Case reports

Carotid plaque inflammation in a patient with unstable angina

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Coronary instability has been associated with multifocal plaque activation in the coronary circulation and in remote vascular districts, suggesting a systemic cause of instability, possibly inflammation. Magnetic resonance imaging offers a great potential for the detection of plaque inflammation.

We describe the case of a 73-year-old female admitted for unstable angina, elevated levels of C-reactive protein and three-vessel disease, in whom carotid ultrasound examination revealed an atherosclerotic plaque of the left proximal internal carotid artery with an irregular profile and a heterogeneous echographic texture, determining a 50% stenosis. Magnetic resonance imaging of the plaque before and after contrast enhancement by gadolinium-DTPA showed the following signs of inflammation: an increased vessel wall thickness, an increased triple inversion recovery-fast spin-echo signal intensity indicative of tissue edema, and a homogeneous plaque contrast enhancement indicative of an increased capillary permeability and neovasculature. As the carotid stenosis was < 70% and did not give rise to any symptom, the patient was submitted to coronary bypass surgery without concomitant carotid endarterectomy. Two days later she developed an ischemic stroke with right brachiocrural hemiplegia.

In the present case report, the simultaneous presence of coronary instability and a carotid plaque with magnetic resonance features suggestive of inflammation, which was probably responsible for the stroke complicating cardiac surgery, may indicate a multifocal plaque instability.

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Introduction

Plaque inflammation plays a pivotal role in the transition from chronic to acute forms of cardiovascular disease[1]. Accordingly, imaging techniques able to reveal vulnerable and inflamed atherosclerotic plaques might considerably improve risk stratification[2,3].

We describe the case of a woman admitted for an acute coronary syndrome associated with elevated systemic markers of inflammation, showing a non-stenotic carotid plaque with ultrasound characteristics of a high-risk plaque and magnetic resonance features suggestive of inflammation, who developed an ischemic stroke after coronary artery bypass grafting.

Case report

A 73-year-old female smoker was admitted to our coronary care unit with a non-ST segment elevation myocardial infarction preceded, during the previous 4 days, by unstable angina. On admission, the ECG showed ST segment depression in the V_3 to V_4 leads; the total creatine kinase (CK), CK-MB and troponin T serum levels were normal, while those of C-reactive protein (CRP), the prototypical marker of inflammation, were elevated (5.6 mg/l, normal values < 3 mg/l). The patient had no signs of infectious or inflammatory disorders. The peak total CK and peak CK-MB serum levels were 255 IU/l and 25 ng/ml respectively (normal values 30-170 IU/l and < 5 ng/ml respectively). Coronary angiography showed three-vessel disease. Therefore the patient was referred for coronary artery bypass surgery.

Before surgery the patient was submitted to a routine B-mode ultrasonography of the carotid arteries. The examination revealed an atherosclerotic plaque of the left proximal internal carotid artery determining a 50% stenosis as evaluated by the minimal residual area/total area ratio in a short-axis section. The plaque showed an irregular profile with a recess > 2 mm in depth and width and a heterogeneous echographic appearance (coexistence of hyperechogenic and hypoechogenic areas) consistent with a complex/complicated atherosclerotic lesion. Magnetic resonance imag-

ing (MRI) of the carotid plaque was also performed using a 1.5T cardiac scanner and a modified quadrature surface coil. Triple inversion recovery-gated fast spin-echo and spin-echo T1 wave sequences before and 15 min after the intravenous administration of gadolinium-DTPA (0.2 ml/kg) were used. The MRI acquisition parameters are listed in Table I. MRI study of the carotid arteries showed: 1) an increased wall thickness of the vessel suggestive of arterial wall edema and/or infiltration (Fig. 1); 2) an increased triple inversion recovery-fast spin-echo signal intensity of both the plaque and the adjacent arterial wall suggestive of tissue edema (Fig. 2); 3) a homogeneous plaque contrast enhancement of the opposite wall, suggestive of an increased capillary permeability and neovasculature (Fig. 3). All these features are considered to be markers of vascular inflammation. As the carotid stenosis was < 70% and no previous history of cerebrovascular accident had been reported, the patient was submitted to coronary surgery without concomitant carotid thromboendarterectomy after 6 days. Two days after cardiac surgery the patient developed an ischemic stroke with right brachio-crural hemiplegia, as documented by two subsequent computed tomographic scans. A transesophageal echocardiography excluded potential cardioembolic sources.

