



Stroke from internal carotid artery occlusion during mumps infection

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Abstract

During the terminal incubation period of severe mumps infection, a 40-year-old patient suffered from large infarction in the right middle cerebral artery territory. The proximal right internal carotid artery (ICA) was occluded on angiography. Computed tomography of the neck detected a hemorrhage located ventromedial to the right common carotid artery. Four months later the right ICA was partly recanalized. Carotid surgery revealed an atherosclerotic plaque and a vessel wall, which was fragile and less compact than usually. A strong inflammatory reaction to mumps infection may have contributed to the pathogenesis of the cervical hemorrhage and to acute thrombosis and occlusion of the ICA. © 1998 Elsevier Science B.V.

Keywords: Severe mumps infection; Cerebral infarction; Cervical hemorrhage

1. Introduction

For almost a century, evidence has been collected that acute and chronic infectious disease may lead to vessel injury and may contribute to atherogenesis (Wiesel, 1906). More recent research indicated that chronic infection with *Chlamydia pneumoniae*, Cytomegalovirus and other microbial agents may play an important role in the pathogenesis of atherosclerosis (Hajjar, 1991; Grayston, 1993). Furthermore, acute infection has been identified as a risk factor for ischemic stroke. Various pathogenetic pathways may be involved in the association of infection and stroke and acute infection appears to increase the risk for several etiological stroke subtypes (Grau et al., 1995a,b). Here we report the unusual case of a patient with stroke from

internal carotid artery (ICA) occlusion during severe mumps infection.

2. Case report

A 40-year-old male patient was admitted after he had acutely developed severe sensorimotor hemiparesis on the left and forced gaze to the right side. He smoked 20 cigarettes per day but had no other vascular risk factors, preexisting diseases or previous trauma. Early cerebral angiography showed proximal right ICA occlusion and mild distal common carotid artery (CCA) stenosis but no signs of atherosclerosis in other arteries visualized. Injection into the left vertebral artery indicated a right proximal middle cerebral artery (MCA) occlusion suggesting arterio-arterial embolism during ICA occlusion. Collateral blood flow to the right MCA territory was poor. Despite intensive pharmacological treatment he developed

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critically elevated intracranial pressure and required intubation and early right-sided craniectomy. Follow-up CT scans revealed a space-occupying right MCA territory infarction.

During the first day after ictus, the patient developed fever which peaked on day 3 (39.4°C). Antibiotic treatment was started. On the 3rd day swelling of the right parotid and submandibular glands was observed. Less swelling of the salivary glands on the left side occurred during the following days. One week after ictus, the left testicle became painful and swollen. Anti-mumps IgM (enzyme immunoassay) was positive one week after ictus; it decreased to a borderline level a few weeks later and was negative 4 months after ictus. There were no findings suggesting mumps myocarditis or meningitis. Lumbar puncture was not done. A cervical CT scan on day 15 showed a hemorrhage located ventromedial to the right CCA but no intramural bleeding in the carotid arteries (Fig. 1). No attempts had been made to puncture the right jugular vein or the right carotid arteries.

The hemiparesis slightly improved but remained severe. Control angiography 4 months later exhibited partial recanalization of the occlusion resulting in a severe stenosis of the proximal right ICA. Angiographically an atherosclerotic lesion was suspected and the decision to perform endarterectomy was made. On operation, findings were strikingly unusual. Periadventitial fibrosis surrounded the carotid artery. The vessel wall was fragile and the adventitial layer was rarefied. A dissecting cleft at the level of the external elastic lamina was found at the distal end of the stenosis. Therefore, resection of the proximal ICA and dacron graft interposition were required.

