

Not just weight loss

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ABSTRACT

Renal cancer (RC) – associated increased calcium is rather frequent among cases of kidney neoplasia; it may be the first sign of presentation that allows the detection of the malignancy; typically representing a poor prognostic factor. Weight loss is part of the panel underlying hypercalcemia - related signs, but also of the malignancy – associated phenotype. We aim to introduce a male case who was admitted for a clinical picture (including weight loss) correlated with alarming high calcium levels; the biochemistry anomaly was actually a paraneoplastic syndrome due to RC. When admitted as emergency, the assays revealed hypercalcemia of 16.9 mg/dl (normal levels between 8.4 and 10.2 mg/dl) with low PTH (Parathormone) and high CrossLaps as bone turnover marker of resorption. Intravenous contrast computed tomography showed a large left retroperitoneal tumor (involving the kidney and adrenal gland) with iodophil pattern, and post-contrast heterogeneous structure of 8.06/11.09 cm (axial), 10.58/12.16 cm (coronal - reconstruction), 9.12/10.59 cm (sagittal - reconstruction), also associating a mixt structure and micro-calcifications as well as hypodense areas. Whole body bone scintigrame did not show metastasis. The calcium levels were controlled under subcutaneous denosumab 60 mg in addition to IV fluids replacement; then the patient was referred to nephrectomy; post-operative confirmation confirmed a clear cell renal cell carcinoma (T4N1Mx). A normalization of calcium and PTH levels was found immediately after surgery. Unintentional weight loss might become a valuable tool in order to assess a routine biochemistry panel that will detect hypercalcemia. Low PTH represents the next step in order to further look for a tumor. Symptomatic control of hypercalcemia in addition to targeted approach of originating tumor are essential to improve the outcome.

Keywords: weight loss, hypercalcemia, malignancy-related hypercalcemia, calcium, parathormone, tumor, parathyroid gland, kidney cancer

INTRODUCTION

Calcium metabolism and kidney status are linked through renal complications of primary hyperparathyroidism (like kidney stones etc.), renal hyperparathyroidism that is associated with long standing renal fail-

ure, as well as malignancy – related hypercalcemia accompanying a renal cancer (1,2). At the point when hypercalcemia becomes symptomatic, the renal tumor might be already diagnosed or not (3,4). Among the cases of cancer – related hypercalcemia, this is a rare cause opposite to other cancers originating from breast

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or lungs or even some particular types of neuroendocrine neoplasia (5,6,7). Weight loss is part of the panel underlying hypercalcemia - related signs, but also of malignancy – related clinical picture (8).

We aim to introduce a male case who was admitted for a clinical picture (including weight loss) correlated with alarming high calcium levels; the biochemistry anomaly was actually a paraneoplastic syndrome due to a renal cancer. The patient' consent is signed.

CASE PRESENTATION

Admission

This is a 63-year old male who is admitted for weight loss (14 kg/6 months), high blood pressure controlled under adequate medication with a 1-year history of mild hypercalcemia complicated as acute type (requiring admission as emergency).

Assessments as emergency

When admitted as emergency, the assays showed hypercalcemia with low PTH (parathormone) and high CrossLaps as bone turnover marker of resorption (Table 1).

TABLE 1. Hypercalcemia on a 63-year old patient who is admitted for massive, unintentional weight loss within the last few months

| Parameter | Value | Normal | Units |
|--|-------|------------|-------|
| Total serum calcium | 16.9 | 8.4-10.2 | mg/dl |
| Serum phosphours | 2.4 | 2.3-4.7 | mg/dl |
| 25OHD (25-hydroxyvitamin D) | 17 | >30 | ng/ml |
| PTH (parathormone) | 1.2 | 16-65 | pg/ml |
| CrossLaps (bone resorption marker) | 1.48 | 0.33-0.782 | ng/ml |
| Osteocalcin (bone formation marker) | 47 | 15-46 | ng/ml |
| 1,25 (OH)D2 | 96 | 18-79 | ng/ml |
| Alkaline phosphatase (bone formation marker) | 173 | 8-105 | U/l |

Imaging assays

Abdominal ultrasound showed a left kidney tumor at superior pole, with inhomogeneous structure, associating necrosis and calcifications (of 10.34 by 10.69 by 9.11 cm as largest diameters) (Figure 1).

