Importance of assessment of carotid plaques in the management of acute ischemic stroke: floating intracarotid plaque

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ABSTRACT

Mobile atheromatous plaques affecting large arteries are a major risk factor for embolic strokes. We report a case of extensive embolic cerebral infarction secondary to a vulnerable internal carotid artery plaque. A 67-year-old female was admitted with sudden left-sided weakness. A computed tomography brain scan revealed early ischemic changes in the right middle cerebral territory. The ultrasound Doppler showed soft mobile plaque with thrombus in the right internal carotid artery causing 90% stenosis. Magnetic resonance imaging brain scan performed later showed extensive right cerebral infarction. A computed tomography angiogram revealed ulcerated non-occlusive soft tissue plaque in the right internal carotid artery. She was also diagnosed with bladder cancer during this admission and was managed medically due to her performance status. Unstable vulnerable plaques can be symptomatic even in the absence of significant carotid stenosis. Hence, early identification of the plaque vulnerability, using new imaging modalities, and its medical stabilization can help to reduce the risk of cerebrovascular insults. The etiopathogenesis of inflammation within unstable vulnerable plaques and its concordance with inflammatory markers is still unclear. It is feasible in our case the malignant process could also be contributing to the inflammation within the blood vessels promoting vulnerability of the plaques.

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Introduction

Large artery atherosclerosis is one of the five etiologies of acute ischemic stroke according to the *Trial of Org 10172 in Acute Stroke Treatment*.[1] It accounts for 20-30% of ischemic stroke cases.

Atherosclerosis is a dynamic inflammatory and immune process that involves arterial walls. Atherosclerotic plaque is the main pathology induced by atherosclerosis.[2] Most plaques are silent and asymptomatic.

Floating plaque is a form of unstable or vulnerable plaque. When present, it is associated with cerebrovascular incidents like transient ischemic attack or ischemic stroke. However, it is uncommon in clinical practice.

We present a case of floating vulnerable plaque in the right internal carotid artery in a woman who presented with left hemiparesis to our stroke unit.

Case Report

A 67-year-old woman was admitted to our stroke unit with significant left-sided weakness and left facial palsy. She didn't have a significant medical history, but she was a heavy smoker (40 pack-years) and drank an excess of alcohol. Her first computed tomography (CT) brain showed an acute cortical infarct in the right frontal lobe. A carotid duplex (Figure 1) was done, and it revealed a right internal carotid artery (ICA) mixed plaques and thrombus causing 80-89% stenosis. The case was discussed by the vascular surgeons and the MDT decision was for medical management and not for surgical intervention in view of the patient's high NIH Stroke Scale.

The patient was treated medically with high-dose aspirin

and high dose statin. After two days, her weakness got worse, and she developed new dysphagia, so a magnetic resonance imaging (MRI) of the brain was requested (Figure 2). There was extensive acute infarction in the right hemisphere in the MRI scan: frontal, temporal, and occipital lobes. A computed tomography angiogram (CTA) showed a soft tissue ulcerated plaque at the right ICA bulb with stenosis of less than 30% (Figure 3). Her laboratory investigations came with iron deficiency anemia and high C-Reactive Protein (CRP). As she gave a history of recent significant weight loss, a CT thorax, abdomen, and pelvis was done. A urinary bladder mass was found, and it was confirmed malignant on cystoscopy examination. She received palliative treatment for her tumor because of her significant stroke-related disability. She had a percutaneous endoscopic gastrostomy tube inserted for feeding and was discharged to a 24-hour care home.

