# Moans and Groans

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## Elenor's fatigue

- Elenor, 63, presents to the ED with a two week history of fatigue and general malaise.
- On further questioning, she also complains of left-hip pain, but denies any history of trauma.
- She has a history of hypertension, hypercholesterolemia and remote breast cancer.
- Her medications include: enteric coated acetylsalicylic acid, hydrochlorothiazide and simvastatin.
- Her physical examination is remarkable for supraclavicular and axillary lymphadenopathy.
- Plain radiographic assessment of her hips and pelvis shows a mixed lytic/blastic lesion (Figure 1).

**For more on Elenor, turn to page 2.**

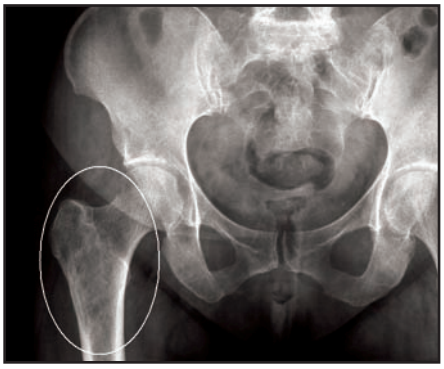

Figure 1. Mixed lytic-blastic lesion in right hip.

## Questions & Answers

### 1. What are the clinical features of hypercalcemia?

The clinical features of hypercalcemia are non-specific and variable. Patients with high calcium levels have decreased neuronal conduction, resulting in a range of symptoms from generalized weakness and fatigue to confusion or a decreased level of consciousness. ECG findings, such as shortened QT, first degree atrioventricular block and QRS widening are characteristic.

Patients are typically volume depleted and the increased calcium level impairs fluid reabsorption at the renal tubule, which further exacerbates hypovolemia. Not surprisingly, patients also complain of polyuria and polydipsia. Common, nonspecific symptoms include abdominal pain and constipation.

### 2. What are the common etiologies of hypercalcemia?

Hyperparathyroidism and malignancy account for over 90% of cases. Malignancy can cause hypercalcemia by increasing osteoclastic activity from metastatic disease, secretion of parathyroid hormone (PTH) related peptide (*i.e.,* paraneoplastic syndrome) or due to the malignancy itself (*i.e.,* multiple myeloma). Milk-alkali syndrome may occur in patients treated with calcium carbonate, such as those with osteoporosis or dyspepsia. Certain drugs like lithium and thiazide diuretics are also known offenders. Other causes of hypercalcemia include granulomatous disease (*i.e.,* sarcoidosis), vitamin D intoxication, Paget's disease and hyperthyroidism.

### 3. What are the complications of hypercalcemia?

Chronic hypercalcemia leads to the often quoted constellation: "moans, bones, stones and psychiatric overtones." These generally occur when calcium levels are chronically elevated and are more likely to appear in the setting of hyperparathyroidism. Abdominal complaints may include constipation (decreased smooth muscle tone), pancreatitis (activation of phospholipases) and peptic ulcer disease (increased gastrin release). Patients may complain of bony pain or tenderness related to significant bone resorption, fractures and calcium pyrophosphate deposition in joints. Nephrolithiasis is

**Table 1**

## Treatment options for hypercalcemia

| | Treatment |
|---|---|
| **Volume restoration** | • Isotonic saline |
| **Renal elimination** | • Saline diuresis: Furosemide 40 mg/day to 160 mg/day |
| **Reduction of osteoclastic activity** | • Bisphosphonates: Pamidronate 60 mg to 90 mg over 24 hours<br>• Plicamycin 25 mμ over four hours<br>• Calcitonin 4 IU/kg every 12 hours<br>• Hydrocortisone 200 mg/day to 300 mg/day<br>• Gallium nitrate 200 mg/m$^2$ over 24 hours |

common and exacerbated by ongoing relative volume depletion. Neuropsychiatric manifestations may be dramatic (*i.e.,* coma) or subtle (*i.e.,* irritability, personality change). Band keratopathy is also well-described.

## 4. *What investigations should be conducted in the setting of hypercalcemia?*

The history and physical examination should provide some direction to the etiology of elevated calcium. For example, in our patient with a history of breast cancer, metastatic disease is the most likely culprit. Acutely, relevant tests include a full electrolyte panel, complete blood count, creatinine, liver enzymes, amylase/lipase and ECG.

In an undifferentiated patient with hypercalcemia, laboratory investigations should delineate the basis of the underlying problem. It is important to obtain an ionized calcium level. While the amount of unbound, ionized calcium can theoretically be calculated based on the albumin level, this method is fraught with error. Once hypercalcemia is confirmed, the next step is to obtain a PTH level. If the level is high or inappropriately normal, a 24-hour urine calcium would be prudent. Low PTH should prompt close evaluation for malignant or other causes. Further tests might include alkaline phosphatase (bone lysis), serum protein electrophoresis (myeloma), chest X-ray (lung mass), calcitriol (elevated in granulomatous diseases) and thyroid stimulating hormone (hyperthyroidism).

## 5. *What are the management options for hypercalcemia?*

Most importantly, treat the underlying cause of hypercalcemia. In symptomatic or severe hypercalcemia (> 3.5 mmol/L), correct the volume status, enhance calcium elimination via the kidneys and decrease osteoclastic activity (Table 1). Dx

Additional references and resources available—contact *The Canadian Journal of Diangosis* at **diagnosis@sta.ca.**

## Back to Elenor

- Her total serum calcium is 3.3 mmol/L.
- Hydration therapy and bisphosphonates are initiated.
- She is admitted to hospital for ongoing treatment. Her symptoms of fatigue and malaise improve.
- As an in-patient, she is referred to both radiation and medical oncology to be evaluated for ongoing management of likely metastatic breast cancer.

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***This department covers selected points to avoid pitfalls and improve patient care by family physicians in the ED. Submissions and feedback can be sent to* diagnosis@sta.ca.**

Publication Mail Agreement No.: 40063348
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