IV (intravenous) contrast CT (computed tomography) showed a large left retroperitoneal tumor (involving the kidney and adrenal gland) with iodophil pattern, and post-contrast heterogeneous structure of 8.06/11.09 cm (axial), 10.58/12.16 cm (coronal - reconstruction), 9.12/10.59 cm (sagittal - reconstruction), also associating a mixt structure (liquid/solid) and micro-calcifications as well as hypodense areas (Figure 2A,B,C).

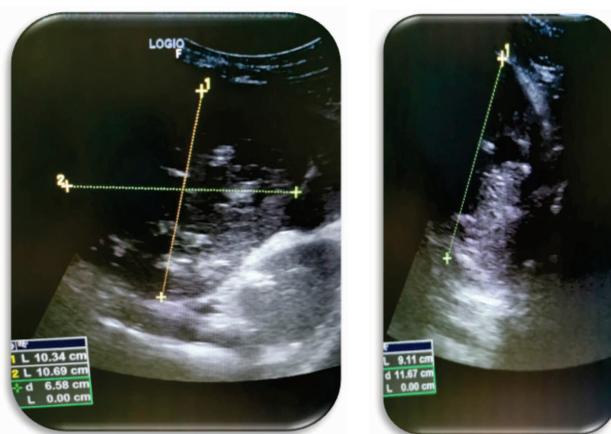
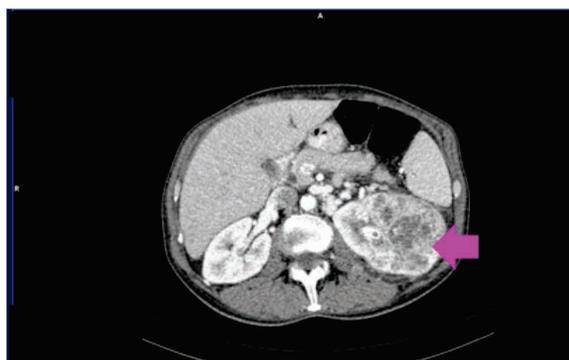


FIGURE 1. Abdominal ultrasound showing a renal mass that was detected starting from high calcium levels



2A. Transversal plan



2B. Coronal plan



2C. Sagittal plan

FIGURE 2. Intravenous computed tomography of renal cancer that was detected starting from hypercalcemia on a 63-year old male

Whole body bone scintigrama showed no distance metastasis, but a renal stasis at left upper kidney level (Figure 3).

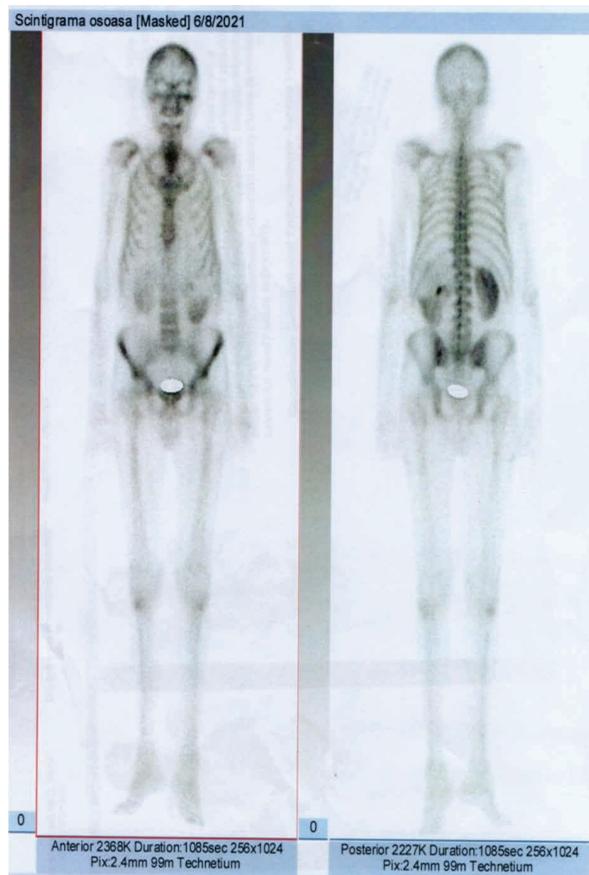


FIGURE 3. Negative whole body scintigram for bone metastases

Follow-up

The calcium levels were controlled under subcutaneous denosumab 60 mg in addition to IV fluids re-

placement; then he was referred to nephrectomy; post-operative confirmation showed a clear cell renal cell carcinoma (T4N1Mx). A normalization of calcium and PTH levels was found immediately after surgery (Figure 4). Lifelong follow-up is essential according to a multidisciplinary team.

