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# RADIATION INDUCED TUMOUR LYSIS SYNDROME IN A PATIENT WITH LEUKAEMIA

Pages with reference to book, From 191 To 193

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Tumour lysis syndrome is a catastrophic complication of treatment of certain neoplasms. It is usually seen with the tumours that have high growth fractions, increased bulk and extreme sensitivity to cytotoxic therapy. Most commonly it occurs in association with hematologic malignancies such as lymphomas and leukaemias. Rarely it has been observed with solid tumours like small cell lung cancer, seminoma and carcinoma of the breast. The syndrome develops due to massive cell lysis occurring within a few hours to a few days of starting the cytotoxic therapy. It is characterized by hyperuricemia, hyperkalemia, hyperphosphatemia and hypocalcaemia. Acute renal failure, cardiac arrhythmias and sudden death may occur. Tumour lysis syndrome has hitherto not been reported as a complication of radiotherapy only. We recently observed a patient with a diagnosis of chronic myeloid leukaemia who received splenic irradiation for massive splenomegaly and developed full-blown tumour lysis syndrome. Pathogenesis and clinical implications are discussed.

## CASE REPORT

A 38 years old male was admitted to The Aga Khan University Hospital with three days history of vomiting, dysuria, haematuria and oliguria. He was also complaining of LUQ pain. Patient had history of LUQ pain and fever since November, 1990. He was found to have massive splenomegaly. A blood count done at that time showed hemoglobin 8.6 g/dl, WBC 257,000/cmm with 40% neutrophils, 9% lymphocytes, 3% eosinophils, 3% basophils, 17% metamyelocytes, 27% myelocytes and 1% blasts. He also had some nucleated red cells in the peripheral blood. A diagnosis of chronic myeloid leukaemia was made. Due to massive splenomegaly, he received splenic irradiation. He did well for three months but in early March he developed LUQ pain again, as well as fever and splenomegaly. His hemogram revealed hemoglobin of 11.3 g/dl, WBC 216,000/cmm with 10% neutrophils, 52% lymphocytes, 2% metamyelocytes, 4% myelocytes and 30% blasts. His platelet count was 45,000. He was re-started on splenic irradiation. He received radiotherapy for five days. No other treatment was given. In the next three days he developed severe nausea and vomiting. He also developed dysuria, haematuria and later on oliguria. With these complaints he was admitted to this hospital for the first time on March 14, 1991. He was afebrile but very sick looking young man in considerable distress. He had generalized lymphadenopathy. His spleen was enlarged upto the umbilicus. His CBC revealed hemoglobin of 6.1 g/dl, WBC 2,300/cmm with 10% neutrophils, 72% lymphocytes and 18% blasts. His platelet count was 9,000. His electrolytes and blood chemistries revealed sodium 133 mEq/L, potassium 8.3 mEq/L bicarbonate 9.2 mEq/L calcium 5.9 mg/dl, phosphorus 31.5 mg/dl, BUN 108 and creatinine 5.0 mg/dl. Serum uric acid was 50 mg/dl. His ECG revealed tented T waves. Bone marrow examination, reported later, confirmed infiltration with blasts. A diagnosis of CML in blast crisis and acute tumour lysis syndrome was made. He was treated with emergency measures to lower serum potassium with calcium gluconate, insulin and glucose and kayexalate. He was hydrated and forced alkaline diuresis was initiated. He received allopurinol for hyperuricemia and aludrox for hyperphosphatemia. His serial electrolytes and other metabolic changes are shown in Figure.

