

Parathyroid Hormone-Related Peptide in Hypercalcemia

Indications for Ordering

Aid in the evaluation of unexplained hypercalcemia, particularly in suspected hypercalcemia of malignancy

Test Description

Quantitative high-performance liquid chromatography/tandem mass spectrometry

Tests to Consider

Primary test

[Parathyroid Hormone-Related Peptide \(PTHrP\) by LC-MS/MS, Plasma 2010677](#)

- Highly specific test for parathyroid hormone-related peptide (PTHrP)
- Aid in the diagnosis of and monitoring of treatment for hypercalcemia
- Amino (N)- and carboxy (C)-terminus PTHrP fragments, such as those produced by some patients with renal insufficiency, do not interfere with this assay

Related tests

- [Renal Function Panel 0020144](#)
- [Parathyroid Hormone, Intact with Calcium 0070172](#)
- [Calcium, Ionized, Serum 0020135](#)
- [Calcium, Urine 0020472](#)
- [Vitamin D, 1, 25-Dihydroxy 0080385](#)
- [Vitamin D, 25-Hydroxy 0080379](#)

Disease Overview

Prevalence – ~33% of cases of hypercalcemia are related to squamous cell carcinoma (often metastatic)

Symptoms – severe hypercalcemia is associated with acute signs and symptoms

- Fatigue, weakness, polyuria, polydipsia, dehydration
- Anorexia, nausea, vomiting, abdominal pain, constipation
- Mental status changes
- Bone pain

Physiology

- Hypercalcemia is a metabolic abnormality frequently related to primary hyperparathyroidism and cancer (hypercalcemia of malignancy)
- Causes of hypercalcemia of malignancy
 - Presence of humoral factors mimicking parathyroid hormone (PTH) action
 - Commonly, secretion of PTHrP by tumor tissue or tumor metastasis
 - Osteolytic or nonosteolytic activity related to bone metastases
 - Ectopic secretion of 1-alpha hydroxylase by tumor tissue
 - Impaired renal function caused by a tumor or a treatment
- Primary hyperparathyroidism and malignancy are responsible for >90% of cases of hypercalcemia
- Hypercalcemia of malignancy is relatively common in patients with cancer (>20% of cases)
- Most patients with symptoms of hypercalcemia of malignancy have
 - Elevated circulating PTHrP
 - Suppression of PTH due to elevated calcium concentrations
 - Some drugs may contribute to hypercalcemia (eg, thiazides, lithium)
- Common cancers associated with hypercalcemia include
 - Squamous cell lung cancer
 - Squamous cell head and neck cancers
 - Breast cancer
 - Multiple myeloma
 - T-cell lymphomas
 - Renal cell cancer
 - Ovarian cancer

Diagnostic issues

- For mild or moderate hypercalcemia, if evaluation for hyperparathyroidism is negative, consider measurement of PTHrP
- In addition to hypercalcemia, patients with elevated PTHrP concentrations may also have
 - Hypercalcuria
 - Hypophosphatemia
 - Hyperphosphaturia
 - Elevated serum alkaline phosphatase

Test Interpretation

Results

- Reference intervals for PTHrP
 - Females – 0.0-3.4 pmol/L
 - Males – 0.0-2.3 pmol/L
- Patients with hypercalcemia due to elevated PTHrP concentration often have low PTH concentration

Limitations

Results should not be interpreted as absolute evidence for the presence of hypercalcemia