Table I. Magnetic resonance scanning parameters.

	SE	IR-FSE
Time of repetition (ms)	440	2 (R-R)
Time of echo (ms)	20	34
No. excitations	2	1
Matrix	256 × 256	256 × 256
Slice thickness (mm)	3	3
Slice gap (mm)	0.3	0.3

IR-FSE = inversion recovery-fast spin-echo; SE = spin-echo.

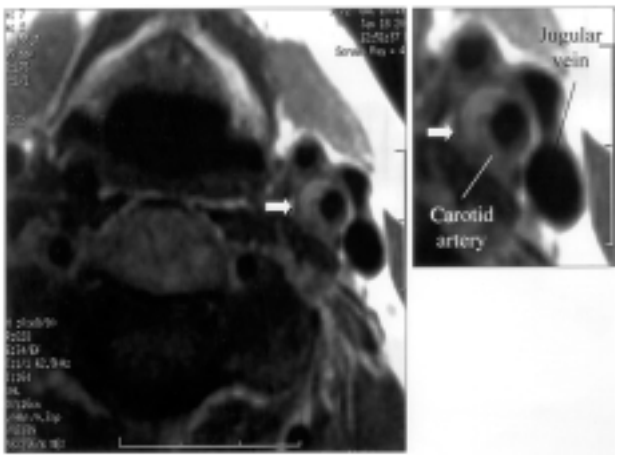

Figure 1. *Magnetic resonance image of the left internal carotid artery: an inversion recovery-fast spin-echo sequence in the axial plane showing proximal arterial wall thickening* (arrow). *In the* right panel *a zoom of the carotid plaque is represented.*

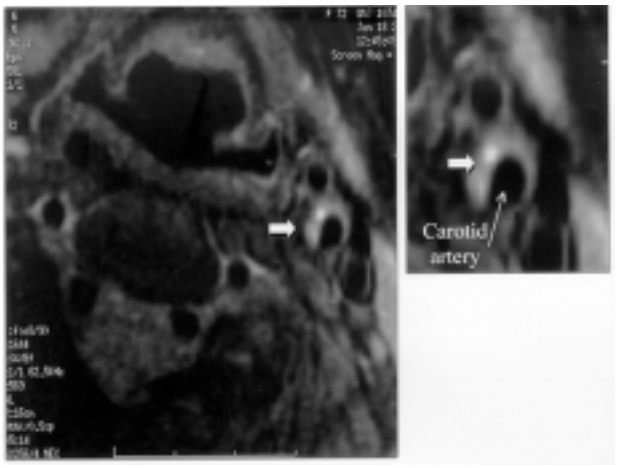

Figure 2. *Magnetic resonance image of the left internal carotid artery: a triple inversion recovery-prepared fast spin-echo sequence in the axial plane showing clear evidence of an inhomogeneous hyperintensity due to edema within an asymmetric carotid plaque* (arrow). *In the* right panel *a zoom of the carotid plaque is represented.*

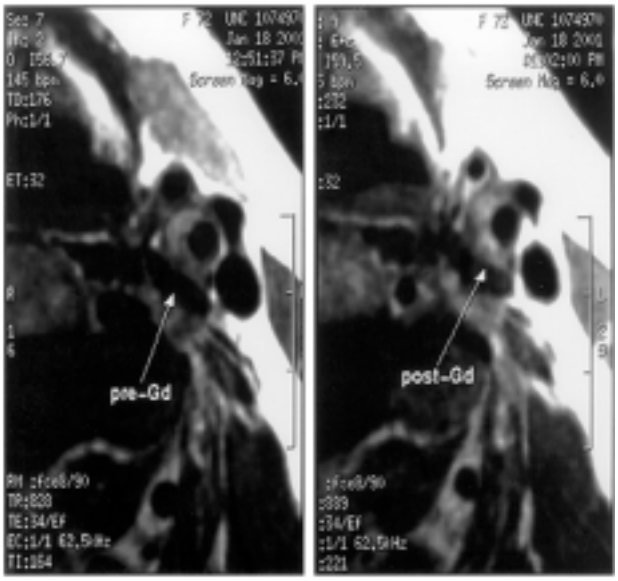

Figure 3. *Magnetic resonance image of the left internal carotid artery: an inversion recovery-fast spin-echo sequence before* (left panel) *and after* (right panel) *gadolinium (Gd)-DTPA administration: contrast enhancement can be appreciated within carotid plaque after Gd-DTPA administration.*

