Bilateral orbital myeloma in a young male: an unusual case with cerebrospinal fluid involvement

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INTRODUCTION

Multiple myeloma is a malignant disease which usually involves the bone marrow. It is responsible for 1% of all malignant diseases and for 10% of the haemotological malignancies. In 98% of all cases it occurs after the age of 40 [30].

The purpose of this report is to describe a case with some atypical features such as patient's age (24 years), proptosis as the first manifestation of the disease, and plasma tumoral cells in the cerebrospinal fluid (CSF) without previous neurological manipulation.

CASE REPORT

A 24-year-old male was admitted on May 29, 1983 complaining of progressive right proptosis for three weeks plus headaches and vomiting for one week. On examination he was moderately pale, normotensive, and afebrile, without lymph node enlargement, and with a discrete pan — cardiac systolic murmur.

The right eye was proptotic and deviated downward and temporally, with limitation of adduction and elevation. A rubbery mass about 5 cm in diameter was palpated at the temporal orbital margin; the upper lid was hyperemic and edematous. The left eye was normal. The fundus and the intraocular pressure were normal in both eyes. Visual acuity OD 20/200 and OS 20/15.

X-rays of the skeleton disclosed diffuse osteoporosis and multiple lytic bone lesions in the skull, hip, and long bones. Abdominal ultrasonography revealed 10.5 cm kidneys with increased cortical density. Orbital mass and bone marrow biopsies confirmed multiple myeloma.

Laboratory tests showed a normocytic and normochromic anemia, haemoglobin 8.3 g/dl, normal leucogram, 150000 platelets per cubic millimeter and the presence of erythrocytes with rouleaux formation. Creatinine 3.2 mg/dl. Total bilirubin 0.4 mg/ml. Sodium 123 mEq/l. Potassium 3.2 mEq/l. Uric acid 4.5 mg/l. Alkaline phosphatase 346 IU/l. Glutamic-oxalacetic transaminase 12 IU/l. Glutamic pyruvic transaminase 18 IU/l. Lactic dehydrogenase 346 IU/l. Gamma-glutamyl transpeptidase 66 IU/l.

Serum electrophoresis showed total protein 12.1 g/dl; albumin 4.6 g/dl; alpha 1 globulin 0.2 g/dl; alpha 2 globulin 0.8 g/dl; beta globulin 1.0 g/dl, and gamma globulin 5.5 g/dl with monoclonal aspect. Serum immunoelectrophoresis revealed a monoclonal precipitation arc with IgG-Kappa chain. Bone marrow aspiration showed 43% plasmoblastic strainlike cells.

Two weeks later the right proptosis had increased markedly (Fig. 1, A) and there was deterioration of renal function. Dialysis and plasmophoresis treatment were instituted with remission of the renal insufficiency in 21 days. A kidney biopsy revealed acute tubular necrosis. Orbital tomography at this time revealed a large tumor pushing the right eye downward and temporally, destroying the orbital roof.

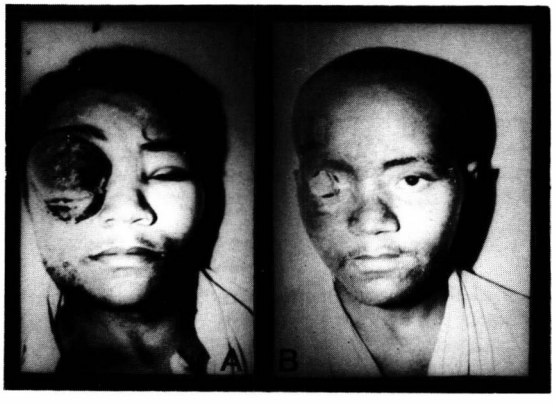

Fig. 1 — Patient before (A) and after (B) treatment.

Meanwhile at the beginning of the dialysis orbital radiotherapy (4000 rads) and

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systemic chemotherapy with Melphalan (10 mg days 1 to 4), Vincristine (2 mg day 1), and Prednisone (80 mg days 1 to 4) were introduced. One and a half months after admission the patient developed left upper lid and facial tumors which disappeared with radiotherapy (left upper lid) and chemotherapy with another combination of drugs (Cyclophosphamide 600 mg day 1, Doxorubicin 50 mg day 1, Vincristine 2 mg day 1, and Prednisone 80 mg days 1 to 5).

Three weeks later symptoms of paraparesis developed with progressive dificulties of blader and bowel evacuation. CSF analysis revealed 20 leucocytes and no erythrocytes per cubic millimeter, 64% cells with tumoral characteristics (plasmoblasts, Fig. 2); proteins 127 mg/dl; immunoelectrophoresis with a serumlike pattern. Methotrexate 12 mg intrathecal was started with complete remission after three applications.

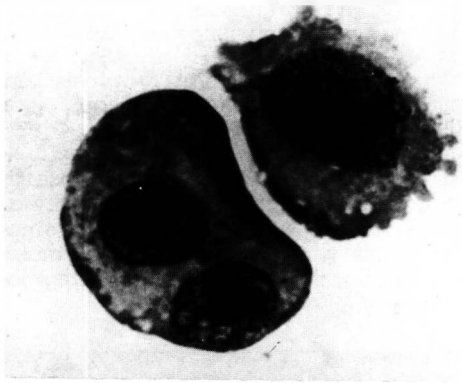

Fig. 2 — Plasmoblasts in the cerebrospinal fluid.

Regression of the proptosis was observed but with right phthisis bulbi (Fig. 1, B). There was clinical and haematological improvement until January of 1984 when the patient was lost to follow-up.

