A CASE OF RECURRENT ACUTE ISCHEMIC STROKE AFTER RTPA FIBRINOLYSIS IN A PACIENT WITH WALDENSTROM'S MACROGLOBULINEMIA

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ABSTRACT

We report the case of a 61-year-old man, with Waldenstrom's macroglobulinemia, who was hospitalized for paresthesias and weakness in lower and upper extremities; during hospitalization he developed acute ischemic stroke for which he received fibrinolytic therapy with rtPA with complete remission of his symptoms; six hours later he developed a new ischemic stroke with progressive aggravation and death.

Key words: Waldenstrom's macroglobulinemia, acute ischemic stroke, fibrinolysis with rtPA, neuropathy

INTRODUCTION

Waldenstrom's macroglobulinemia is a low grade lymphoplasmacytic lymphoma which was first described in 1944. The disease is characterized by neoplastic proliferation of B lymphocytes and excessive production of monoclonal immunoglobulin M (IgM). The leading clinical features are lymphadenopathy and/or splenomegaly, anemia and hyperviscosity syndrome.

CASE REPORT

We report the case of a 61-year-old male patient who was referred to the Neurology Department of our hospital for paresthesias and weakness in lower and upper extremities.

The patient was diagnosed with Waldenstrom's macroglobulinemia six months before on the basis of skin and bone marrow biopsy and elevated serum concentration of IgM. He was treated with five sessions of plasmapheresis and was on ongoing treatment with hydroxychloroquine 400mg/day and methylprednisolone 8mg/day. Besides, he had no other significant medical history.

The present episode began two weeks before presentation with paresthesias in lower and upper extremities which aggravated progressively and were accompanied by weakness at the same level in the last week. Before referring to our hospital he was investigated at the territorial hospital with a brain computer tomography which showed normal aspect and a lumbar puncture which was also normal.

At presentation the patient was afebrile, pale, with splenomegaly but no other clinical signs of organ enlargement, normal vital signs and normal cardiac and pulmonary findings. The neurologic examination showed no disorientation, no meningeal signs, no cranial nerves deficits, no visual and hearing impairments and no signs of aphasia, distal weakness involving the lower and upper limbs with

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paresthesias at this level, with amyotrophies in upper and lower limbs, distal hypoesthesia, absence of osteotendinous reflexes.

The laboratory tests revealed a discrete leukocytosis with increased erythrocyte sedimentation rate and fibrinogenemia, mild anemia and normal count of thrombocytes. The serum IgM level was 590mg/dl (normal 60-280) and serum viscosity was increased. Serum electrophoresis showed an IgM kappa monoclonal gammopathy. The hepatic and renal tests were normal, including the markers for viral hepatitis B and C.

The electromyographic examination showed severe sensory-motor axonal polineuropathy involving the four limbs.

Since admission in our service the patient received treatment with methylprednisolone, hydroxychloroquine, proton-pump inhibitor and aspirin (100mg/day).

In the fifth day of hospitalization the patient developed suddenly dysarthria accompanied by right-sided hemiparesis. The biologic reevaluation (but no immunologic tests were repeated) showed no significant changes. The brain computer tomographic examination revealed no ischemic lesions and no signs of hemorrhage (Figures 1a and 1b). The diagnosis was acute ischemic stroke and the fibrinolysis was considered. As the patient had no contraindications he received intravenous Actylise in weight-adjusted dose with 10% of the dose given as a bolus followed by a 60-minute infusion, as is specified in the European Stroke Organization's Guidelines for Management of Ischaemic Stroke and Transient Ischaemic Attack. The thrombolysis was free of incidences but the first twenty-four hours were characterized by a raise of blood pressure with a maximum of 205/135 mmHg which was cautiously lowered using intravenous beta blockers and enzyme-converting antagonists (as labetalol or sodium nitroprusside are not available in Romania for the moment). The repeated brain CT scan performed immediately after thrombolytic therapy showed no pathological findings. A carotid Doppler ultrasonography was performed as well but showed no atherosclerotic lesions.

The neurological evolution was favorable, with slow but complete recovery of the motor deficit and disappearance of dysarthria. Unexpectedly we remarked the appearance of persistent high-grade fever with no other signs of infection, reluctant to antitermic measures.

