Diagnostic approach to hypercalcemia

Elevated serum calcium

Check repeat (total calcium corrected for albumin or ionized calcium)

Hypercalcemia confirmed by repeat measurement

Measure intact PTH

Elevated

Primary hyperparathyroidism

Mid to upper normal or minimally elevated

Primary hyperparathyroidism likely, consider FIH

Low-normal or low

Non-PTH mediated hypercalcemia

Measure:
-PTHrP
-1,25-dihydroxyvitamin D
-25-hydroxyvitamin D

Is PTHrP elevated?

Yes

Is 1,25-dihydroxyvitamin D elevated?

Yes

Hormonal hypercalcemia of malignancy more likely

Lymphoma, granulomatous diseases (sarcoidosis, tuberculosis) more likely

No

Is 25-hydroxyvitamin D elevated?

Yes

Vitamin D intoxication more likely

Measure:
- S.P.E.P.
- S.G.E.P.
- Serum free light chain assay

Normal

Multiple myeloma

Abnormal

Assess for other diagnoses (vitamin A intoxication, hypervitaminosis A)


* Serum PTH typically ranging from 35 to 65 pg/mL in an assay whose normal range is 10 to 60 pg/mL.

† Serum 25-hydroxyvitamin D must be markedly elevated before hypercalcemia develops. Although the serum concentration of 25-hydroxyvitamin D at which hypercalcemia typically occurs is undefined, many experts define vitamin D intoxication as a value >150 ng/mL (374 nmol/L).

‡ Refer to UpToDate content on primary hyperparathyroidism.

§ Refer to UpToDate content on primary hyperparathyroidism and familial hypocalciuric hypercalcemia for details.

¶ Additional work-up is warranted to identify malignancy.