Myeloma and benign intracranial hypertension

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Benign intracranial hypertension is uncommon, with a prevalence of 0·9 per 100 000 and a noticeable female predominance (8:1). Several associations have been reported including with proliferative haematological disease such as polycythaemia rubra vera, essential thrombocythaemia, and paroxysmal nocturnal haemoglobinuria. In a series of 29 men with benign intracranial hypertension an empty sella was noted on 55% of computed tomograms, and nine of them required a shunt.[1] We report on three patients with myeloma and benign intracranial hypertension without other features consistent with Shimpo's disease[2] or the POEMS syndrome[3]—for example, polyneuropathy, hyperpigmentation, scleroderma, ascites, hepatosplenomegaly, lymphoadenopathy, gynaecomastia, impotence, amenorrhoea, diabetes mellitus, polycythaemia, and osteosclerosis.

Case reports

The characteristics of the three patients are given in the table.

Case 1—The first patient presented with a six month history of headache, nausea, dysphagia, dysarthria, and psychomotor retardation. Lumbar puncture showed a high cerebrospinal fluid opening pressure and subsequent investigations detected myeloma (table). He required weekly lumbar puncture for removal of cerebrospinal fluid to obtain symptomatic relief. He was referred to this hospital, where chemotherapy with verapamil, cyclophosphamide, vincristine, doxorubicin hydrochloride, and methylprednisolone was given according to our current protocol. Opening pressures of only 13 and 4 cm H_2O on days 6 and 13 respectively were recorded at repeat lumbar puncture, obviating the need for further removal of fluid. This coincided with complete resolution of his symptoms. After five courses of the chemotherapy he achieved complete remission and has remained well taking maintenance interferon alfa treatment over the past six months.

Case 2—The second patient presented with blurred vision, diplopia, headaches, and severe back pain. Subsequent investigations showed myeloma (table). At lumbar puncture the cerebrospinal fluid opening pressure was raised. He was treated with high dose melphalan (140 mg/m^2) without autologous bone marrow transplantation and his symptoms and condition improved (paraprotein concentration fell from 89 to 7 g/l). Nine months later he had a relapse, which improved marginally with chemotherapy (vincristine, doxorubicin hydrochloride, and methylprednisolone), and he then received high dose melphalan (140 mg/m^2) with autologous bone marrow transplantation. He responded completely but had a relapse four months later and died despite further chemotherapy, two years after his initial presentation.

Case 3—The third patient was referred to this hospital after having presented to a neurologist initially with visual disturbance, nystagmus, and unsteady gait. Subsequently myeloma was diagnosed (table), and he received chemotherapy. On arrival here he still had symptoms; his paraprotein concentration was 20 g/l and bone marrow infiltration 15%. He had an empty sella on computed tomography and the cerebrospinal fluid opening pressure at lumbar puncture was 43 cm H_2O. He was given high dose melphalan with total body irradiation and an allogeneic bone marrow transplant. He entered complete remission within five months, but three months after transplantation he still had neurological symptoms requiring lumbar puncture. These symptoms resolved after a lumboperitoneal shunt had been inserted.

Characteristics of patients at presentation

Case No	Age (years)	Examination	Sella	Paraprotein	Bone marrow infiltration	Skeletal survey
1	49	Papilloedema, enlarged blind spots	Normal	IgG1 33 g/l	56%	Positive
2	45	Papilloedema	Normal	IgG1 89 g/l	38%	Positive
3	38	Papilloedema	Empty	IgK NA	Positive	Positive

NA=Not available at presentation.

Comment

We found no description of an association between benign intracranial hypertension and myeloma in published work. Sugita *et al* and Collier and Ashworth described raised intracranial pressure with myeloma, but this was in the presence of an intracerebral and cranial plasmacytoma respectively.[4,5]

The mechanism of benign intracranial hypertension is obscure but probably related to an imbalance between overproduction of cerebrospinal fluid and its absorption at the arachnoid villi. Hyperviscosity has not been implicated in clinical or experimental studies and benign intracranial hypertension has not been reported in Waldenström's macroglobulinaemia. All our cases of myeloma were of the IgG subtype, and none had evidence of hyperviscosity or an intracerebral mass lesion. The symptoms of benign intracranial hypertension responded rapidly to treatment for myeloma in two of our three patients.

Although the association is rare, we believe that all patients presenting with benign intracranial hypertension should have investigations to exclude myeloma, including serum immunoelectrophoresis, urine analysis for Bence Jones protein, and bone marrow aspiration and trephination. Myeloma is treatable and may obviate the need for repeated lumbar puncture and insertion of a shunt.

1 Digre KB, Corbett JJ. Pseudomotor cerebri in men. *Arch Neurol* 1988;45: 866-77.
2 Bardwick PA, Zvaifler NJ, Gill GN, Newman D, Greenway GD, Resnick DL. Plasma cell dyscrasia with polyneuropathy, organomegaly, endocrinopathy, M protein, and skin changes: the POEMS syndrome. *Medicine* 1980;59: 311-22.
3 Shimpo S. Solitary plasmacytoma with polyneuritis and endocrine disturbances *Japanese Journal of Clinical Medicine* 1968;24:2444-56.
4 Collier A, Ashworth B. Multiple plasmacytoma presenting as raised intracranial pressure. *J Neurol Neurosurg Psychiatry* 1987;50:495-6.
5 Sugita K, Kayama T, Ohwada K, Chinose M, Takasugi R, Shizaki R, *et al.* A case of multiple myeloma showing intracranial hypertension due to large cranial mass lesions. *No To Shinkei* 1986;38:6259.

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