Discussion

Atherosclerosis is a systemic disease. The atherosclerotic plaque is composed of a lipid core and a covering fibrous cap (FC). There are continuous changes within the plaque itself during the development of atherosclerosis.[3] The plaque will be symptomatic once the changes lead to significant vascular stenosis or occlusion. However, few plaques cause damage apart from the degree of stenosis. These are called vulnerable or unstable plaques.[4]

A cascade of changes converts the stable plaque into a vulnerable plaque. This starts with endothelial activation by numerous factors that include infectious agents, nicotine, homocysteine and oxidized low-density lipoprotein (LDL).[5] Dysfunctional endothelium allows inflammatory cells and LDL to pass into the subendothelial space and lipid core. Then LDL is oxidized by free radicals to form a reactive and cytotoxic compound. This oxidized LDL stimulates inflammatory cells to produce proteases like matrix metalloproteinases (MMPs) and cytokines. MMPs degrade the plaque cap exposing the underlying thrombogenic core to luminal blood. Finally, a thrombus forms at the site of rupture and this may lead to embolism depending on local coagulation and fibrinolytic mechanisms.

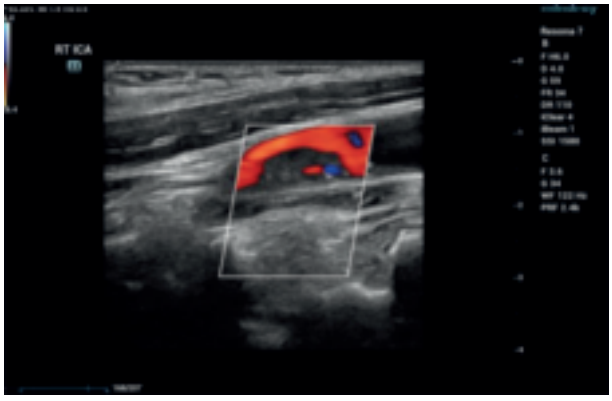

Figure 1. Carotid Doppler shows intra-arterial mixed plaque and thrombosis.

Histologically, the vulnerable plaque has a large lipid core and a thin fibrous cap. The high lipid content decreases the load-bearing capability of the plaque and increases the stress in the overlying fibrous cap.[6] Under certain extrinsic factors, like high blood pressure and vasospasm, the plaque can easily rupture.[7] Other features of plaque vulnerability are neovascularization and

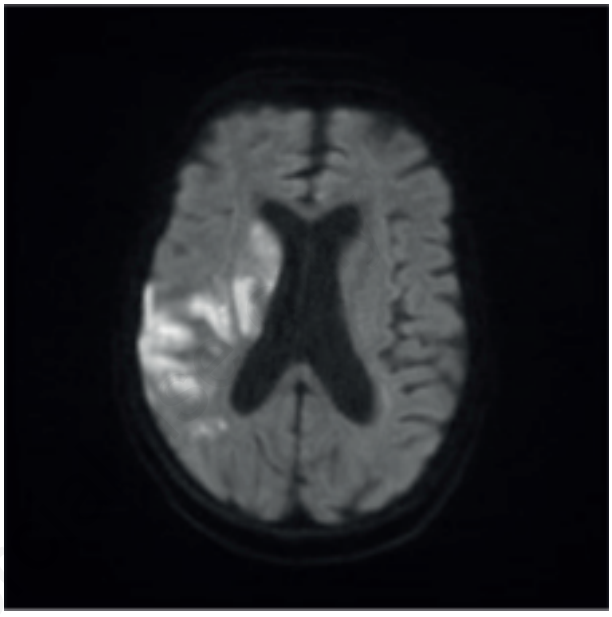

Figure 2. Magnetic resonance imaging of the brain shows extensive right cerebral infarcts.

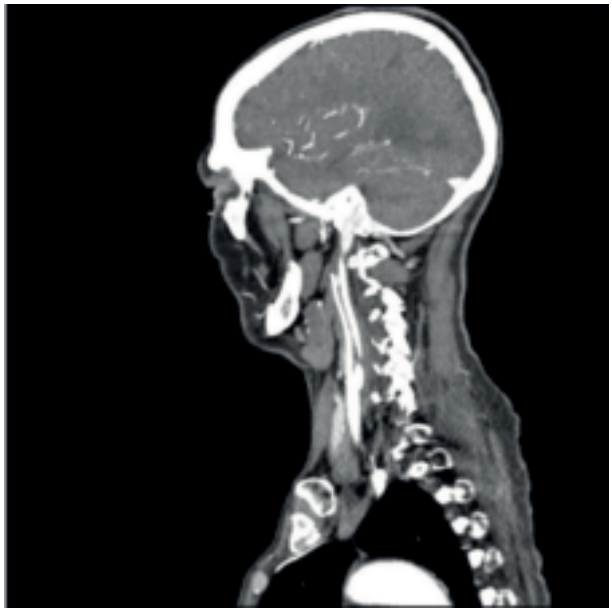

Figure 3. The computed tomography angiogram shows an ulcerated plaque at the right internal carotid artery bulb.