Six hours after thrombolysis the patient's state deteriorated with appearance of coma with a score of 6 on Glasgow scale and polypnea. A new brain

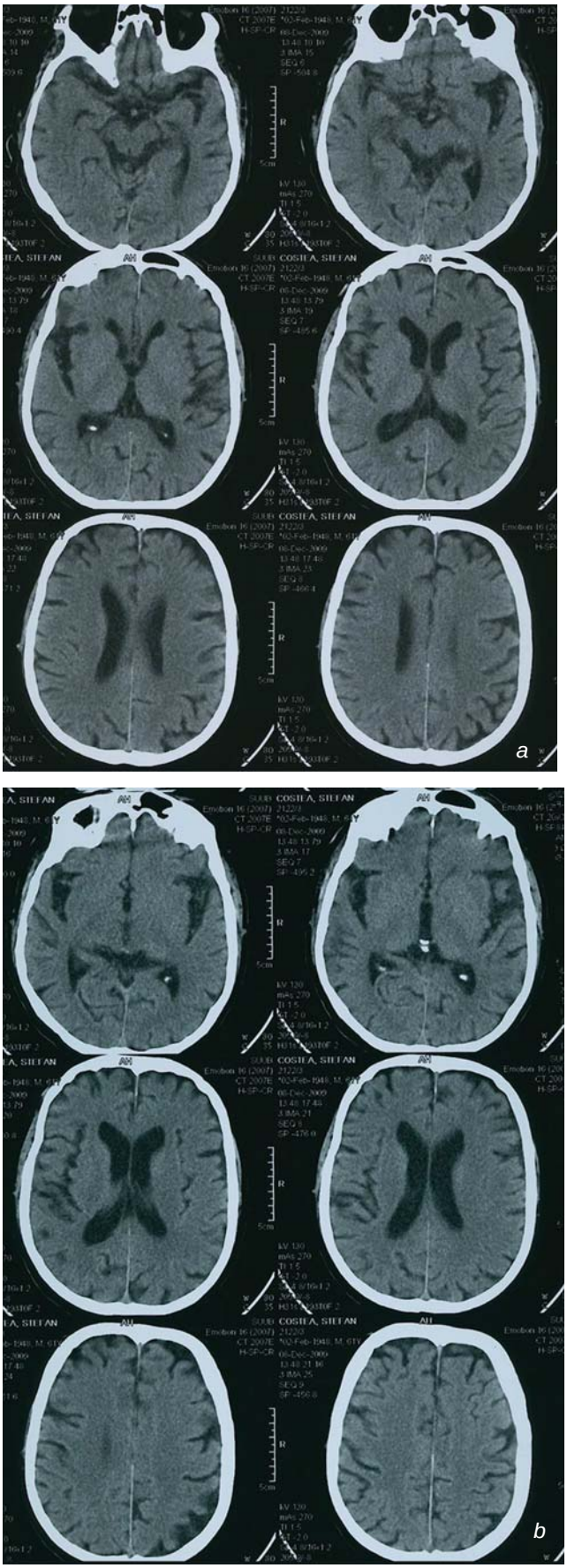

FIGURE 1. *a) Cerebral CT scan showing no acute ischemic signs and moderate brain atrophy; b) Cerebral CT scan showing no acute ischemic signs and moderate brain atrophy*

CT imaging was performed after 24 hours in order to exclude a hemorrhagic complication after thrombolysis and it revealed ischemic lesions of different ages situated left pontomesencephalic, in the posterior limb of left internal capsula and in the head of left caudate nucleus (Figure 2). From this point the clinical status of the patient was progressively aggravating, with deep coma combined with fever and lowering of blood pressure and culminating with irreversible cardiorespiratory stop and death.

