

Learning Objectives

1. Learn a structured approach to malignancy-associated hypercalcemia
2. Understand the effect of humoral hypercalcemia on the outcomes in patients with HCC

Case

Presentation:

A 67-year-old male with hx of HCV (treated with SVR) c/b cirrhosis and previously treated HCC (MWA in 2013, TARE 2021) with recurrence presented to the ED with subacute confusion, constipation, and lower extremity weakness.

Exam:

- Tangential thinking, somnolent
- Soft, mildly distended abdomen, no ascites, +BS
- No asterixis, CN II-XII intact, normal reflexes, oriented to person, place, time

Relevant Labs:

- **Serum calcium 14.8 (corrected to 15.3)**
- **Cr 1.36 (baseline 0.8), AST 141, ALT 32, AFP 135**

Imaging: Evidence of metastatic disease (Figures 2 and 3)

Hospital Course:

- Serum calcium levels normalized with IV fluids, calcitonin, and zoledronic acid
- Periorbital mass biopsied and revealed HCC metastases
- PTHrP elevated to 79; Vit D, PTH, SPEP and UPEP normal

Dx: PTHrP-mediated hypercalcemia due to HCC

Clinical Course:

- Patient was discharged but returned one week later with recurrent, severe hypercalcemia
- No further cancer treatments available so hospice was consulted and pt died at home within 1 week