DISCUSSION

Multiple myeloma affects the eye and adnexa in multiple forms which can be classified, according to Ashton [2], as follows:

I — lesions resulting directly from the neoplasm itself: involvement of the orbital bones, mainly the roof and frontal bone [10]; invasion of the orbital cavity; compression of the cranial nerves with loss of vision and ocular motor paralysis; optic nerve [12], intraocular, lacrimal gland [23], and conjunctival infiltration [11,17], papilledema from elevated intracranial pressure.

II — lesions resulting from the blood changes: the hyperproteinemia and the increased blood viscosity found in multiple myeloma give rise to crystal deposits in the cornea, vascular tortuosity and engorgement, exudates and haemorrhages in the fundus.

Orbital involvement is rare in multiple myeloma and when it does occur proptosis is observed in the majority of cases [22]. Proptosis was the first sign of the disease in 23 out of 30 cases. In two series, one with 465 and the other with 676 consecutive orbital tumors, there were only two cases of multiple myeloma in each [13]. Until 1981 there were only 35 cases of orbital involvement in multiple myeloma described in the literature and cases of bilateral implication were still rarer [21].

Although a biopsy of the left upper eyelid was not performed a myelomatous infiltration was probably present. The tumoral characteristics and the therapeutic response enable us to presume the presence of a bilateral tumoral growth. Multiple myeloma should be considered in the differential diagnosis of patients with proptosis, even in young subjects.

Considering the complications of the central nervous system (CNS) with respect to multiple myeloma it can be seen that they are relatively frequent, with variable physiopathological causes. Compression of the spinal cord is the most common involvement, caused by an extradural myeloma or by a destructive bone lesion leading to a vertebral collapse [6]. Other factors such as vascular lesions by amyloidosis, increased blood viscosity, peripheral neuropathy, uremic and hypercalcemic metabolic changes are additional factors of the nervous lesions found in this disease [3,6].

Intracraneal plasmocytomas, leptomeningeal and CSF involvement by myelomatous cells are very rare indeed. Unlike acute lymphoid leukemia in which the CNS is frequently infiltrated by blastic cells, this findings is very seldom reported in multiple myeloma in spite of the extensive literature on the subject, which includes necropsy studies [15]. The blood-brain barrier is permeable to proteins with sedimentation rate up to 9 S [29] and therefore immunoglobulins of the IgM class (19 S) and some of the IgA (between 7 S and 13 S) [5] would not be detected in the CSF of patients with high serum levels. In myelomas secreting IgG, IgE, or IgD the presence of these paraproteins in the CSF cannot be used to diagnose infiltration of the meninges. For this reason the finding of neoplastic cells of the plasmocytariam family in the CSF is the best way of diagnosing "in vivo"

involvement of the meninges by a myelomatous process; but routine CSF tap is not always justifiable because of the rarity of this finding. A study of 869 cases makes no mention at all of affected meninges in this disease [15]. Another investigation, specifically directed toward different forms of neurological implications of multiple myeloma, emphasizes medular compressions and intracranial plasmocitomas and makes no mention of infiltration of the meninges by plasmoblasts [6].

At the present time there are 12 studies in the literature [1,4,7,16,18-20,24,28], which cite only 14 cases of infiltration of the meninges by myeloma. All of these patients presented isolated affected leptomeninges, except for one whose duramater was involved [16].

There are various ways in which the meninges can be involved but none of them has been entirely cleared up:

I — Invasion of the CNS by neoplastic peripheral blood cells: Corroborating this hypothesis 43% (6 out 14) of cases presented peripheral plasmocytosis on occasions close to the time of the diagnosis of meningeal infiltration [4,16,18-20,27].

II — CSF contamination by myelomatous cells through previous manipulation during laminectomies or myelographies [1,25].

III — Contiguity: In the present case is the most probable explanation. The meninges could have been invaded either through the orbital roof or at the portion coating the optic nerve.

This is the 11th case in the literature to present myelomatous cells in the CSF while one of the 10 previous cases had no diagnosis of concomitant meningeal infiltration which could explain this finding [1].

An excellent result was obtained in our patient with intrathecal Methotrexate after the first administration. Of the 14 cases previously described in the literature, 4 were treated with intrathecal Methotrexate only [20,23,24,28] and only 1 [20] improved. Therefore this is the second case with gool response to this therapeutic procedure.

The kidney biopsy showed acute tubular necrosis without the characteristic abnormalities of the "Myelomatous Kidneys". This finding has been infrequently described in the medical literature [8,9].

Contrary to the customary biological behavior of multiple myeloma this case presented a rapid growth of the tumor and no response to initial chemotherapy (Melphalan, Vincristine, and Prednisone). There is a tendency to find a relationship between the cinectis of the myelomatous cells and the malignancy of the disease. Our patient responded only to the use of CHOP (Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone), a more effective drug association in neoplasias with a rapid cellular cycle. This behavior is contrary to the idea that multiple myeloma in young patients has a less severe course [14].

SUMMARY

A 24-year-old male was admitted with right proptosis for three weeks, headaches and vomiting for one week. The right eye was displaced forward, downward, and temporally; a rubbery mass was palpated at the orbital margin. Visual acuity OD 20/200 and OS 20/15.

X-rays disclosed multiple lytic bone lesions in the skull, hip, and long bones. Computorized tomography revealed a large mass destroying the right orbital roof. Myelogram showed 43% plasmoblastic strainlike cells. In cerebrospinal fluid analysis 20 white cells per cubic millimeter were found, 64% with tumoral characteristics (plasmoblasts). Biopsy of the orbital mass confirmed multiple myeloma.

Six weeks later the left orbit was involved but not as severely. The mechanism of central nervous system invasion is discussed.

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