Histology revealed an atheromatous plaque with small calcifications and few infiltrates of mononuclear leukocytes at the border of a broad fibrous luminal layer. In the adventitial and periarterial connective tissue, there were focal inflammatory infiltrates mainly localized around small blood vessels and consisting of CD68-positive

monocytes/macrophages and few elastase-positive polymorphonuclear leukocytes as evidenced by immunohistochemistry. Testing for CD markers expressed on T-lymphocytes or natural killer cells (CD3, CD4, CD8, CD16, CD56, CD57) was negative. Immune complexes were not detected. Tissue analysis for mumps virus using a reverse transcriptase (RT)-PCR assay was negative. Testing for human leukocyte antigens (HLA) in our patient showed the following alleles: A2/A3, B7/B49, Cw7/–; Dr13/Dr15.

3. Discussion

Microbial agents may participate in atherogenesis (Hajjar, 1991; Grayston, 1993) and can cause stroke from vasculitis. Mumps virus is not a known candidate in this respect and to our knowledge only few reports related mumps infection to ischemic diseases. During mumps infection, a young girl developed cerebral infarction presumably caused by cerebral venous thrombosis (Banker, 1961). Pulmonary embolism in mumps orchitis probably resulted from thrombosis of pelvic and prostatic veins during testicular inflammation (Ray, 1983). As with the cited cases, we cannot prove that mumps infection contributed to the pathogenesis of stroke in our patient. However, several points favor such hypothesis. Mumps virus can infect and damage human endothelial cells *in vitro* (Friedman et al., 1981). During the incubation period, mumps virus presumably replicates in the upper respiratory tract and in cervical lymph nodes (Wolinsky and Waxham, 1990), therefore close to extracranial brain supplying arteries. The host immune response seems to determine the severeness of clinical manifestations of mumps as in immunosuppressed patients mumps infection usually takes a subclinical course. Specific responses of cytotoxic T lymphocytes (CTLs) to mumps virus infected target cells develop during the incubation period at the end of which stroke occurred in our patient. The magnitude of the CTL response appears to be genetically determined by the HLA system (Wolinsky and Waxham, 1990). It is not sufficiently known whether any of the HLA alleles of our patient are associated with a particularly strong response. However, it is likely that an intense inflammatory response in our patient may have participated in focal tissue injury including the ICA vessel wall. Injury to the endothelium and/or connective tissue caused by vasculitis during such inflammatory response may have contributed to manifestation of the cervical hemorrhage detected on CT scan. Most pronounced swelling of salivary glands, cervical hemorrhage and ICA occlusion all occurred on the same side and had a close spatial relationship. This may also support the idea that periarterial inflammation contributed to ICA occlusion.

Our patient was a smoker and angiography and histopathology indicate that he suffered from atherosclerosis of the right ICA already at the age of 40. The operative



Fig. 1. Cervical CT revealed a hemorrhage which was localized ventromedial to the right common carotid artery (arrow).

specimen showed mononuclear leukocytes in (peri-)adventitial tissue, a finding which is common around atherosclerotic plaques. Vascular risk factors are associated with an increased activation of hemostatic and proinflammatory mechanisms in response to endotoxin, probably resulting from a more vigorous interaction of monocytes and perivascular macrophages with the endothelium (Sirén et al., 1992). In parallel, the assembly of monocytes/macrophages in and around the atherosclerotic lesion in our patient may have predisposed to a strong local inflammatory response to mumps virus and activated monocytes/macrophages and endothelial cells may have contributed to thrombosis. The striking periadventitial fibrosis and the fragile, vessel wall on operation can be understood as the result of such immune-mediated and inflammatory processes. Standard endarterectomy can be technically impossible in these patients and vein or prosthetic graft interposition should be preferred. Mumps virus could not be detected in the tissue specimen, however, this is not surprising as the infection had occurred 5 months before. In summary, supported by the cervical hemorrhage on CT and by the intraoperative findings we hypothesize that a strong local inflammatory response to mumps infection contributed to ICA occlusion and stroke in our patient. Genetic predisposition and leukocyte accumulation due to preexisting atherosclerosis could have been important factors in this process. The case of the patient presented may be uncommon. However, the interaction between atherosclerotic and other preexisting vascular lesions, infection with various microbial agents and genetically determined immunological responses may be more important in the pathogenesis of stroke than previously recognized and such interactive mechanisms deserve further research.

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