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MALIGNANT HYPERCALCEMIA IN A CASE OF SMALL BOWEL GASTROINTESTINAL STROMAL TUMOUR

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Background and Aims: Malignant hypercalcemia is the most common cause of hypercalcemia, occurring in 30% of cancer patients and rendering a poor prognosis. Most cases have a humoral cause, the majority mediated by parathyroid hormone related peptide (PTHrP), rarely by 1,25-dihydroxyvitamin D3 ($1,25(OH)_2D$) and very rarely by parathyroid hormone (PTH) ectopic production; other cases are due to local osteolysis. In the literature, there are only 5 reported cases of hypercalcemia associated to gastrointestinal stromal tumour (GIST), only 2 of them due to $1,25(OH)_2D$ overproduction.
Method: Case report.
Results: Sixty-two years-old male with small bowel GIST diagnosed in 2014, subjected to enterectomy and on tyrosine kinase inhibitor (TKI) since 2017. TKI was changed from imatinib to sunitinib 25mg since August 2020 to the present date due to disease progression with liver metastasis. In March 2022, a PET scan showed no bone or soft tissue metastasis and there was a finding of right ureteral lithiasis with asymptomatic mild pyelocaliceal dilation. The patient had also subclinical hypothyroidism and several episodes of acute kidney injury (AKI) associated with hypercalcemia and hyperphosphatemia managed in outpatient clinic. He did not take any other medication besides the TKI. In April 2022, symptoms of disequilibrium, confusion, asthenia, and anorexia drove the patient to the Oncology Department. At physical examination the patient had an ECOG 3, was disoriented, cachectic and

dehydrated, with no other noticeable findings. Blood lab tests showed a serum creatinine (sCr) of 2,86 mg/dL (baseline 1,10 mg/dL, estimated glomerular filtration rate of 72 mL/min/1,73 m^2), a corrected serum total calcium (sCa) of 16,6 mg/dL and a normal serum phosphate of 4,0 mg/dL. The patient was admitted in the oncology ward with the collaboration of the nephrology department and was started on fluid therapy with 3000–4000cc NaCl 0,9%/day for a target urinary output of 75–200 mL/h. Hypercalcemia work-up showed low PTH of 8,8 pg/dL (reference range: 12–65 pg/dL). Measurement of PTHrP and $1,25(OH)_2D$ were requested but took longer. After 3 days, despite the improvement of both sCr (2,23 mg/dL) and sCa (13,6 mg/dL), zoledronic acid was started. Results revealed an increased $1,25(OH)_2D$ of 309 pg/dL (reference range: 10,9-79,3 pg/dL) and negative PTHrP. At the 6^{th} day, a clear improvement of analytical (sCr 1,60 mg/dL; sCa 11,9 mg/dL) and clinical status, so the patient was discharged. The diagnosis was GIST $1,25(OH)_2D$ overproduction causing malignant hypercalcemia and prednisolone on 20mg id was started. In June 2022, the patient had tumour progression, presenting lethargic, disoriented, and dehydrated; blood lab results showed AKI (sCr 1,97 mg/dL) and worsening hypercalcemia (sCa 14,7 mg/dL). He was admitted for fluid therapy and bisphosphonates but, even though there was a recovery of the hypercalcemia and renal function, the patient's clinical status got worse and he had a fatal outcome in the following days.

Conclusion: Malignant hypercalcemia caused by GIST $1,25(OH)_2D$ overproduction is a rare condition. The work-up of an oncological patient with ureteral lithiasis and recurrent hypercalcemia should prompt us to a more in-depth investigation.