

Case report:

CRYPTOGENIC STROKE AS A VERY EARLY MANIFESTATION OF PANCREATIC NEOPLASM

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ABSTRACT

We present two cases of middle-aged women who sustained definite cerebro-vascular infarctions without predisposing risk factors. Work-up did not reveal any underlying etiology. Treatment with antiplatelets and anticoagulants improved the patients' symptoms. Two and five years later, both patients developed pancreatic cancer. In this article, we discuss the association between cryptogenic stroke and pancreatic cancer and review the cases described in the literature with this association.

Keywords: Stroke, malignancy, pancreas, thrombosis

INTRODUCTION

Stroke is seldomly encountered as the first manifestation of cancer. When it occurs, it usually precedes its diagnosis by days or months (Peres-Lazaro et al., 2004). The cause of stroke in cancer patients is usually embolic taking place in the setting of a hypercoagulable state. A clear definition of all the pathogenic mechanisms contributing to stroke in cancer patients has not yet been elucidated (Cestari et al.; 2004, Adams et al., 1993)

Case 1: A 45 year-old female, previously healthy, presented with expressive aphasia. Neurologic exam revealed normal cranial nerves with no motor or sensory deficits. Brain MRI showed an ischemic lesion in the left hemisphere. MRA did not reveal any thrombotic lesion in the extra- or intracranial circulation. Transthoracic echocardiography was normal. Laboratory work-up ruled out the presence of diabetes mellitus, dyslipidemia, liver or kidney diseases. Hypercoagulability studies including

ANA, protein C, protein S, anticardiolipin antibodies, and factor V Leiden, antithrombin III, MTHFR mutations were negative. PT, PTT, and D-dimers were within normal. The patient was started on antiplatelet therapy with consequent clinical improvement. Two years later, the patient presented with a painful abdominal mass. CT scan of the abdomen revealed a pancreatic lesion that turned out to be, on pathologic examination, an extensive pancreatic anaplastic sarcomatoid tumor. The patient died 5 months later.

Case 2: A 60 year-old female, known healthy, presented with acute severe vertigo and headache. Neurologic examination revealed right finger-to-nose dysmetria, ataxic gait, and an abnormal Tandem walking. The patient did not have any motor or sensory deficits, cranial nerve dysfunction, or neck stiffness. Brain MRI revealed a large infarct of the right cerebellar hemisphere and vermis. Transthoracic echocardiography was normal. Blood studies were normal excluding diabetes, dyslipidemia,

renal or liver failure. Hypercoagulable studies were negative. The patient was started on oral anticoagulation with complete resolution of her symptoms. Three years later (one year after discontinuation of anticoagulation), the patient presented with vertigo, horizontal nystagmus, and headache. Brain MRI revealed an enlargement of the previously present right cerebellar infarct. MRA of the intra- and extra-cranial vessels showed no evidence of obstructive pathology or aneurysmal formation. Transesophageal echocardiography did not reveal any cardiac thrombus. Anticoagulation was resumed with progressive clinical improvement. Two years later, the patient developed an abdominal pain; CT scan of the abdomen revealed a pancreatic mass. Pathology revealed a moderately differentiated pancreatic adenocarcinoma.

DISCUSSION

An association between venous thrombosis and malignancy (mainly pancreatic cancer) was first suggested in 1865 by Trousseau (Sack et al., 1977). Arterial thrombosis as a paraneoplastic manifestation is much less common. In a series of 311 patients with adenocarcinoma of the pancreas described by Schattner et al., only 2 cases developed arterial thromboembolism (Schattner et al., 2002). Cerebral artery occlusion associated with pancreatic neoplasm has been reported in only 4 cases (Perez-Lazaro et al., 2004; Schattner et al., 2002; Medina et al., 2000; Chen et al., 2004). We are reporting in this article 2 additional cases. Cases of cerebral stroke associated with cancer described in the literature usually appear in close temporal proximity to the diagnosis of cancer, and might be even a preterminal event (Chen et al., 2004). However, our cases developed stroke several years before the diagnosis of their pancreatic tumor. Whether this is just a coincidental finding or a peculiar, though rare, presentation of pancreatic neoplasm remains to be elucidated. The pathophysiologic mechanisms of ischemic stroke in

cancer patients are multiple. The majority of cases are embolic as a manifestation of a cardioembolic event, a nonbacterial thrombotic endocarditis (NBTE), an infectious endocarditis, or a paradoxical brain embolism in the setting of a right-to-left shunt (Sack et al., 1977). Some cases may be secondary to in situ thrombosis. Autopsy studies revealed that cerebral infarctions related to cancer can be symptomatic or asymptomatic. Asymptomatic strokes are usually secondary to atherosclerosis while symptomatic cerebral infarctions are secondary to non-bacterial thromboembolism (Sack et al., 1977). The most plausible etiology in our two patients based on the clinical presentation and the negative work-up would be NBTE. However, a transesophageal echocardiography (TEE) was not done to confirm this diagnosis because we did not have a suspicion of malignancy. Based on the TOAST classification system, our two patients fall under the category of acute stroke of undetermined etiology (Schattner et al., 2002). In all the reported cases, strokes occurred days to months after the diagnosis of cancer. The fact that our patients sustained their stroke years before the diagnosis of a highly malignant condition defies the theory that the only causes of stroke in cancer patients are thrombosis and non-bacterial embolism. We speculate that in some cancers, possibly only pancreatic, the pathological process starts very early with a so far undetermined coagulopathy affecting medium or small vessels and undiagnosed by the present laboratory panel. We conclude from these two cases that patients who present with cerebral infarction, with neither risk factors for stroke nor associated systemic illnesses must be followed up meticulously for an underlying malignancy, possibly of pancreatic origin, even several years after the diagnosis of the stroke.

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