Dementia reversible by plasmapheresis in multiple myeloma

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Although hyperviscosity syndrome may lead to cerebral hypoxia and produce some degree of dementia, this condition is rarely recognized. We report a patient in whom moderate dementia was the only manifestation of a hyperviscosity syndrome due to an IgG- κ myeloma. Dementia dramatically improved following plasmapheresis.

Keywords: Dementia – Hyperviscosity – Plasmapheresis

INTRODUCTION

Among the many dementing diseases (Cummings and Benson, 1992), clinically of greatest importance are those in which dementia is potentially reversible (Cummings *et al.*, 1980). A condition which can cause reversible cerebral hypoxia is hyperviscosity syndrome (HVS) as occurring in Waldenstroem's macroglobulinaemia (Waldenström, 1944), hyperlipidaemia (Heilman and Fisher, 1974), leukaemia (Preston *et al.*, 1978), multiple myeloma (Mueller *et al.*, 1983), etc. HVS includes bleeding from mucosal membranes, retinopathy, congestive heart failure and a broad spectrum of neurological symptoms. Although HVS is not uncommon, dementia as a leading symptom is rarely described (Mueller *et al.*, 1983).

CASE REPORT

This 67-year-old housewife had an uneventful medical history until one year ago when she started suffering from pain in the lumbar and thoracic region and from nocturnal sweating. On admission complete medical and neurological examinations were normal and remained normal throughout the course of the illness. In particular there was no mucosal membrane bleeding, nor abnormalities of the fundus or hearing. Mental status at admission revealed minimal difficulties with short-term memory and word finding. A diagnosis of multiple myeloma of the IgG- κ type was made on the basis of multiple osteolytic lesions in the skull and spine together with laboratory data: BSR 110 mm/h, bone marrow infiltration of 23% plasma cells,

haemoglobin 8.5 g%, haematocrit 27.2%, total protein 156 g/l (normal 65-80 g/l), serum globulins 114 g/l (35-40 g/l), albumin 38.5 g/l (35-50 g/l). Serum immunoelectrophoresis demonstrated IgG- κ monoclonal gammopathy of the IgG₁ subclass of 74.5 g/l (normal 7-19 g/l), IgA of less than 0.3 g/l (0.7-4.0 g/l) and IgM of less than 0.3 g/l (0.6-2.8 g/l). The plasma viscosity could not be directly measured, but was estimated to be between 5 cp [according to the linear correlation between monoclonal protein concentration and plasma viscosity described by Crawford *et al.* (1985)] and 8 cp [according to the averaged viscosity values described by Pruzanski and Watt (1972)] (normal 1.62 ± 0.05 cp). All other laboratory data were normal.

Between Days 2 and 7 in hospital chemotherapy with melphalan 15 mg/day and prednisone 100 mg/day orally was performed. She did not suffer any adverse effect of chemotherapy, but deteriorated during the first 2 weeks in hospital, became disorientated and lethargic, and developed mild paranoid ideation. CT scan of the head was normal and ^{99m}Tc-HMPAO-SPECT did not show areas of focal hypoperfusion, but EEG was abnormal with a diffuse slowing in the theta and delta range with repeated occurrence of bi- and triphasic wave complexes with frontal accentuation. CSF was normal.

Comprehensive neuropsychological examination at Day 15 in hospital revealed a picture of marked subcortical dementia (Cummings, 1990) with severe impairment of learning and recall in the presence of mild deficits of recognition memory, strongly impaired figural and verbal

fluency, difficulties with concept identification and interference suppression and an altered affect with some depressive and paranoid components. There were no signs of aphasia, apraxia or agnosia, but some word finding difficulties.

Plasmapheresis was started at Day 19. On two consecutive days 2.3 l plasma were exchanged. The paraprotein fell to 27 g/l (less than 50% of the initial value). This resulted within 24 h in a dramatic improvement of her mental status. She became more alert, completely orientated in time and space and memory functions improved. After an interval of 2 days plasmapheresis of 2.3 l was twice more performed, without further clinical improvement. At Day 25 she was given another course of chemotherapy consisting of 100 mg/day prednisone and 15 mg/day melphalan over 5 days, during which the paraprotein rose and the patient again showed signs of increased apathy, slowness in thinking and a lack of spontaneity. At Day 37 this decline in mental status prompted plasmapheresis on two following days, which resulted in an immediate restoration of the mental state observed after the initial plasmapheresis. The EEG normalized. Neuropsychological examination on the day of the last plasmapheresis had normalized except for a minimally impaired recognition memory and some paranoid ideation. One month after discharge neuropsychological examination was entirely normal.

DISCUSSION

We have presented a patient in whom a marked subcortical dementia of subacute onset was the only manifestation of HVS in an IgG- κ myeloma. After plasmapheresis the dementia cleared dramatically. A second course of plasmapheresis was necessary when dementia recurred together with a rise of paraprotein, probably due to a wash-out from extracellular fluid compartments. Following the second plasmapheresis the patient returned to her normal state and has remained symptom-free for the past 6 months.

HVS is common in a wide variety of diseases (Waldenström, 1944; Heilman and Fisher, 1974; Preston *et al.*, 1978; Mueller *et al.*, 1983). Its frequency in IgA and IgG myelomas is estimated at 10% and 4%, respectively.

Although neurological deficits such as hemiparesis, lethargy, coma, seizures or acute confusional states are not infrequent in HVS, dementia is uncommon, particularly as isolated as in the present case. This is surprising, since generalized but mild cerebral hypoxia, as expected to occur by hypoperfusion due to HVS, quite early leads to disturbances in memory and frontal lobe functions when encountered in other mild to moderately hypoxic conditions, such as exposure to high altitude (Regard *et al.*, 1989). Thus the observation of mild to moderate subcortical dementia in diseases known to produce HVS should alert the clinician, particularly since this condition is potentially reversible by plasmapheresis.

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