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Tumor Lysis Syndrome under Concurrent Chemoradiation for Rectal Cancer in a Patient with Dihydropyrimidin Deficiency

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Abstract

Tumor Lysis Syndrome (TLS) is a major oncological emergency involving metabolic perturbations. TLS is usually observed after aggressive treatment or spontaneously in rapidly growing hematological malignancies and exceptionally in solid cancers.

Dihydropyrimidine Dehydrogenase (DPD) is the first enzyme acting in the catabolism of 5-fluorouracil (5FU). Patients with a partial deficiency of this enzyme are at risk for developing a severe 5FU-associated toxicity.

We report here a rare case of TLS secondary to DPD deficit in a patient treated with concurrent chemoradiation for a locally advanced rectal cancer.

Introduction

Tumor Lysis Syndrome (TLS) is a major oncological emergency involving metabolic perturbations such as hyperuricemia, hyperkaliemia, hyperphosphatemia hypocalcemia, and increased serum creatinine.

TLS is usually observed after aggressive treatment or spontaneously in rapidly growing leukemias, high grade lymphomas and exceptionally in solid cancers. Dihydropyrimidine Dehydrogenase (DPD) is the initial and rate-limiting enzyme in the catabolism of 5-Fluorouracil (5FU). Patients with a partial deficiency of this enzyme are at risk for developing a severe 5FU-associated toxicity due to 5FU accumulation.

We report here a case of TLS secondary to DPD deficit in a patient treated with concurrent chemoradiation for a locally advanced rectal cancer.

Case Presentation

A 43-year-old man with a family history of Familial Adenomatous Polyposis (FAP) and past medical history of hypertension and dyslipidemia, consulted for rectorragia.

Colonoscopy showed multiple sessile polyps involving the entire colon with presence of as two exophytic lesions in the medium rectum and sigmoid. Biopsies confirmed a bifocal adenocarcinoma. Work-up did not show distant metastases. Pelvic MRI showed a medium rectal lesion staged cT2N1. The patient started neoadjuvant chemotherapy with oral capecitabine (850 mg BID twice a day) concomitant with pelvic-radiotherapy. No toxicity was reported for the first two weeks. At a dose of radiotherapy of 23 Gy and 17 days of oral capecitabine, the patient was admitted in emergency for hypovolemic shock secondary to grade 3 vomiting and diarrhea. Blood tests showed (Table 1) a creatinine serum level of 653 µ mol/l and grade 4 neutropenia.

Abdominopelvic ultrasonography was performed to explore the cause of the Acute Kidney Failure (AKF) and didn't show renal nor Ureteral obstruction. Patient was managed for his digestive chemoradiation toxicity by intravenous hydration, oral allopurinol and symptomatic treatment for his STL. After treatment increased creatininemia persisted after 5 days and other tests confirmed and further laboratory exams (Table 1). The diagnosis of TLS excepting for hypokaliemia (explained by massive diarrhea).

A DPD determination by phenotypic technique showed a partial deficiency. Patient status improved slightly after and fully recovered from all toxicities. A secondary surgery by anterior

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Table 1: Biochemical Parameters.

Biochemical parameter	Before chemoradiation	Hospitalisation			Normal range
		Day 1	Day 5	Day 6	
Uric Acid (µ mol/l)	-	-	639.4	571	209-429
Lactate dehydrogenase (UI/L)	-	-	267	119	135-145
Creatinine (µ mol/l)	48.62	653	566	422	59-104
Urea nitrogen (mmol/L)	-	38.9	40.5	39.37	2.8-7.2
Potassium (mmol/L)	-	4.45	3.8	2.58	3.5-4.5
Phosphorus (mmol/L)	-	-	2.7	2.17	0.87-1.45
Calcium (mmol/L)	-	-	1.82	1.96	2.2-2.55
PH	-	7.31	-	7.4	7.38-7.42
Bicarbonate (mmol/L)	-	10.1	-	13.6	22-28

resection was performed and histologic exam showed a pathological complete response.

Discussion

TLS is an expectable complication in hematologic malignancies, like aggressive acute leukemia's and lymphoma's resulting from a rapid destruction of tumor cells and a massive release of cellular breakdown products. Its occurrence in solid cancers is exceptional with only 45 cases collected by Baeksgaard and Sorensen JB published between 1977 and 2002 [1]. Thus, prognosis is poorer than with hematological malignancies due to a lack of early recognition and prevention.

We collected other cases of TLS in patients treated for metastatic colorectal [2-6]. Factors implicated to promote cell lysis or inhibit compensatory mechanisms included high tumor volume, metastatic presentation, bulky liver metastasis, high LDH and uric acid levels, and pre-existent renal insufficiency [7]. In our case, the TLS occurrence after 2.5 weeks of concomitant chemo radiotherapy and rapid impressive tumor shrinkage was mainly due to DPD deficiency. The tumor volume was moderate and TLS couldn't be anticipated.

Therefore, TLS diagnosis has to be discussed in patients with solid cancers, regardless the treatment regimen, due to its high risk of mortality and the need of immediate management, conversely to hematological tumors where prophylactic measures are anticipated [8-14].

DPD screening for any patient receiving 5FU is now a recommendation, it is rare but toxicity can be lethal. In February 2018, the National Agency for the Safety of Medicines and Health Products (ANSM) had advocated the search for a DPD deficiency for any patient concerned by chemotherapy incorporating fluoropyrimidines. In December 2018, the National Cancer Institute (INCA) and the Haute Autorité de Santé (HAS) recommended the search for DPD D.

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