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# HYPOCALCEMIC TETANY IN A CHILD WITH ACUTE LEUKEMİA*

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Serious metabolic abnormalities in acute leukemia result from spontaneous or chemotherapeutically induced cell lysis. These abnormalities generally occur during the active stage of the disease and are not to be expected during remission[1].

Hypocalcemic tetany has been shown in acute leukemic patients secondary to hyperphosphatemia, the result of rapid cell lysis[2]. In our patient there was neither hyperphosphatemia nor hypoalbuminemia. Clinical and laboratory findings and progress suggested that the hypocalcemic tetany was related to malabsorption, a side effect of methotrexate (MTX). We wanted to point out this rare complication by this presentation.

## Case Report

A nine-year-old boy was admitted to Hacettepe Children's Hospital with the complaints of fever, paleness, weakness and weight loss. He had been diagnosed as having acute lymphoblastic leukemia (ALL) in another hospital. During the previous year and a half he had not been receiving chemotherapeutic agents regularly.

On physical examination the patient was pale, the liver and spleen were palpable 12 cm and 9 cm respectively below the costal margin. There were petechiae on the legs.

On laboratory examination the hemoglobin level was 3.3 g/dl, the leukocyte count was 17000/$mm^3$, a peripheral blood smear showed thrombocytopenia and almost one hundred percent lymphoblastic cells; bone marrow was replaced by

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lymphoblasts. Blood was given until the patient's hemoglobin level reached 10.5 g/dl. He was treated weekly with IV vincristine and daily with oral prednisolone. Complete remission was attained in four weeks. Intrathecal MTX 0.5 mg/kg and cranial irradiation 2400 rad were given for central nervous system prophylaxis.

Maintenance therapy consisted of MTX and 6-mercaptopurine (6 MP) given orally. Three months after remission, he returned with the complaints of diarrhea, weakness and oral ulcers. There were extensive petechiae on the skin all over his body.

The hemoglobin level was 5 g/dl, the leukocyte count was 3000/$mm^3$ and the peripheral blood smear showed thrombocytopenia. Bone marrow was mildly hypocellular and revealed megaloblastic changes, but no lymphoblasts were seen. Since he was in remission it was thought that all the abnormal clinical and laboratory findings were the result of the toxic effects of the chemotherapy. MTX and 6-MP were stopped and folinic acid started and the clinical and laboratory findings began to go back to normal.

During the follow-up period, however, when MTX was resumed, the hemoglobin, leukocyte and thrombocyte counts fell, and oral ulcers and diarrhea again appeared. During these 8 months of remission bone marrow needle aspiration was repeated three times and the same morphology was observed as described above.

While he was in hospital for close observation the occurrence of carpopedal spasms was noted and Chvostek's sign. The serum calcium level, 7.5 mg/dl, was compatible with the clinical findings. Other laboratory results were phosphate 4 mg/dl, alkaline phosphatase 4.5 BU, total protein 7.4 g/dl and albumin 4 g/dl.

After treatment with calcium gluconate, intravenously, at the acute stage and with calcium lactate orally for ten days, the level of serum calcium was found to have increased to 10 mg/dl.

The patient was given half the normal daily dose of MTX. Two months later there was a relapse and he died of septicemia within one week.

## Discussion

Serum mineral and electrolyte changes, hyperuricemia, hyperphosphatemia, hypercalcemia and hypocalcemia are the best known metabolic complications in acute leukemia. However, hypocalcemia is not frequent and the mechanism is not always clear. Patients are at an advanced stage of the disease when hypocalcemia becomes symptomatic[3-6].

Hypocalcemia may be observed in acute leukemic patients with high white blood cell counts during the period of remission induction. The high phosphate load, a consequence of the dying leukemia cells, appears to lower the serum calcium

levels significantly. But hypocalcemia has also been determined in some patients before and during remission induction therapy. In the case of these patients the leukocyte and phosphate levels were within normal limits[7]. With our patient too, the high phosphate level was not responsible for the hypocalcemia. In a patient in remission but on MTX therapy, mouth ulcers, diarrhea, reduced hemoglobin, leukocyte and thrombocyte counts and bone marrow megaloblastic changes would seem to be the side effects of the MTX.

It has been shown that there is a relationship between a defective D-xylose test and the amount and interval between the MTX doses in a group of patients with ALL[8]. The morphological changes of human proximal small bowel mucosa have also been shown in serial observation[9]. Experimental studies which revealed morphological alterations in small bowel mucosa and amino acid malabsorption offer further supporting evidence[10].

Diarrhea was the only clinical finding which suggested malabsorption in our patient. Tests related to malabsorption were not carried out. However, the mouth ulcers, the reduced hemoglobin, leukocyte and thrombocyte values together with the megaloblastic bone marrow changes observed in our patient were all suggestive of the side effects of MTX. Since there were no other findings to explain why hypocalcemia developed during remission it would seem logical, in the light of the above clinical and laboratory findings, to regard the hypocalcemia in our patient as most probably being the result of malabsorption caused by MTX-induced mucosal changes of the intestine. However, more detailed laboratory investigations of these patients are needed to throw more light on this subject.

## Summary

The case is presented of a nine-year-old boy who developed hypocalcemic tetany while on a methotrexate regimen for acute lymphoblastic leukemia. While the patient was in remission diarrhea, mouth ulcers, pancytopenia and megaloblastic changes in the bone marrow occurred. With these clinical and laboratory findings it is suggested that the hypocalcemic tetany was the result of malabsorption, a side effect of the methotrexate treatment.

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