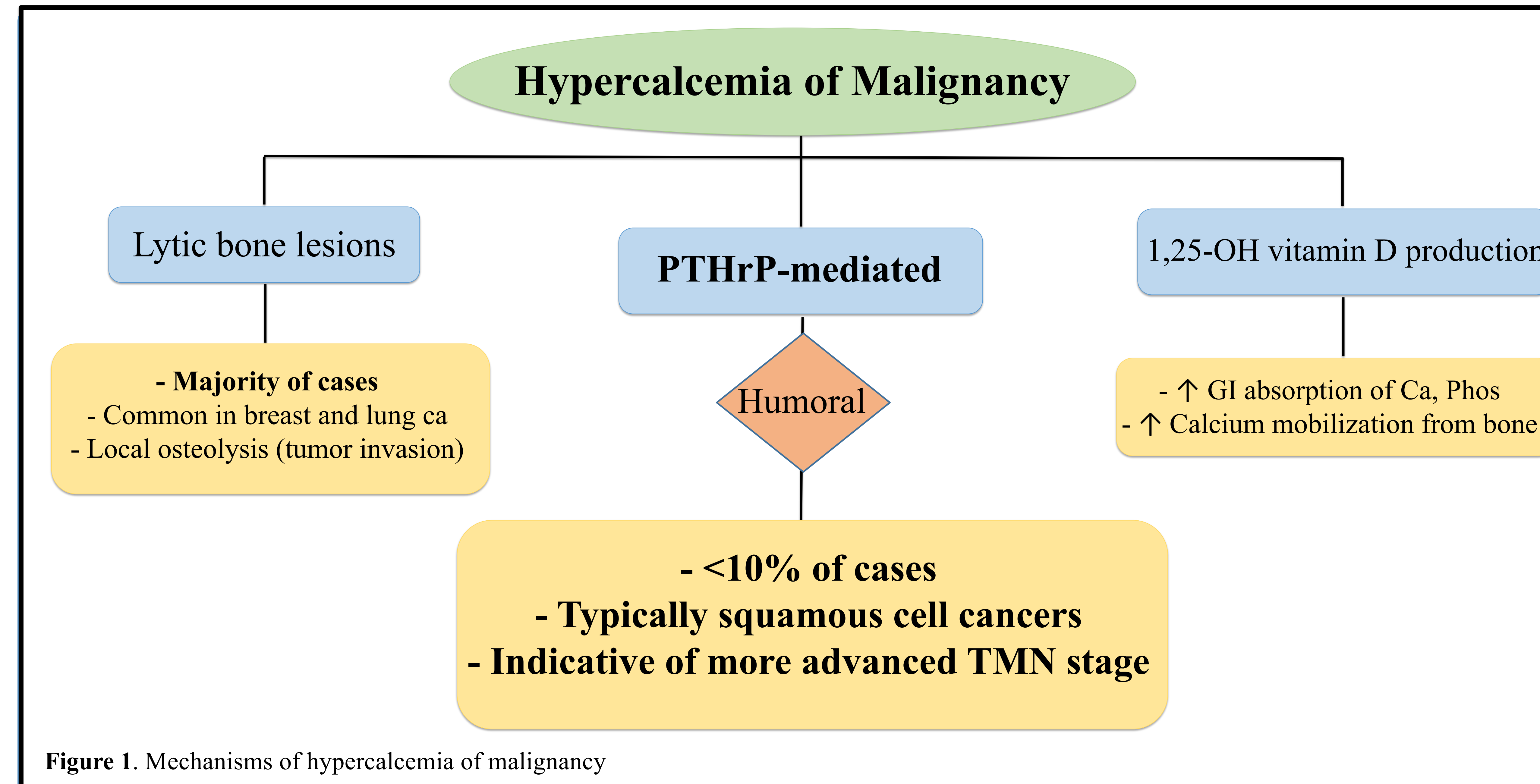
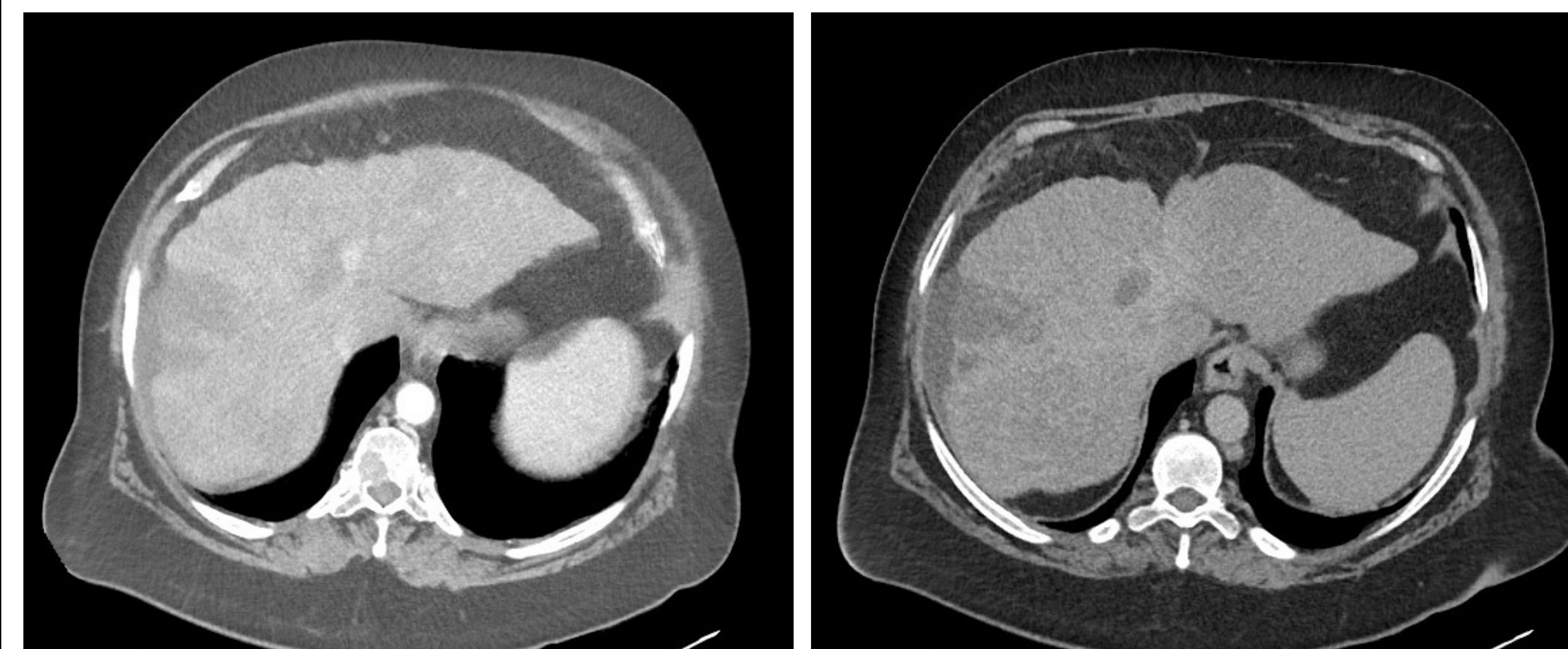


Figure 1. Mechanisms of hypercalcemia of malignancy

Figure 2. Triple Phase CT Abdomen/Pelvis: New liver lesions in multiple segments, enlarged LN in the porta hepatis, widespread spinal lytic lesions