intraplaque haemorrhage.[8] There are controversies regarding the effect of arterial calcification on plaque nature. Some studies suggest that calcification gives the plaque more stability,[9] while others consider it a sign of vulnerability, irrespective of the degree of stenosis.[10]

There is an asymmetrical distribution of the mechanical stress levels along the symptomatic carotid plaques according to Thrysøe *et al*.[11] Around 50% of the mechanical stress was proximal (upstream side) while 25% was distal (downstream side) to the point of maximal stenosis. This stress level has an inverse correlation with the thickness of the fibrous cap (FC). The upstream side of the stenosis is considered the oldest part of the plaque. It is proved that it has more neovascularization and hemorrhage with the thinnest FC.[12] This could explain why vulnerable carotid plaque mostly ruptures in this region.[13] Different imaging modalities are in use now, to improve the identification of rupture-prone plaques, like intravascular ultrasound, intravascular ultrasound elastography, high-resolution MRI and optical coherence tomography.

It is proved that inflammation is the main feature of the atherosclerotic process, especially in the stage of destabilisation.[14] Hence, the relation of the inflammatory markers to vascular events has been under study with particular attention to serum Amyloid-A and CRP. Their levels were positively correlated to recurrent coronary events in *The Cholesterol Recurrent Events Study.*[15]

There has been rising evidence that CRP level is associated with the severity of atherosclerosis and cardiovascular risk.[16] There is an increased risk of myocardial infarction and sudden cardiac death in patients with angina and high CRP level.[17] The effectiveness of statins in the reduction of high CRP levels and risk of vascular events, independently of lipid-lowering, was clear in patients with low cholesterol and high CRP.[18] Healthy males with high CRP levels have the greatest benefit from antiplatelet therapy.[19]

In the present case, our patient had a floating atheromatous plaque with a formed thrombus making significant stenosis of the right ICA. This mobile plaque/thrombus sent a first embolus which caused her left-sided hemiparesis. This was shortly followed by a complete detachment of the carotid lesion and its lodgment in the anterior circulation of the right brain hemisphere. This resulted in the worsening of her neurological deficit and left a carotid ulcer seen in the CTA.

Although she didn't have the usual vascular risk factors: hypertension, diabetes or hyperlipidemia, her lifelong heavy smoking could be the culprit for developing a vulnerable carotid plaque. She had persistently high CRP during her stay in the hospital for five-month which had never been back to a normal level. Her records showed normal CRP six-month before her admission to our hospital. The robust association between high CRP and cancer risk is yet debatable: whether elevated CRP levels cause cancer, occult cancer increases CRP levels or a third factor, *e.g.*, inflammation, increases both CRP levels and the risk of cancer. Our case raises again the concern about the role of high CRP in the transformation of carotid plaque into a vulnerable one even if it was high secondary to malignancy. The site of rupture of the vulnerable plaque in our case was the bulb of the ICA. This comes in agreement with the literature,[20] showing that carotid ulceration was most often seen in the upstream part of the plaque where the wall shear stress was highest.

Conclusions

Unstable plaques can be symptomatic even in the absence of significant carotid stenosis. Hence, early identification of the plaque vulnerability, using new imaging modalities, and its medical stabilization can help to reduce the risk of cerebrovascular insults. The etiopathogenesis of inflammation within unstable vulnerable plaques and its concordance with inflammatory markers is still unclear. It is likely that in our case the malignant process could also be contributing to the inflammation within the blood vessels promoting vulnerability of the plaques.

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