References


Technetium-99m sestamibi scintigraphy in monitoring patients with multiple myeloma

Technetium-99m-Sestamibi (99mTc-sestamibi) scintigraphy has been shown to be capable of differentiating patients with multiple myeloma (MM) in remission from those with active disease.1-10 We studied 5 patients with MM (2 females and 3 males, age 53±17 years) before and after treatment. 99mTc-sestamibi scintigraphic results were concordant with clinical status.

99mTc-sestamibi scintigraphy was performed as previously described.10 The patients were clinically and biochemically evaluated at the time of both 99mTc-sestamibi scans to determine their clinical status. Case #1. A 72-year old man with MM. X-ray skeletal survey was negative, while 99mTc-sestamibi scan showed intense and diffuse bone marrow uptake (spine, pelvis, ribs, proximal part of both humeri and femora) with no focal increased uptake (Figure 1A). After 2 courses of VAD chemotherapy, increased plasma cell infiltration (72%) was found in the bone marrow, monoclonal component was 0.6 g/dL, and Hb was 10.6 g/dL. A second 99mTc-sestamibi scintigraphy showed intense and diffuse uptake in the spine and focal abnormality in T5 and T9 as well as in the skull (fronto-parietal region). Case #2. A 66-year old woman with micromolecular MM. 99mTc-sestamibi scan showed several focal areas of increased radiotracer uptake in thoracic vertebrae (T5, T9). After 2 courses of VAD chemotherapy, increased plasma cell infiltration (72%) was found in the bone marrow, monoclonal component was 0.6 g/dL, and Hb was 10.6 g/dL. A second 99mTc-sestamibi scintigraphy showed intense and diffuse uptake in the bone marrow (pelvis, ribs, proximal part of both humeri and femora) without focal increased uptake. After receiving 12 courses of melphalan and prednisone, the patient’s bone marrow was normal and 99mTc-sestamibi scintigraphy did not show abnormal bone marrow uptake of the radiotracer. Case #3. A 30-year old man with juvenile micromolecular MM. 99mTc-sestamibi scan showed several focal areas of increased radiotracer uptake.
The patient received chemotherapy (VAD x3, MTX+CTX+prednisone x3), and underwent radiotherapy of the cervical tract, clavicles and skull. After 6 months X-ray skeletal survey showed all the pre-existing plus new osteolytic lesions. 99mTc-sestamibi scintigraphy showed no uptake in the radio-treated lesions, while new areas of focal uptake in the skeleton were observed.

Case#5. A 55-year old man with MM. X-ray skeletal survey showed a few osteolytic cranial lesions, the largest one (2.5 cm diameter) located in the right fronto-parietal region. Osteolytic lesions with pathologic fractures were also seen in the 5th left rib and in the 5th and 6th right ribs. In the same period a 99mTc-sestamibi scan was normal (Figure 2A). On the basis of hematologic findings (bone marrow plasma cells 6%, monoclonal component 1.6 g/dL, Hb 11.5 g/dL) the patient was considered in continuous clinical remission. After 6 months 99mTc-sestamibi scan showed focal radiotracer uptake in the left clavicle (Figure 2B). This clavicle fractured one week later and X-ray confirmed the presence of a pathologic fracture through an osteolytic lesion.

Our findings in this small group of patients affected by MM suggest that 99mTc-sestamibi scintigraphy is a suitable method for evaluation of therapeutic response and for monitoring patients during follow-up. Whole body scanning with this tracer provides a simple and sensitive index of the biological activity of disease.

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References
Might arsenic trioxide be useful in the treatment of advanced myelodysplastic syndromes?

Failure of conventional therapies is dramatic in patients with advanced myelodysplastic syndromes (MDS), thus therapeutic approaches that increase the apoptotic rate of myelodysplastic syndrome (MDS) cells might be advantageous. We studied the behavior of cells exposed to $\text{As}_2\text{O}_3$ in vitro from patients with advanced MDS. Our data show that therapeutically useful concentrations of $\text{As}_2\text{O}_3$ increase the rate of apoptosis in short-term cultures. Moreover, pre-treatment with GM-CSF increased the sensitivity of the cells to the effect of $\text{As}_2\text{O}_3$.

Sir,

The search for therapy of myelodysplastic syndromes has so far been unsuccessful. Single agent chemotherapy as well as acute myeloid leukemia (AML)-type chemotherapy, alone or in combination with human growth factor (HGF), have not shown a clear beneficial effect on survival in MDS or in MDS-related AML.

Morphologic features of apoptosis are easily demonstrable in MDS cell populations.\(^1\) Moreover, data about fas expression in CD34+ MDS cells show that the myeloblast populations that emerge with disease progression are more resistant to fas-induced cell death.\(^2\) Thus, it is possible to hypothesize that, in advanced phases of MDS, an increase in the apoptotic rate of MDS cell populations might be advantageous.

Recently, much attention has been drawn to the use of $\text{As}_2\text{O}_3$ as a useful agent in the treatment of AML-M3 that has become resistant to standard retinoic acid treatment.\(^3\) In a patient with retinoic-resistant AML-M3 treated with arsenic trioxide we observed a very good correspondence between the levels of drug-induced apoptosis in affected cells in vivo and that observed in vitro in liquid culture. This correspondence was maintained during progression of the disease (4 and AD, personal communication).

In the present study, we collected blood samples from 14 patients with the diagnoses shown in Table 1. Bone marrow or peripheral mononuclear cells were seeded in 6-well plates (250,000 cells/mL IMDM/10% FCS). After 24 hours, $\text{As}_2\text{O}_3$ was added at concentrations of 0.1, 0.5, 1 and 2 $\mu$M. After 5 days in culture, culture aliquots were stained with propidium iodide and analyzed by FACS using Lysis II software. The percentage of cells in the hypodiploid peak was used to assess the percentage of apoptotic cells. A minimum of 10,000 events were taken for each sample.

The result obtained show that micromolar concentrations of $\text{As}_2\text{O}_3$ were effective at inducing apoptosis in 7/11 advanced MDS cases. No apoptosis was induced in cases of AML-M0 and Ph+ALL.

We also observed that the drug was more effective in inducing apoptosis when the initial spontaneous levels of apoptosis were low, suggesting that the drug might preferentially act on cycling cells. To test this hypothesis we repeated the experiments adding the...