Discussion

The present case report refers to a patient with systemic signs of inflammation who presented with coronary instability and an irregular, although non-obstructive, carotid plaque with MRI features suggestive of inflammation. Even though other etiologies could not be excluded, embolization from this plaque was the most probable cause of the stroke which complicated cardiac surgery. Thus, with regard to this patient we hypothesize a multifocal plaque instability in different and remote vascular territories, probably due to a systemic

cause of instability, possibly inflammation. Other factors promoting plaque rupture such as a genetic predisposition to complex/vulnerable plaques could be hypothesized.

A growing body of evidence indicates that coronary instability is associated with multifocal plaque activation in the coronary circulation[4-7]. The mechanisms responsible for multifocal plaque activation in the coronary circulation might also involve remote vascular districts. In the European Carotid Surgery Trial patients, the presence of carotid plaques with an irregular morphology at one site was frequently associated with the presence of irregular contralateral plaques and also with a history of previous myocardial infarction and with the risk of non-stroke vascular death at follow-up[8]. Considered together, these findings suggest a systemic cause of instability of the atherosclerotic lesions, possibly of an inflammatory nature. Indeed, several clinical observations link inflammation to acute coronary syndromes: about 65% of patients with severe persistent unstable angina as well as nearly 100% of patients with preinfarction unstable angina have elevated levels of CRP on admission[9]. Furthermore, high CRP levels predict the risk of complications in patients with acute coronary syndromes, the risk of future cardiovascular events (including stroke) in both low- and high-risk patients and the development and/or progression of peripheral vascular disease[10,11]. Moreover, our preliminary studies suggest, in patients with unstable angina, an association between elevated CRP levels and irregular carotid plaques compared to smooth plaques[12].

The ultrasonographic carotid and aortic plaque characteristics including their echolucency and the presence of an irregular surface and a heterogeneous structure (reflecting both a mixed material – lipid, hemorrhage, thrombus – and possibly a dynamic process of rupture and healing) have been associated with a higher risk of cerebrovascular events[13]. Although B-mode ultrasound cannot reliably predict the histological plaque composition in detail, homogeneous plaques predominantly contain fibrous tissue while complex/heterogeneous plaques predominantly contain lipids and hemorrhagic material[13,14].

Recently, MRI has emerged as the non-invasive imaging technique of choice for the assessment of atherosclerotic vessels, offering a great potential for carotid plaque characterization *in vivo*. High-resolution MRI has been shown to recognize and quantify the lipid and fibrous components and to visualize the fibrous cap thickness and rupture within atherosclerotic plaques *in vivo*[15,16]. Gadolinium-enhanced MRI has been employed to detect arterial wall inflammation in large vessel vasculitis, such as active Takayasu arteritis and giant cell arteritis[17-19]. Indeed, since the distribution of contrast media depends on the extracellular volume and since the microvascular permeability in inflamed tissues is increased, vascular inflammation will result in an enhanced tissue contrast[20]. Very recently, signal enhancement following infusion of gadolinium has been shown to correlate with histological areas of neovascularization within unstable human carotid plaques[20]. Moreover, contrast enhancement has been found to correlate with the clinical and laboratory markers (CRP) of disease activity[18,21]. In the present case report we have taken three established markers of vascular tissue edema into consideration to detect vascular inflammation in atherosclerosis: the increased vessel wall thickness, the increased triple inversion recovery-fast spin-echo signal intensity and gadolinium enhancement. Recently, accumulation of superparamagnetic iron oxide particles has been observed in atherosclerotic plaques. As superparamagnetic iron oxide uptake has been observed in macrophage infiltrates, it might represent a more specific marker of inflammatory activity[22].

In conclusion, this case report suggests the possibility of multifocal plaque instability in two remote vascular districts. If these data are confirmed by larger controlled studies, contrast-enhanced MRI might play an important role in the identification of high-risk unstable atherosclerotic plaques.

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