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REGULAR ARTICLE

Sialic acid is an inflammation marker associated with a history of deep vein thrombosis

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Triglycerides

Abstract

Introduction: Deep vein thrombosis (DVT) induces a systemic chronic inflammation and it has been associated with atherosclerosis. Increased levels of total sialic acid (TSA) have been shown to correlate with inflammation and atherosclerotic processes. The aim of this study was to investigate whether or not increased levels of TSA are associated with a history of DVT and with inflammation and coagulation markers, as well as with the lipid profile.
Materials and methods: TSA, fibrinogen, C-reactive protein (CRP), fibrin D-dimer (D-dimer), prothrombin fragment 1+2 (F1+2), endogenous thrombin generation, cholesterol and triglycerides were measured in 68 patients who had suffered, in the previous 6—12 months, a first episode of idiopathic DVT, and in 68 age- and sex-matched healthy subjects.
Results: Levels of TSA, fibrinogen, CRP and D-dimer observed in patients were significantly higher than those detected in healthy subjects. TSA positively correlated with fibrinogen ($R=0.47$, $p<0.01$), cholesterol ($R=0.46$, $p<0.01$), triglycerides ($R=0.38$, $p<0.01$) and CRP ($R=0.28$, $p<0.05$). The logistic regression analysis confirmed that both high fibrinogen (≥ 340 mg/dl) and cholesterol (≥ 267 mg/dl) levels significantly and independently influence the TSA concentration. TSA levels above the 95th percentile of controls (>72 mg/dl) were detected in 33% of patients (OR=8.9; $p<0.0001$; 95% CI 2.4 to 31.7).

Abbreviations: DVTdeep vein thrombosisTSAtotal sialic acidCRPC-reactive proteinD-dimerfibrin D-dimerF1+2prothrombin fragment 1+2ETGendogenous thrombin generationCHcholesterolTGtriglycerides.

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Conclusions: Patients with a history of DVT had associated high levels of TSA. In these patients, TSA correlated to markers of inflammation activity and lipid profile. Thus, TSA appears to be a useful vascular inflammatory marker in idiopathic DVT.

Introduction

Deep vein thrombosis (DVT) is considered as a multifactorial disease. In spite of its extreme frequency, little is known about the pathogenic mechanisms that initiate venous thrombosis. Furthermore, about 50% of patients with DVT do not have an underlying thrombophilic defect [1]. Recently, it has been suggested that patients with atherosclerosis may be at increased risk for venous thrombosis [2]. On the other hand, evidence suggests involvement of inflammation not only in the pathophysiology of arterial thrombosis but also in DVT [3,4]. However, relatively little is known about the relationship between inflammation and venous thrombosis. Several factors are currently under investigation in relation to inflammatory markers of atherothrombosis. TSA and fibrinogen may provide such markers. Measure of TSA levels has been shown to provide a useful tool for evaluating inflammatory status in chronic disease [5] as well as to correlate with the presence of atherosclerosis [6,7]. It has been reported that high levels of TSA have been considered as a risk factor for cardiovascular disease [8,9]; however, there are no data about the association between TSA and DVT. Prospective studies have shown a significant association between an increase of fibrinogen and the risk of venous thrombosis [10,11]. Hyperfibrinogenemia, independently of other risk factors, is associated to both the atherosclerotic progression [12] and the acute and chronic inflammatory processes [13]. Fibrinogen levels have been reported to strongly correlate to TSA levels in several chronic diseases [6,14—16]. Thus, TSA concentration may be related to fibrinogen either as a key of the blood coagulation and as a marker of the inflammatory process.

Taking together all these data and, on the other side, the fact that the nature of the relationship between inflammation and venous thrombosis has not yet been established, we decided to determine the significance of TSA concentration as a marker of both inflammatory activity and atherosclerotic progression in patients who suffered their first venous thrombotic event in the previous 6—12 months. We evaluated the possible relationship among TSA concentration and the levels of fibrinogen, CRP, D-dimer, F1+2, endogenous thrombin generation, cholesterol and triglycerides, in order to eventually employ them as sensitive markers of inflammation, coagulation and lipid profile.

Materials and methods

Subjects

A total of 68 consecutive patients who had suffered, between 6 and 12 months before, a first episode of venous thrombosis were referred to us for study. Sixteen patients (23.5%) suffered from pulmonary embolism. Their age ranged from 18 to 71 years (mean 40 ± 14 years). Forty-five percent of these patients were male.

The selection of patients was based on the following entry criteria: (1) if they had suffered a confirmed (by means of ultrasonography or venography) DVT, without a risk situation (immobilization or postoperative state); (2) they have not inherited origin thrombophilic risk factors (factor Leiden, prothrombin mutation, protein C or S deficiency, antithrombin deficiency, lupus anticoagulant and anticardiolipin antibodies); (3) they do not suffer from organic diseases (renal and hepatic), malignancy, or previous ischemic events (stroke, myocardial infraction, angina pectoris or peripheral occlusive arterial disease) and (4) they were not under pharmacological treatment for diabetes and/or hyperlipidaemia. None of the patients were on the oral anticoagulant at the time the blood samples were withdrawn.

The control group comprised 68 healthy subjects with a similar age and sex distribution to the patients (41 ± 16 years, 50% male), and without a previous history of venous or arterial thrombosis. The healthy voluntary subjects were recruited during the time that the study lasted.

The study was approved by the Hospital Clinic Research Ethics Committee. All the patients and healthy subjects who participated in this study gave their informed written consent to the protocol.

Blood sampling and processing

Blood samples were collected into Vacutainer tubes containing 0.129 mol/l sodium citrate. The ratio of anticoagulant to blood was 1:9 (v/v). Each sample was immediately centrifuged at $3000 \times g$ for 30 min