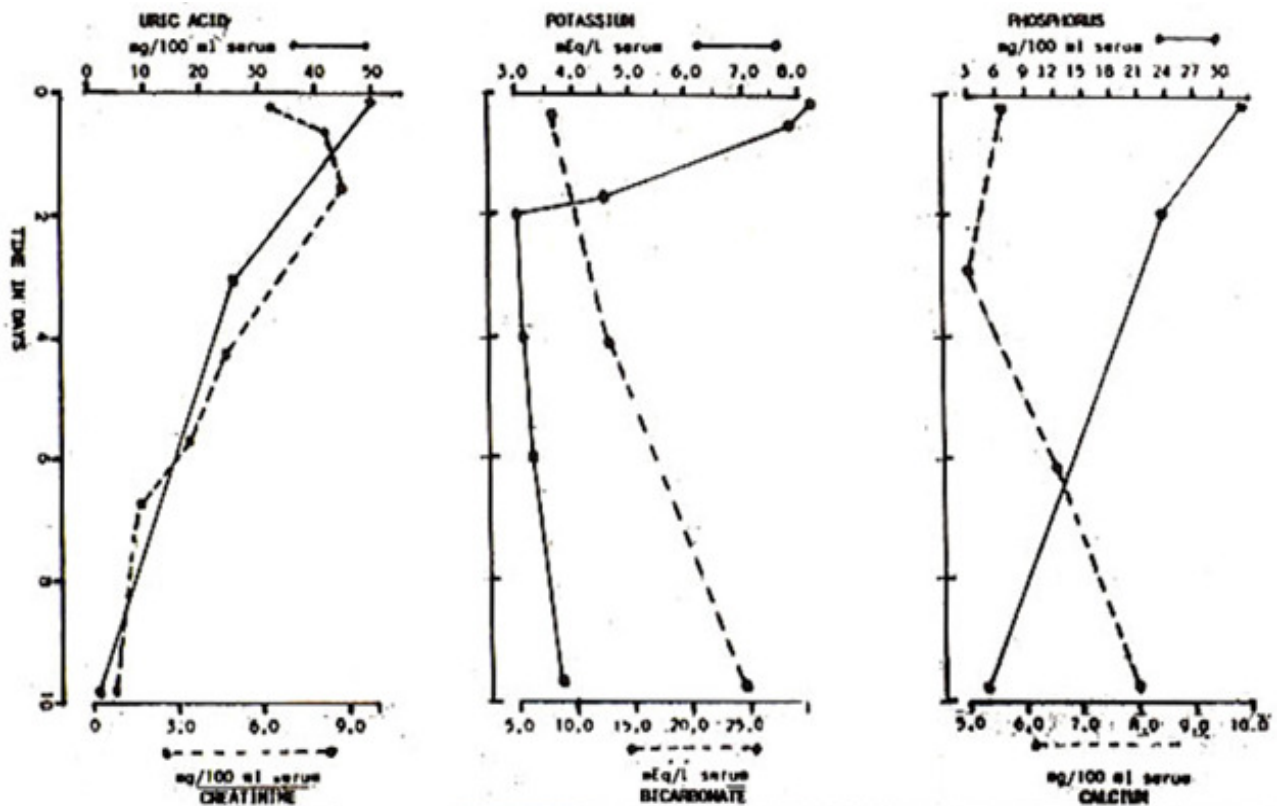


Figure. Temporal course of metabolic abnormalities. Splenic irradiation was done for 5 days, 3 days prior to the admission.

With these aggressive measures, he survived the tumour lysis syndrome. On normalization of his metabolic abnormalities he was started on antileukaemia therapy.

## DISCUSSION

Certain malignancies, particularly those with high tumour burden and growth fractions may respond dramatically to cytotoxic therapy resulting in the tumour lysis syndrome<sup>1</sup>. Most often it is seen with tumours that are exquisitely sensitive to treatment such as lymphomas and leukaemia<sup>2-7</sup>. Infrequently it has been observed during the treatment of certain solid tumours such as small cell carcinoma of lung, breast cancer or seminoma<sup>8-10</sup>. The syndrome develops due to massive release of products of cell destruction, i.e., uric acid, potassium and phosphate into the circulation. The risk of developing this syndrome is increased in patients with high tumour bulk, high LDH, presence of hyperuricemia prior to the initiation of therapy, extreme leukocytosis and pre-existing renal impairment. Our patient had a very high tumour burden as reflected by extremely high leucocyte count. Presence of other factors remains unknown since patient had previously been treated elsewhere. Tumour lysis syndrome, however, is most commonly observed after the institution of chemotherapy. Even small doses of cytotoxic drugs such as given for intrathecal therapy, may precipitate tumour lysis syndrome in an exquisitely chemosensitive cancer<sup>11</sup>. Only rarely have been precipitated by other agents, ag., steroid, tamoxifen and alpha interferon<sup>9,12-15</sup>. Our patient developed this complication after splenic irradiation. This is most unusual and hitherto unreported complication of this therapy. However, development of tumour lysis syndrome in this patient can easily be explained by extremely high white cell count, high growth fraction of leukaemic cells, massive splenomegaly, increased blood supply of an enlarged spleen that would have exposed very high number of blood cell to the destructive effect of radiation

and exquisite radiosensitivity of myeloid and lymphoid cells. There are many complications that follow the development of this syndrome. Hyperuricemia can cause acute renal failure. This is due to the precipitation of urates in the collecting tubules. Hyperphosphatemia can cause hypocalcaemia due to the sequestration of calcium in the bones. If the product of calcium and phosphate exceeds 70, these may precipitate in different organs resulting in organ dysfunction. If it happens in the kidney, acute renal failure may ensue. Severe hyperkalemia may lead to cardiac arrhythmias and sudden death. Metabolic acidosis may be caused by hyperuricemia, acute renal failure or lactic acidosis. Death may be the result of acute renal failure or arrhythmias. The best management of this syndrome is by prevention. Delaying the cytotoxic therapy, until the pre-existing metabolic derangements have been corrected, may decrease the chances of developing tumour lysis syndrome. This could be achieved by intravenous hydration, usage of allopurinol to control hyperuricemia, alkalization of urine with sodium bicarbonate and maintenance of good urinary output may be helpful. However, at times, this complication may develop in spite of all these measures. The treatment of the syndrome, once established, is extremely difficult<sup>16</sup>. The usual measures include correction of hyperkalemia with dextrose and insulin, sodium bicarbonate infusions for metabolic acidosis, intravenous calcium to correct hypocalcaemia and aluminum hydroxide to decrease hyperphosphatemia. Hemodialysis may be indicated if potassium is over 6 mEq/L, uric acid over 10 mg/dl, serum creatinine over 10 mg/dl, phosphate above 10 mg/dl, volume overload or symptomatic hypocalcemia<sup>5</sup>. In spite of these measures mortality may be high. In conclusion, we described a case of full blown tumour lysis syndrome that occurred as a complication of splenic irradiation in a patient with chronic leukaemia who had undergone blast transformation. With aggressive management, the patient survived the consequences of severe metabolic derangement.

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