

HYPERCALCEMIA OF MALIGNANCY

Grill V, Martin TJ. *Hypercalcemia of malignancy. Rev Endocr Metab Disord.* 2000 Nov;1(4):253-63.

Mundy GR, Guise TA. *Hypercalcemia of malignancy. Am J Med.* 1997 Aug;103(2):134-45.

Major P, et al. *Zoledronic acid is superior to pamidronate in the treatment of hypercalcemia of malignancy: a pooled analysis of two randomized, controlled clinical trials. J Clin Oncol.* 2001 Jan 15;19(2):558-67.

Take home points:

1. PTH-rP is the leading cause of hypercalcemia in malignancy (80% of cancer pt.'s with hypercalcemia have PTH-rP-related hypercalcemia).
2. Hypercalcemia in malignancy occurs abruptly, is severe, and portends a very poor prognosis (median survival only six weeks).
3. Zoledronic acid, a new bisphosphonate, is significantly more potent than older bisphosphonates and has been FDA-approved for treatment of hypercalcemia of malignancy.

Overview:

- Hypercalcemia is common in cancer (occurs in 10-20% of patients).
- There are three main mechanisms of hypercalcemia in malignancy:
 - PTH-rP related hypercalcemia
 - Osteolytic metastases
 - Tumor production of calcitriol
- Most common cancers associated with hypercalcemia are *breast cancer, lung cancer, and multiple myeloma.*
- Hypercalcemia in malignancy occurs abruptly, is severe, and portends a very poor prognosis (median survival only six weeks).

PTH-related protein (PTH-rP):

- PTH-rP is the leading cause of hypercalcemia in malignancy (80% of cancer pt.'s with hypercalcemia have PTH-rP-related hypercalcemia).
- Also known as HHM (humoral hypercalcemia of malignancy)
- PTH-rP is produced by a number of cells (neuroendocrine, epithelial, mesoderm-derived tissues)
- Can be associated with any solid tumor (most commonly breast cancer) and occasionally humoral malignancy.

Osteolytic metastases:

- Remember the pneumonic *BLT with a Kosher Pickle, Mustard & Mayo:*
Breast, **L**ung, **L**ymphoma, **T**hyroid, **K**idney, **P**rostate, **M**ultiple **M**yeloma
- Most commonly caused by breast cancer and NSCLC

Tumor production of calcitriol:

- Predominant cause of hypercalcemia in Hodgkin's disease and in 1/3 of patients with NHL
- Similar to mechanism of hypercalcemia in granulomatous disease
- Usually responds to corticosteroid administration

Treatment of hypercalcemia of malignancy

- Treat hypercalcemia with aggressive hydration (usually normal saline)
- Check urine sodium periodically (goal $U_{Na} > 20$)
- Once patient well hydrated, can give bisphosphonate – Zoledronic acid is a new bisphosphonate that is more potent and effective than older bisphosphonates. The patient must be well-hydrated ($> 2L/day$ urine output). Give zoledronic acid 4 mg over ≥ 15 minutes (IV infusion).
- Once the patient is adequately hydrate (see above), you can also give furosemide to further reduce the calcium.