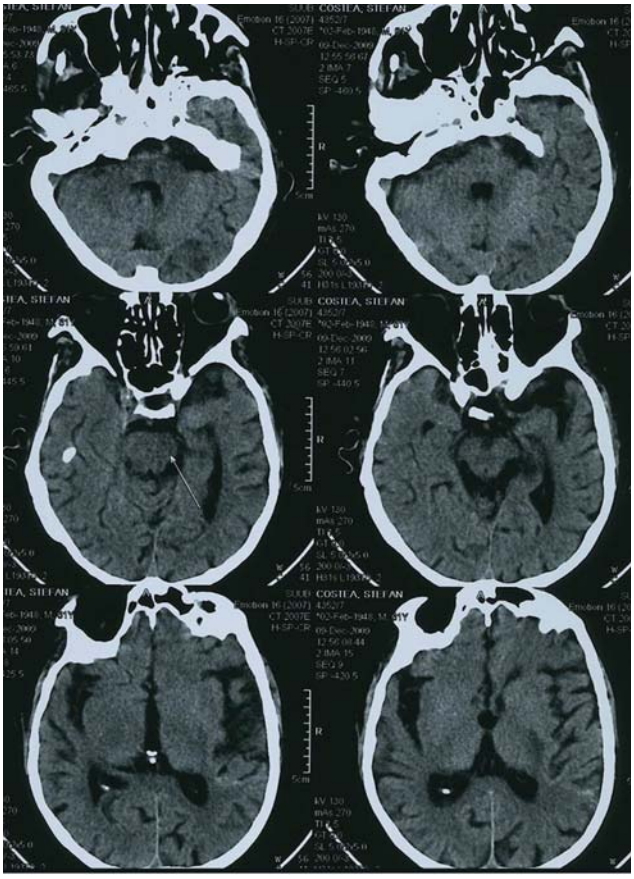

FIGURE 2. *Cerebral CT scan showing ischemic lesions situated in the left side of the pons and mesencephalon*

DISSCUSSIONS

Waldenstrom's macroglobulinemia is a rare disorder with an incidence of approximately three per million people per year. In the United States 1400 new cases are reported each year. The median age at diagnosis is 64 years; less than 1 percent of patients are under 40 years of age, and approximately 60 percent are males. Waldenstrom's macroglobulinemia is much more common in Caucasians than in other ethnic groups.

The neuropathy is the most frequent neurologic manifestation, specifically a distal, symmetric, and slowly progressive sensorimotor peripheral neuropathy causing paresthesias and weakness. The reported incidence of this abnormality is around 20 percent of patients at time of diagnosis. Other neurologic manifestations can occur but are less common. These include cranial nerve palsies, mononeuropathy, mononeuritis multiplex, multifocal leukoencephalopathy, and sudden deafness.

Other frequent neurological symptoms are those related to hyperviscosity which are present in up to 30 percent of patients. These include blurring or loss of vision, headache, vertigo, nystagmus, dizziness, tinnitus, sudden deafness, diplopia, or ataxia. Rarely, confusion, dementia, disturbances of consciousness, stroke, or coma could appear.

The particularity of the case is that the patient suffered the both types of neurologic complications mentioned above.

First, he presented a sudden onset and rapid progress of peripheral neuropathy which affected in an equal manner the upper and lower limbs, although in Waldenstrom macroglobulineamia usually the lower extremities are more involved than the upper ones.

Second, he developed acute ischemic stroke as primary manifestation of hyperviscosity, which is also unusual. The appearance of persistent fever during hospitalization and lack of any clinical and laboratory signs of infection suggest a relapse of hematologic disease. Same, the patient had no other evident cause for stroke as cardioembolic source or carotid atherosclerosis or even thrombophilia.

This patient referred to our service for evaluation and treatment of the polineuropathy associated to his hematological disease. He had no indication to receive immunoglobulins and for technical reasons we couldn't perform plasmaferesis. He developed the first stroke while he was hospitalized so we could immediately perform fibrinolysis with rtPA as he had no contraindications (Waldenstrom's macroglobulinemia and subsequent hiperviscosity syndrome does not contraindicate rtPA fibrinolysis) with complete resolution of symptoms. He had a second stroke, six hours after the first one, but in this case we couldn't repeat fibrinolysis as he had received rtPA a few hours earlier.

CONCLUSION

The patient represents a case of Waldenstrom's macroglobulinemia complicated with typical but rapidly aggravating peripheral sensorimotor polyneuropathy and with recurrent acute ischemic stroke as rare and severe manifestation of hyperviscosity.

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