Arterial Phase

Delayed Phase

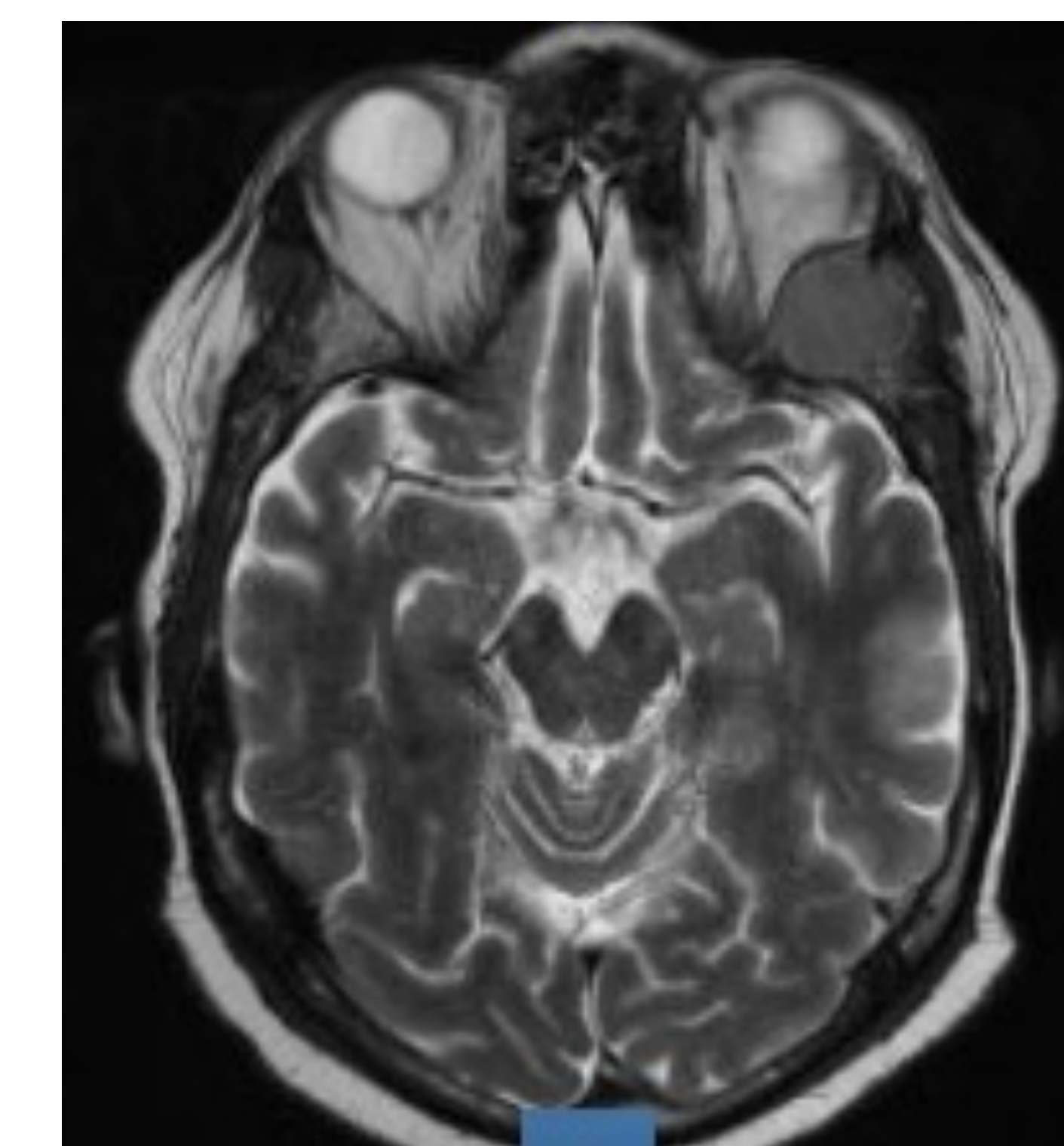


Figure 3. MRI brain/orbits w/w contrast: Lytic lesions throughout calvarium, skull base, and facial bones with a 3.4 cm x 2.4 cm left orbital wall mass

Discussion

Malignancy is the most common cause of hypercalcemia in the inpatient setting

PTHrP-Mediated Hypercalcemia (Humoral):

- Unknown mechanism – possible underlying paraneoplastic syndrome and downstream metabolic derangements
- Associated with a more advanced TNM stage and higher tumor burden in patients with HCC
- Study of 534 patients with HCC: 6.3% had humoral hypercalcemia and had worse Child-Pugh scores
- Study of 165 patients with HCC + humoral hypercalcemia: median survival time of 15 days

Conclusions

Patients with heavy disease burden of HCC may be at risk for developing malignancy associated hypercalcemia.

Given its association with higher mortality, early recognition of PTHrP-mediated hypercalcemia is essential to help providers expedite locoregional therapy and guide goals of care discussions.

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