Malignant phaeochromocytoma and hypercalcaemia

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Summary: We describe a case of hypercalcaemia secondary to recurrent malignant phaeochromocytoma. Parathyroid-related protein (PTHrp 1–86) immunoreactivity was identified in plasma and PTHrp was identified by immunocytochemistry in tumour tissue.

References

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This is a page from a publication, and the content is clearly formatted in a readable manner. The text is related to medical and scientific topics, specifically focusing on extramedullary hematopoiesis and its manifestations.

The image contains a page from a document discussing the clinical aspects of thalassemia and extramedullary hematopoiesis. The page includes references and a summary of a clinical case involving hypercalcaemia and the treatment outcomes. The text is written in a formal, academic style, typical of medical journals.

The page also includes a section on references, which lists various sources cited in the text. These references are likely scientific articles and books that provide further information on the topics discussed in the main text.

The content is structured logically, starting with an introduction to the conditions discussed, followed by case descriptions and treatment outcomes. The use of proper citation and referencing is evident, showing the thorough research involved in the preparation of this document.

Overall, the page provides comprehensive information on a medical condition, its clinical aspects, and the outcomes of treatment, making it a valuable resource for those interested in the field of hematology and thalassemia.
Introduction

The association of pheochromocytoma with hypercalcaemia is infrequent but well documented, and usually (although not always) occurs with multiple endocrine adenomatosis type II. Hypercalcaemia in this context has been attributed to either stimulation of bone resorption, excess parathyroid hormone (PTH) production secondary to catecholamines or increased production of PTH
d. or a PTH-like humoral agent by the tumour.

In 1987, a hypercalcaemic factor with potent PTH-like bioactivity, structurally homologous with PTH at its NH3-terminus was isolated from tumours and cancer cell lines. This factor, called PTH-related protein (PTHRp) is now thought to be an important humoral mediator of hypercalcaemia in patients with solid tumours. Thus mRNA for PTHrp has been identified in tumours associated with humoral hypercalcaemia of malignancy and PTHrp has been localized in tumour tissue by immunohistochemistry. Recently plasma levels of PTHrp have been shown to be increased in a high proportion of patients with cancer-associated hypercalcaemia.

The recent demonstration of PTHrp mRNA and PTHrp immunoreactivity in a benign pheochromocytoma prompted us to report our own case of hypercalcaemia secondary to PTHrp in recurrent malignant pheochromocytoma.

Case report

A 68 year old retired taxi driver was first noted to have hypertension in 1978, easily controlled with a modest dose of metoprolol and chlorthalidone. Routine measurement of catecholamines prior to entry into a clinical trial revealed noradrenaline concentrations of 17.1 nmol/l supine and 18.1 nmol/l standing (reference range 0.5-3.5 nmol/l supine). Urinary vanillylmandelic acid (VMA) was 80 µmol/24 hours (reference range 9-36). Computed tomographic (CT) scan confirmed the presence of a 7 cm left pheochromocytoma. Surgical excision of the tumour occurred without incident and serum catecholamines returned to normal. Subsequently he was treated with a combination of enalapril and bendrofluazide which kept pressures in the range of 140/80 mmHg, pulse 72 supine, 118/80 mmHg, pulse 92 standing.

Eight years following resection of his original tumour, he presented with symptoms of intermittent constipation, malaise and worsening memory. He was found to be anaemic (haemoglobin 8.0 g/dl normocytic and normochromic), hypercalcaemic (calcium 3.24 mmol/l, albumin 36 g/l) and to have an erythrocyte sedimentation rate (ESR) of 128 mm/hour. An abdominal ultrasound and CT scan located a left para-aortic mass thought likely to be recurrent pheochromocytoma.

The hypercalcaemia was treated with a single intravenous infusion of pamidronate (15 mg) with some improvement in his mental state but investigations including parathyroid ultrasound, technetium bone scan, serum parathyroid hormone < 1.5 pmol/l (reference range 1-5), serum 1, 25-OH vitamin D 15 ng/ml (reference range 3-30), calcitonin 0.08 µg/ml (reference range < 0.08) and myeloma screen were negative. Plasma PTHrp 1-86, measured by a sensitive two-site immunometric assay, was raised (0.7 pmol/l (reference range < 0.25)). One month following treatment with pamidronate, the serum calcium began to rise again (calcium 2.82 mmol/l, albumin 36 g/l) but not to levels requiring further treatment.

Although the para-aortic mass was felt most likely to be a recurrent pheochromocytoma, it was difficult to prove it. The patient was normotensive off antihypertensive treatment, urinary VMA values were only borderline, the MIBG scan was normal and a CT-guided needle biopsy of the para-aortic mass did not yield a histological diagnosis. Laparotomy, however, revealed malignant para-aortic lymphadenopathy, the histology of which was pheochromocytoma, very similar to histology obtained 8 years earlier. Immunohistochemical staining of the laparotomy tumour specimen using a rabbit antiserum to PTHrp 37-67 was positive.

Only immediately preoperatively (and postoperatively), did he become hypertensive requiring intravenous labetalol. Plasma noradrenaline (12.6 pmol/ml (0.5-3.5)) and urinary VMA (70 µmol/24 hours (9-36)) was elevated but plasma adrenaline remained normal – characteristic of a non-adrenal source of catecholamine. Blood pressure returned to normal without treatment 5 days later. He subsequently died of bronchopneumonia one month following laparotomy.

Discussion

This case illustrates several interesting aspects of pheochromocytoma. Long-term recurrence is well described up to 30 years but continues to surprise. Recurrence as a malignant tumour is less common and has a less favourable prognosis. Episodic hypertension is described as commonly as 50% and in our patient was only present immediately pre- and post-operatively. This hypertension was easily controlled with relatively small doses of labetalol. Presentation with hypercalcaemia is uncommon but well described, although only in non-malignant cases. Serum and tissue identification of PTHrp makes it likely that PTHrp was the cause of hypercalcaemia in this patient.
References


