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Case Report

Spontaneous Tumor Lysis Syndrome Revealing a Hematological Malignancy: A Case Report

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Abstract: Tumor lysis syndrome is a metabolic emergency in oncology. It is the direct outcome of the massive destruction of tumor cells, with the release of their components in quantities that exceed the body's homeostatic regulatory capacity. Often observed following the initiation of cytotoxic treatment, we report the observation of a 13-year-old Moroccan female who developed a spontaneous tumor lysis syndrome, in the absence of any cytotoxic treatment, which led to the diagnosis of hematological malignancy, later confirmed and characterized as acute lymphoblastic leukemia.
Keywords: Tumor Lysis Syndrome, Acute Leukemia, Metabolic Emergency, Pediatric, Oncology.

INTRODUCTION

Tumor lysis syndrome (TLS) is one of the most common life-threatening emergencies encountered in the management of cancer and hematological diseases. It results from an inadequate balance between the body's homeostatic regulatory capacity and the massive release of metabolites into the bloodstream due to tumor cell lysis [1]. We report the case of a 13-year-old patient admitted with fever and abdominal pain who presented a highly proliferative spontaneous tumor lysis syndrome leading to the fortuitous discovery of acute lymphoblastic leukemia.

OBSERVATION

We report the case of a 13-year-old girl admitted to the pediatric department of the Mohammed V Military Training Hospital (HMIMV) in Rabat for fever, abdominal pain and vomiting. The history of the illness goes back one month with the development of osseous aches and diffuse myalgia with asthenia and 3 kg of weight loss.

Upon admission, the patient was conscious, pale, apyretic with a stable hemodynamic and respiratory status. The mucocutaneous examination revealed discolored conjunctivae, purpuric spots on the palate, both feet and ecchymotic spots on the outer surface of the left thigh. The rest of the clinical examination showed no particularities.

During hospitalization, the child presented a significant biological and clinical tumor lysis syndrome (TLS). The biological TLS was characterized by hyperuricemia greater than 331 mg/L (39-78 mg/L), hyperkaliemia at 7.20 mmol/L (3.7-5.3 mmol/L) with a hemolysis index of 0, hyperphosphatasemia greater than 253 mg/L (30-40 mg/L) and hypocalcemia at 40 mg/L (80-105 mg/L). The aspartate aminotransferase value reached 96 IU/L, about 3 times the normal value (<35 IU/L), with a normal alanine aminotransferase value (19 IU/L). Lactate dehydrogenase reached 5124 IU/L, 21 times the normal value (125-243 IU/L) and the lipase was up to 574 IU/L, 7 times the normal value (<78 IU/L). The child also had a very low alkaline reserve of 8 mmol/l (21-28 mmol/L).

This biological tumor lysis syndrome was further complicated by a clinical TLS that manifested as an acute renal failure with an urea level of 2.68 g/L (0.15-0.38 g/L) and a creatinine level of 15 mg/L (5-9 mg/L). The patient also experienced seizures as a result of hypocalcemia during her hemodialysis session and was transferred to the intensive care unit for the management of the lysis syndrome.

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The hematological tests showed normochromic normocytic anemia, hyperlymphocytosis at 12.9 x 10^3/µL and thrombocytopenia at 11 x 10^3/µL. The blood smear showed and infiltration at 65% of the peripheral blood by blasts of various sizes. The diagnosis of acute lymphoblastic leukemia (ALL) was confirmed on the myelogram, that was further supplemented by an immunophenotyping test.

Following her stabilization and the positive outcome of her stay in intensive care, the patient was referred to the pediatric hematology and oncology center at the Children's hospital in Rabat.

DISCUSSION

TLS is a metabolic emergency in oncology, involving a series of metabolic disorders that occur as a result of the sudden and massive lysis of cancer cells, with the release of their components in quantities that exceed the capacity of renal excretion.

The frequency of TLS has not yet been established [2], but it is the most common complication in patients with large tumors, or with high proliferation rates and tumors that are highly sensitive to cytotoxic therapies. [1- 3]

TLS is the direct consequence of the massive destruction of tumor cells, which releases large quantities of intracellular compounds into the bloodstream, overloading the body's homeostatic regulatory capacity. This lysis is primarily responsible for hyperkaliemia and hyperphosphatemia. This acute hyperphosphatemia will lead to the precipitation of phosphocalcic crystals in soft tissues, particularly the heart and kidneys, resulting in paradoxical hypocalcemia.

Secondly, the nucleic acids released are progressively metabolized (de novo purinosynthesis) into uric acid, leading to hyperuricemia [1], [4- 7]. Uric acid, which is usually filtered by the glomeruli, precipitates in large quantities in the renal tubules, particularly at acid pH. This metabolic acidosis is due to mitochondrial dysfunction and acute renal failure, which is a turning point in the evolution of the tumor lysis syndrome [4].

