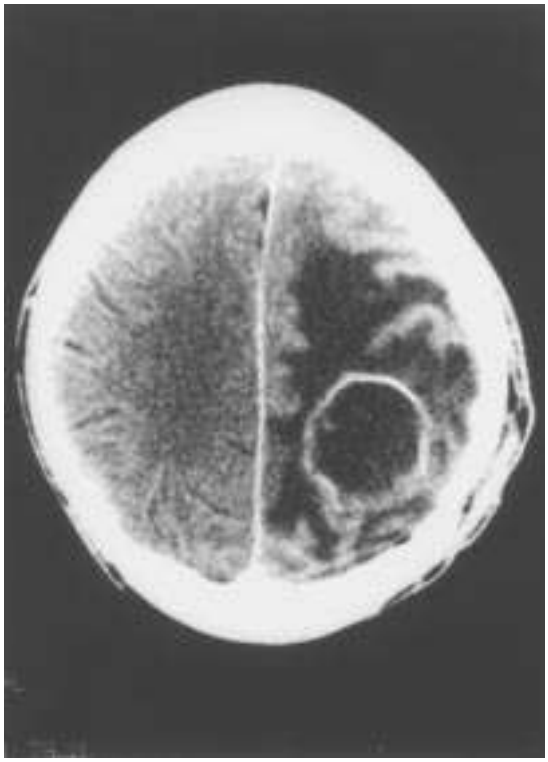

**Figure 2.**

reviewed by various authors.[2,5-7] The treatment of survivors included a combination of antimycotics and/or neurosurgery. We began therapy with conventional amphotericin without response and it was not possible to increase the dose because of the nephrotoxicity which developed. Liposomal amphotericin at a low dosage led to resolution of the clinical picture, and was well tolerated in spite of the high cumulative dose.

The action of itraconazole against Aspergillus is good both *in vitro* and *in vivo*[8] and some publications have compared its effectiveness with that of amphotericin in patients with cerebral aspergillosis.[9,10] In our patient, a high dose was not effective. As plasma concentrations were not measured we do not know if a suitable therapeutic level was reached.

The duration of treatment of IA in neutropenic patients is not well established. There is a consensus that treatment should be maintained until disappearance of lesions and/or recovery from the neutropenia.

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*Aspergillus, cerebral abscess, liposomal amphotericin, neurosurgery, immunosuppression*

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## Transient response of myeloma clone to pamidronate therapy

Sir,

Several studies have previously reported that IL-6 mediates the growth of multiple myeloma cells in either an autocrine or paracrine fashion. More recent studies indicate the paracrine mechanism as that being mainly responsible for the growth of myeloma cells. Tumor cells trigger IL-6 secretion by interacting through adhesion molecules with the bone marrow stromal cells which are the major source of IL-6 production in MM.[1] The efficacy of pamidronate, a second-generation bisphosphonate, in inhibiting osteoclastic activity and reversing cancer-associated hypercalcemia has been widely demonstrated.[2] Berenson *et al*.[3] also showed in a randomized study that pamidronate was effective in reducing skeletal events.

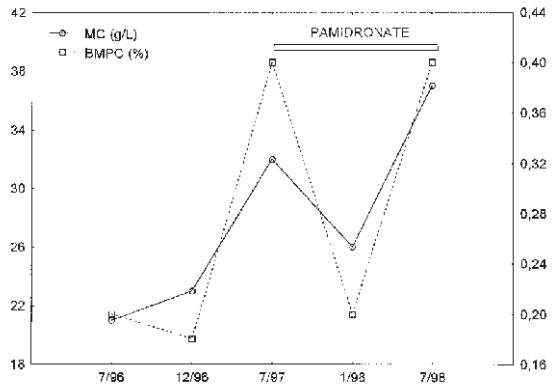


**Fig. 1 Temporal changes of M-component (MC) and percentage of bone marrow plasma cells (BMPC) in a multiple myeloma patient treated with monthly cycles of pamidronate.**

In the same study the authors remarked on the possibility of pamidronate improving survival in MM patients, probably by reducing IL-6 production. Other authors have also shown that *in vitro* pamidronate inhibits the production of IL-6 and induces apoptosis of myeloma cells.[4] Recently, Dhodapkar *et al.*[5] reported on 2 MM patients whose disease stabilized well with monthly cycles of intravenous pamidronate. Thus, they conclude that this therapy directed at the myeloma microenvironment might alter the natural history of myeloma delaying the requirement for chemotherapy.

We report here the case history of a patient with MM evolved from a MGUS, whose myeloma clone after treatment with monthly cycles of pamidronate showed a transient response.

### *Case Report*

A 32-year-old man came to our attention in July 1996 with an IgG κ monoclonal component incidentally detected one month earlier during a routine control. The serum level of IgG was 21 g/L. Blood counts, serum calcium, creatinine, urea, LDH, $\beta_2$ microglobulin, and CRP were within normal limits. Bence Jones proteinuria was undetectable. The patient was asymptomatic and the physical examination yielded no significant findings. Skeleton survey did not show lytic lesions or osteoporosis. A bone biopsy revealed 20% bone marrow plasma cells (BMPC) without atypical morphologic features.

One year later, the disease progressed with an increase of the M-component (MC) up to 32 g/L and of the BMPC up to 40%. The other clinical or laboratory parameters remained stable and no lytic lesions were detected radiologically. Pamidronate was begun at the dosage of 90 mg, in a 3-hour i.v. infusion, every month. No chemotherapeutic agents or corticosteroids were associated. After 6 months of pamidronate treatment a reduction of the percentage of BMPC to 20% and of the MC to 26 g/L was observed (Figure 1). Treatment was continued for further 6 months. Clinical and hematologic examinations performed 6 months later, after a total of 12 cycles, showed a return to the initial hematologic condition (BMPC 40%, MC 37 g/L) (Figure 1). A chemotherapy program with the VAD protocol was started and the patient is presently under treatment.

The case described here gives further evidence of the anti-myeloma effect of pamidronate. In fact, albeit transiently, bisphosphonate treatment improved the hematologic condition with a significant decrease of BMPC and of the MC. Further controlled trials are needed to confirm these isolated case reports, and to define how such therapy can integrate cytotoxic treatment in the management of myeloma patients.

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***Keywords***

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## A paradoxical side-effect of antiaggregating treatment with ticlopidine: the Moschowitz syndrome

Sir,

Ticlopidine is a widely used antiplatelet drug that achieves its antiaggregating activity by irreversibly blocking platelet ADP receptor. The effect requires 3-5 days to became manifest and persists for several days after treatment has been stopped.[1,2]

Neutropenia is a well recongized hematologic