Isolated brachial vein thrombosis in a patient with hyperhomocysteinemia

Trombose isolada de veia braquial em paciente com hiper-homocisteinemia

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INTRODUCTION

Thrombosis of the deep veins of upper limbs account for around 4% of all cases of deep vein thrombosis (DVT) and the brachial vein is the least often affected (26%), while the subclavian vein is the most common site (73%)[1]. Clinical presentation may include pain, edema and functional impairment or may be asymptomatic. Diagnosis is accurately confirmed by B-mode, color Doppler and spectral ultrasonography, on which the vein will exhibit incompressibility and dilatation with thrombus in the interior and no blood flow. Phlebography is no longer used.

Secondary causes of upper limb thrombosis are more common and are related to central venous catheterization and pacemaker placement. Venous thrombosis of the upper limb due to primary causes has an incidence of two in every 100 thousand people per year and is often associated with malignant diseases, effort thrombosis (Paget-Schroetter Syndrome) and thrombophilias[1,2].

The most prominent acquired thrombophilia is antiphospholipid antibody syndrome, while primary thrombophilias include Factor V Leiden disorder and prothrombin G20210A mutation, for example. Excess homocysteine can cause idiopathic vascular thrombosis and can be responsible for increasing recurrence rates by up to 2.7 times, 24 months after withdrawal of anticoagulants[3,4].

This paper describes the clinical case of a patient with isolated thrombosis of the brachial vein and hereditary hyperhomocysteinemia.

PART I – CASE DESCRIPTION

A 23-year-old female secretary, born and resident in Goiânia, GO, Brazil, with no history of abortion or miscarriage and one full term delivery without intercurrent conditions 3 years previously presented complaining of pain and edema in the upper left limb with onset 7 days earlier. Physical examination detected all pulses and dilated superficial veins (Pratt's sign - Figure 1). The patient said she had not suffered a trauma to the limb and had never had a similar complaint before.

Color Doppler echography of the affected limb (Figure 2) showed incompressibility and absence of blood flow on color and spectral mode in the left brachial veins only.

PART II - WHAT WAS DONE

After initiating investigation of possible causes, clinical treatment was prescribed using an active selective Factor X inhibitor (Rivaroxaban). An X-ray of the cervical spine did not show cervical rib or any other anatomic abnormalities. Antithrombin III, C and S proteins and Factor V Leiden were all assayed before the first dose of medication was administered and found to be within normal limits. Anticardiolipin IgG and IgM were negative. A homozygous mutation for homocysteine (genetic mutation C677T) was identified and serum concentration was 105.0 µmol/L (normal value: 14.0 µmol/L), according to high performance liquid chromatography.

Treatment was continued and the patient referred for outpatients follow-up. At 15-day follow-up,

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Figure 1. Day of hospital admission. Edema of entire upper left limb.

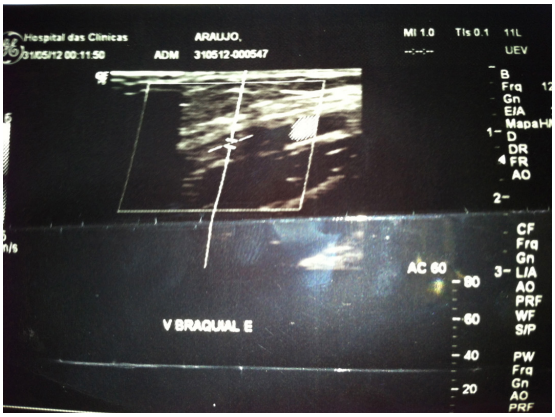

Figure 2. Brachial vein without blood flow.

an imaging exam showed partial recanalization of the affected vein and symptoms had improved considerably. We decided to keep the patient on anticoagulation for 6 months with continuous folic acid supplementation and periodic follow-up consultations.

DISCUSSION

Venous thrombosis of upper limbs is a rare clinical condition, particularly so when only the brachial vein is involved. The primary complications that can result from upper limb venous thrombosis are pulmonary embolism and postthrombotic syndrome[1,4]. Standard treatment is clinical, with oral anticoagulants and heparins. Thrombolysis may occasionally be a treatment option.

Hyperhomocysteinemia, which is a disorder of homocysteine metabolism, has recently been recognized as a risk factor for thromboembolic disease[5]. Homocysteine is a by-product of sulfur-containing amino acids and in excess it appears to be related to endothelial damage caused by oxidative and inflammatory mechanisms, and by reducing bioavailability of nitric oxide, which is a powerful endogenous vasodilator[4-8]. The homozygous methylenetetrahydrofolate reductase C677T mutation detected in our patient is related to high plasma homocysteine concentrations (phenotypical expression) and hyperhomocysteinemia confers even higher risks of thromboembolic phenomena such as DVT, pulmonary embolism, myocardial infarction and ischemic cerebral vascular accidents.

Serum homocysteine levels can increase in response to smoking and to deficiencies of folate and vitamin B12, which should be borne in mind when no etiologic diagnosis is found. Furthermore, genomic change (mutation) is not synonymous with phenotypical expression (high homocysteine levels)[6]. The normal range is from 5 to 15 µmol/L; figures above this level characterize hyperhomocysteinemia[8].

Treatment for thrombosis should be initiated as soon as diagnosis is made, but duration is not consensus[9]. Some authors prefer perennial anticoagulation because of the thrombophilia. In contrast, other choose to treat the first event for 3 to 12 months during the acute phase and only prescribe continual anticoagulation in cases of repeat thrombosis. High risk patients (two or more thrombosis episodes, atypical site, a DVT and more than one genetic mutations, cancer patients, and others) should be considered for indefinite anticoagulation in order to avoid recurrence[5,9].

Another situation that should be mentioned is how to manage pregnant or recently-delivered women, since the changes to the hematological system that take place during these periods predispose to thrombotic events. For high risk expectant mothers, low molecular weight heparin or unfractioned heparin are recommended throughout gestation and the postnatal period. For moderate risk expectant

mothers, heparin should be started from the second or third trimester of pregnancy and maintained postnatally.

For hyperhomocysteinemia, folic acid and vitamin B6 and B12 supplementation and dietary changes can reduce plasma levels effectively, but the impact this has on cardiovascular disease morbidity and mortality is a controversial subject and different studies contradict each other[10-12].

The case described here is of importance because of its rarity, but this possibility should not be forgotten when investigating patients complaining of pain in an upper limb, even when there is no obvious cause of venous thrombosis.

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