DISCUSSIONS

Renal cancer-associated increased calcium is actually frequent among cases of kidney cancer; it may be the first sign of presentation that allows the detection of the malignancy; typically representing a poor prognostic factor (9,10). Multiple mechanisms are involved in this condition: humoral subtype due to the production of PTHrP (parathormone related peptide), one third of cases associate bone metastasis (which may also cause pain, fragility fractures, spinal cord compression depending on site) and even anomalies of vitamin D metabolism (11,12). PTH is typically suppressed (unless an ectopic production of PTH is the underlying cause, not extra PTHrP), while PTHrP might become a useful tool to differentiate humoral mechanism (with high PTHrP) from osteolytic metastases (with low PTHrP) (13,14). However, PTHrP assessment in daily practice is not routinely feasible (15,16). Non PTHrP-related molecules that cause increased calcium levels are also interleukins as, for instance, IL-6, IL-1 as well as TNF- α , transforming growth factors alpha & beta (17,18). PTHrP uses PTH receptor type 1 of PTH which explains calcium anomalies; but it does not stimulate the production of active form of vitamin D as PTH while PTHrP shares an inhibitor feedback with PTH (19). Symptomatic control of hypercalcemia in addition to targeted approach of originating tumor are essential to a good outcome (20).

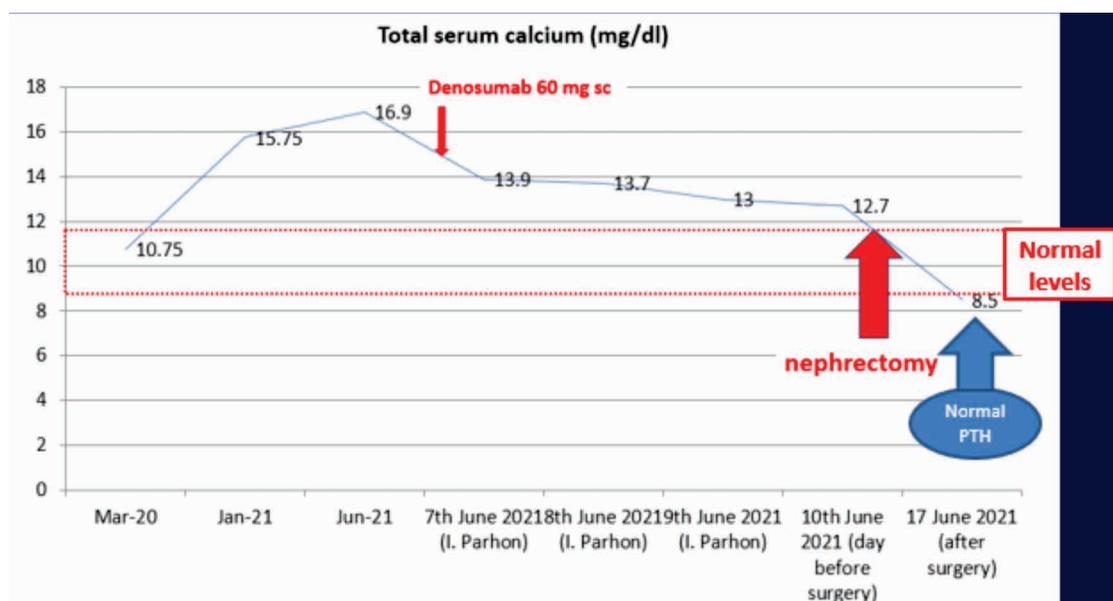


FIGURE 4. The evolution of calcium and PTH levels under medication and after surgery

CONCLUSIONS

Unintentional weight loss might become a valuable tool in order to assess a routine biochemistry panel

that will detect hypercalcemia. Low PTH represents the next logical step in order to further look for a tumor, for instance, a kidney cancer.

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