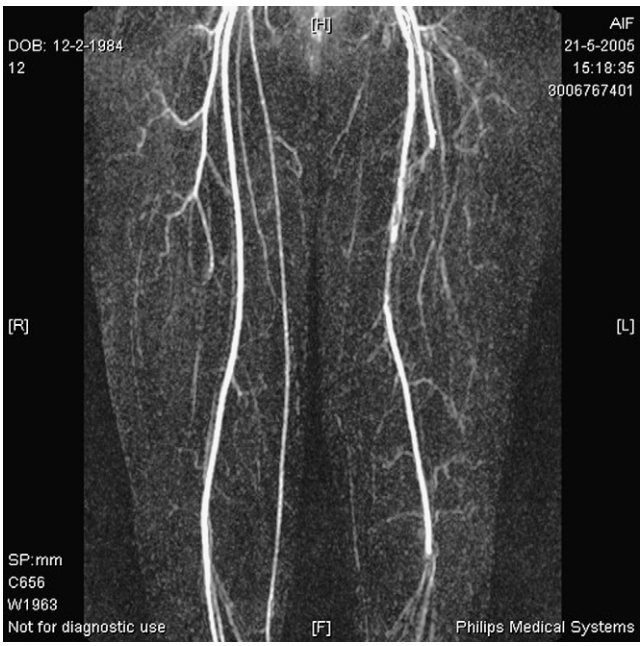

Fig. 2. Preoperative MRA, showing ooclusion of the left profound femoral artery and popliteal artery.

Discussion

A floating aortic thrombus is a rare condition in an otherwise healthy 21-year old. Coagulation cascade activation leading to aortic thrombus formation usually occurs as a result of atherosclerotic plaque rupture, but is not seen in adolescents. Although the patient was found to have a heterozygote mutation of the fVL gene, this finding does not provide an explanation for spontaneous thrombus formation in this high-flow vessel. Hypercoagulability can arise from a mutation in the fVL gene, but a relationship with aortic thromboemboli has never been established. Hypothetically, OC-induced protein S or C deficiency may have enhanced the mild hypercoagulability due to a heterozygote fVL mutation, although these deficiencies were never consistently demonstrated.[1] Onwuanyi reported of mural aortic thrombi resulting from protein S and C deficiency.[2] However, according to literature high fVIII serum levels are clearly associated with both venous and arterial thrombosis.[3,4] This may have contributed significantly to our patient's thrombophilia.

Often no satisfactory explanation can be found when spontaneous thromboembolic events occur in healthy adolescents. In such patients, it is believed to result from external factors (e.g. oral contraceptives, smoking) combined with previously unknown inborn coagulopathies. In our patient, combined factors (elevated fVIII, heterozygote fVL mutation, OC, smoking) may have led to thrombus formation.

The non-aneurysmatic aorta is likely to be unrecognized as a source of systemic embolism, specifically in adolescents. TEE and CT-angiography are reliable methods to identify thoracic and abdominal aortic thrombi, and should be performed in case of peripheral embolism, particularly in low-risk patients.[5] Also, the presence of any coagulopathies including elevated fVIII should be investigated. The detrimental effects of (ongoing) peripheral embolism justify an aggressive diagnostic and therapeutic approach. Although rare, this diagnosis must not be overlooked in the quest for an etiology of recurrent peripheral

ischemic events because of the gross functional risk resulting from a delayed diagnosis and therapy.

References

1 Koenen RR, Christella M, Thomassen LG, Tans J, Rosing G, Hackeng TM. Effect of oral contraceptives on the anticoagulant activity of protein S in plasma. *Thromb Haemost* 2005;**93**(5): 853–859.

2 Onwuanyi A, Sachdeva R, Hamirani K, Islam M, Parris R. Multiple aortic thrombi associated with protein C and S deficiency. *Mayo Clin Proc* 2001;**76**(3):319–322.

3 Kawasaki T, Kaida T, Arnout J, Vermylen J, Hoylaerts MF. A new animal model of thrombophilia confirms that high plasma factor VIII levels are thrombogenic. *Thromb Haemost* 1999;**81**(2): 306–311.

4 Bank I, Libourel EJ, Middelkoop S, Hamulyak K, Van Pampus EC, Buller HR *et al*. Elevated levels of FVIII:C within families are associated with an increased risk for venous and arterial thrombosis. *J Thromb Haemost* 2005 Jan;**3**(1):79–84.

5 Lau LS, Blanchard DG, Hye RJ. Diagnosis and management of patients with peripheral macroemboli from thoracic aortic pathology. *Ann Vasc Surg* 1997;**11**(4):348–353.

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