Case report

Successful treatment of severe bone pain and acute arthritis in chronic myelomonocytic leukaemia by cytosine arabinoside

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SUMMARY An elderly patient with chronic myelomonocytic leukaemia developed severe bone pains and acute gonarthritis. Intravenously administered cytosine arabinoside brought dramatic relief of the bone pains and led to a rapid subsidence of the arthritis, without achieving haematological remission.

Chronic myelomonocytic leukaemia occurs mainly in elderly patients and usually runs a relatively benign course (Zittoun et al., 1972; Miescher and Farquet, 1974; Zittoun, 1976). Intensive chemotherapy is generally not applied in such patients because of poor tolerance (Miescher and Farquet, 1976). Bone pains are a rare feature of this condition and mostly are of mild degree (Zittoun et al., 1972; Geary et al., 1975; Zittoun, 1976).

We describe a patient with chronic myelomonocytic leukaemia in whom the disease manifested by severe generalized bone and joint pains and by acute knee joint arthritis, which did not respond to analgesics, anti-inflammatory agents, or to corticosteroids. The pains subsided after treatment with cytosine arabinoside, in spite of no haematological improvement.

Case report

A 60-year-old male was admitted to the medical department because of severe pains in both shoulders of one week's duration. He was afebrile, physical examination was noncontributory, and no lymphadenopathy or hepatosplenomegaly was found. Haemoglobin was 10.8 g/dl; white blood cell count 12 × 10⁹/l (12 000/mm³) with 11% metamyelocytes, 10% myelocytes, 16% neutrophils, 8% band forms, 20% lymphocytes, and 35% monocytes; platelet count was 250 × 10⁹/l (250 000/mm³). Ultrastructural study of the peripheral blood showed the presence of immature monocytes. Bone marrow was hypercellular with a myeloid:erythroid ratio of 16:1, with 6% blasts, 12% promyelocytes, 33% myelocytes, 18% metamyelocytes, 10% band forms, 5% neutrophils, 3% lymphocytes, and 7% monocytes. Serum lysozyme was 56 µg/ml (normal 10-27±1.46 SD) and urine lysozyme 7-8 µg/ml (normal 1.02±1.46 SD). Cytogenetic studies showed no chromosomal abnormalities. Serum vitamin B12, uric acid levels, and neutrophil alkaline phosphatase score were normal. Rheumatoid factor and anticardiolipin antibodies were not found and the LE test was negative. Liver and spleen scans were normal. Extensive roentgenographic examination was normal. The findings in the peripheral blood and in the bone marrow were consistent with the diagnosis of chronic myelomonocytic leukaemia.

Within 9 days of admission bone pain became generalized and unbearable, his temperature rose to 39°C and acute arthritis of the right knee with effusion appeared. 10 mm³ of clear synovial fluid was aspirated; its viscosity, mucin clot, glucose content, and complement level were normal. The fluid contained mononuclear cells, 200/mm³, of normal appearance on light microscopy. There was no evidence for bacterial infection and no tubercle bacilli or fungi were found. Polarized light examination showed no crystals. X-ray skeletal examination and bone scan were normal. Bone pains were not
alleviated by acetylsalicylic acid 3 g daily, or indomethacin 300 mg daily, or by prednisone 40 mg daily, given successively for a period of 4 weeks while the gonarthritis fluctuated in severity. Subsequently, cytosine arabinoside, 100 mg daily, was given intravenously for 5 consecutive days. By the third day of treatment a dramatic relief of pain was noted and the temperature returned to normal; the signs of arthritis disappeared within 5 days. A similar second course was given after a 7-day interval. The white blood cell and differential count remained essentially unchanged. The patient was maintained on thioguanine 40 mg daily.

Two similar episodes of severe bone pains but without manifest arthritis occurred after 6 and 11 months, respectively, and in both a 5-day course of cytosine arabinoside 100 mg daily was as effective as the first time. 15 months after the patient’s first admission, on thioguanine maintenance 40 mg daily, he was symptom free. His peripheral blood picture and bone marrow findings remain essentially unchanged.

Discussion

The haematological features, the high lysozyme levels in the blood and urine, and the benign course in this patient are consistent with chronic myelomonocytic leukaemia (Miescher and Farquet, 1974). There was no evidence for other disease which may be accompanied by monocytosis such as chronic infection, lymphoma, or carcinoma (Miescher and Farquet, 1974; Zittoun, 1976).

Bone and joint pains are known features of acute leukaemia (Thomas et al., 1961; Silverstein and Kelly, 1963; Rodnan, 1972). and are particularly frequent and often severe in leukaemia of childhood (Silverstein and Kelly, 1963; Gunz and Baikie, 1974). Bone pains in acute leukaemia have been attributed to a number of factors: increased intramedullary pressure, periosteal lesions, osteolytic lesions, and osteoporosis (Thomas et al., 1961). Acute arthritis has been related to leukemic infiltration of the synovia and the metaphysael and the juxta-articular portions of the bones or to haemorrhage (Thomas et al., 1961; Rodnan, 1972). Secondary gout rarely occurs in acute leukaemia (Talbott, 1959; Thomas et al., 1961). In chronic leukaemia articular involvement is much less frequent and less severe than in acute leukaemia (Rodnan, 1972). Severe bone pains and arthritis with effusion have not, to our knowledge, been described in chronic myelomonocytic leukaemia.

Aggressive chemotherapy in myelomonocytic leukaemia is usually limited to patients with the acute form (Zittoun, 1976). Thomas et al. (1961) stated that in patients with acute leukaemia receiving anti- leukaemic treatment, disappearance of bone and joint pains is often the first indication of improvement.

In patients with chronic myelomonocytic leukaemia intensive chemotherapy does not prolong survival nor does it prevent transformation to the acute form of myelomonocytic leukaemia. According to Zittoun (1976), in some patients with chronic myelomonocytic leukaemia early death was caused by aggressive treatment. In our patient with chronic myelomonocytic leukaemia the severe bone pains were a major therapeutic problem since analgesics, anti-inflammatory agents, and corticosteroids were of no avail. The dramatic improvement after cytosine arabinoside administration in this patient may be ascribed to reduction of leukemic infiltration in the bones. The beneficial effect of cytosine arabinoside suggests that in chronic myelomonocytic leukaemia cautious cytotoxic treatment, although ineffective in achieving haematological remission, can be worthwhile as a symptomatic measure.

References


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