The clinical manifestations usually observed are, firstly, renal failure resulting from mechanical obstruction of the renal tubules by phosphocalcic and uric acid crystals, but also from the direct nephrotoxicity of uric acid [5], [8, 9]. Then there are cardiovascular anomalies, mainly rhythm and conduction disturbances linked to hyperkaliemia, hyperphosphatemia and metabolic acidosis. Neurological abnormalities such as hypocalcemia-related seizures have also been observed. These are rare and mainly observed in the pediatric population. [4].

There are four main risk factors for TLS [4]: The nature of the tumor disease, particularly tumors with a rapid duplication time such as hematological malignancies. Tumor mass, which in the case of solid tumors is assessed by radiological criteria (size > 10 cm) and in the case of hemopathies by the level of circulating blasts, lactate dehydrogenase (LDH > 2 times normal) and/or leukocytes (hyperleukocytosis > 25 Giga/L) [4, 5]. Cycle-dependent chemotherapy is also a main risk factor, but up to a third of tumor lysis syndromes occur spontaneously before any chemotherapy [4]. Finally, the patient's background contributes to the increased risk, essentially through renal function. A pre-existing renal failure causes a clearance reduction and an increased risk of metabolic disorders [5].

In the current classification by Cairo and Bishop, the clinical and biological presentations of the lysis syndrome are separated. A biological tumor lysis syndrome includes the presence of at least two of the following metabolic disorders in the 3 days preceding or up to 7 days following the start of cytotoxic treatment: hyperuricemia (> 476 µmol/L (80mg/L)), hyperkaliemia (> 6 mmol/L), hyperphosphatemia (> 1.5 mmol/L (46. 5mg/L) for adults, and (> 2.1mmol/L) (65.1mg/L)) for children, hypocalcemia (< 1.75 mmol/L (70mg/L)), or a variation greater than 25% in these parameters compared to the patient's initial values. [7] Clinical tumor lysis syndrome is a complication of biological TLS and is present when the biological TLS is accompanied by one or more of the following clinical criteria: an increase of 26.5 µmol/L (3 mg/L) in serum creatinine levels indicating acute renal failure, convulsions, cardiac rhythm dysfunction or death. [1- 5] Howard and al. have proposed some modifications that could improve this biological and clinical classification; two or more metabolic abnormalities must be present simultaneously, a variation of 25% from baseline should no longer be considered a criterion, and any symptomatic hypocalcemia should represent a clinical tumor lysis syndrome [5]. Cairo and Bishop have also developed a graded classification of clinical TLS, including 6 grades that are defined by the severity of the clinical manifestations observed. [7].

In total, our patient in her admission met Cairo and Bishop's classification criteria of grade 1 biological and clinical TLS, which complicated into grade 2 TLS after seizures, resulting in her transfer to an intensive care unit. This spontaneous tumor lysis syndrome led to a diagnosis of hematological malignancy, which was subsequently confirmed as acute lymphoblastic leukemia. The fact that 65% of the peripheral blood was invaded by blasts, and the values for lactate dehydrogenase and Aspartate aminotransferase, indicate the size of the tumor mass, and the infiltration of secondary hematopoietic organs such as the liver, as well as cardiac and renal involvement. This spontaneous form has been reported mainly in Burkitt's lymphoma and acute leukemia [10].

Preventive measures should be introduced systematically for patients at high risk of developing lysis syndrome. Specific treatment targets the electrolyte and organ complications of TLS. It is based on rigorous intravenous hydration of 3 L/m2/day, with an isotonic fluid, in the absence of cardiac contraindication [6- 11]. Three molecules are currently used to treat hyperuricemia: Rasburicase, Allopurinol and Febuxostat [5, 6], [12]. The management of threatening hyperkaliemia (> 6.5 mmol/L) includes insulin infusions (accompanied by glucose), and/or treatment with high-dose inhaled beta-agonists to promote the transfer of potassium into the intracellular compartment. If these measures are exceeded, the use of ion exchange resins or loop diuretics should be considered. [11] Phosphate binders can be used to treat hyperphosphatemia while avoiding any administration of this element. [3- 5] Hypocalcemia should only be treated in severe symptomatic cases [1- 5] In this case, an infusion of calcium gluconate should be administered at the lowest dosage required [1]. Finally, emergency hemodialysis is indicated if acute renal failure develops and if electrolyte disturbances persist despite treatment [3- 5], [11].

All these therapeutic measures must, of course, be accompanied by regular, and continuous clinical and biological monitoring in order to orientate the management. This should include a clinical examination, strict quantification of diuresis, monitoring of blood pressure, heart rate and electrocardiogram, as well as biochemical tests (Serum levels of potassium, phosphates, calcium, uric acid and creatinine).

CONCLUSION

Often reported after the initiation of chemotherapy, in our case, the spontaneous tumor lysis syndrome was the main feature pointing to the suspicion of acute leukemia. The treatment is intended to reduce the biological abnormalities and thereby prevent clinical complications. Clinical and biological monitoring are the central elements of this process.

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