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