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Case Report

Thymic hyperplasia due to excess growth hormone stimulation: A case report☆

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ABSTRACT

Growth hormone has a strong role in stimulation of the thymus. We report a case of thymic hyperplasia due to excess endogenous growth hormone in the setting of acromegaly. Acromegaly often presents with systemic manifestations that may be confused with a systemic hematologic malignancy or infection, especially if an anterior mediastinal mass is present but unrecognized as a benign thymic hyperplasia. It is important for radiologists to be aware of this association between growth hormone and thymic stimulation because it may increase confidence diagnosing thymic hyperplasia in this setting, and avoid unnecessary mediastinal biopsy or surgery.

Introduction

The thymus is a target organ for growth hormone (GH), although it's effects may be underappreciated by radiologists because they are rarely visualized on imaging. Thymic hyperplasia may be induced by endogenous growth hormone excess, such as acromegaly, or exogenous growth hormone administered in cases of immunodeficiency or growth hormone deficiency. Here we report a case of thymic hyperplasia in a patient presenting with a complex constellation of symptoms mimicking malignancy and infection, but ultimately found to be due to a GH-secreting pituitary macroadenoma. To our knowledge, this is the second reported case of thymic hyperplasia due to acromegaly.

Case Report

A 37-year old previously healthy male was in his usual state of health when he developed a complex constellation of symptoms with sore neck, hoarse voice, coughing, arthralgias, weight loss, swollen neck glands, fatigue, headache, night sweats, enlargement of his right testicle, and trouble with comprehension and memory.

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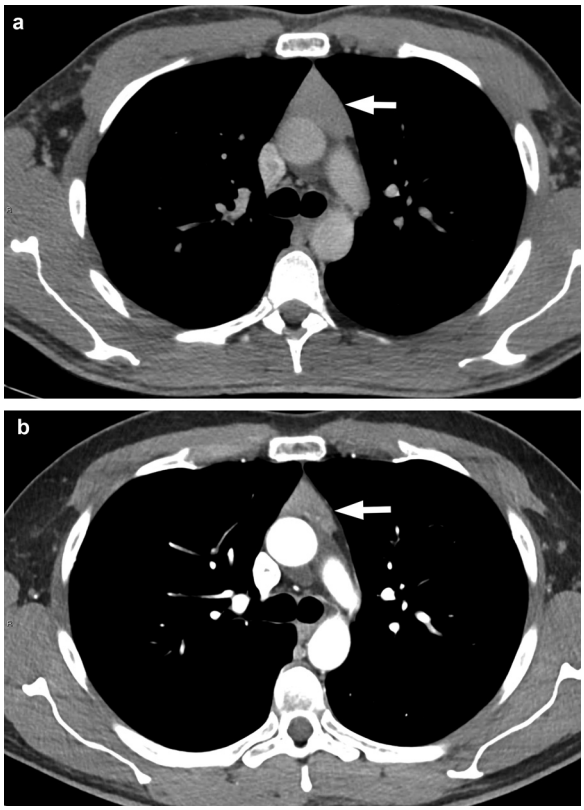

Fig. 1 – (A) Contrast-enhanced CT of the chest at the time of presentation showed an anterior mediastinal mass (white arrow), initially read as possible lymphoma or thymic mass at outside hospital. (B) Contrast-enhanced CT of the chest performed 4 months following resection of the GH-secreting pituitary macroadenoma showed decreased size of this triangular-shaped well-demarcated anterior mediastinal mass (white arrow), consistent with decreasing thymic hyperplasia.

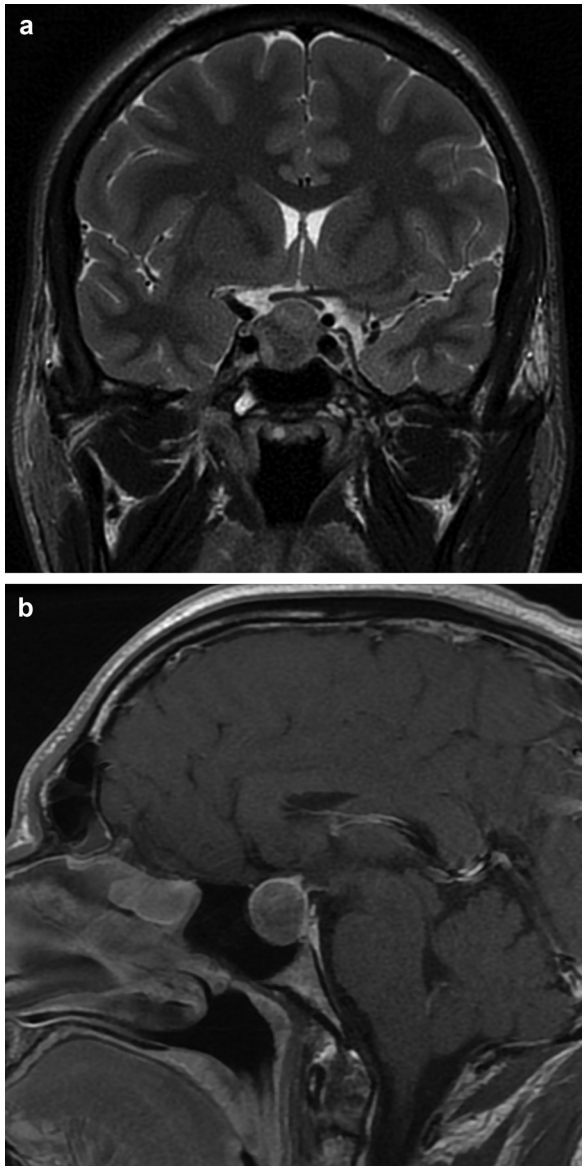

Fig. 2 – (A) Coronal T2-weighted and (B) sagittal post-contrast T1-weight imaging of the brain showed a 2 cm sellar mass with suprasellar extension, consistent with a pituitary macroadenoma.

Infectious disease testing including Covid-19, HIV, mononucleosis, and Lymes disease were all negative. CT of the chest, abdomen and pelvis revealed an anterior mediastinal mass, which was initially read as suspicious for lymphoma or thymic mass at an outside hospital (Fig. 1A). Cervical lymph node biopsy was negative for malignancy. MR of the brain was obtained due to the headaches and difficulties with mentation, and showed a large 2 cm pituitary mass with suprasellar extension (Fig. 2). Laboratory evaluation showed markedly elevated IGF-1 of 623 ng/ml (normal <331 ng/mL), and elevated Growth Hormone of 17.7 ng/mL (normal <7.1 ng/mL). Prolactin was also elevated at 85.2 ng/mL (normal <18.0 ng/mL). These findings were consistent with acromegaly due to a growth-home secreting pituitary macroadenoma.

The patient underwent transphenoidal resection of the pituitary macroadenoma nine months after initial presentation. Pathology of the surgical specimen showed a mammosomatotroph pituitary adenoma. Following surgical resection of the pituitary adenoma, his Growth Hormone dropped to a nadir of 0.7 ng/mL.

Follow-up CT of the chest obtained 4 months following resection of the pituitary macroadenoma showed an anterior mediastinal mass with triangular shape and smooth contours (Fig. 1B). The mass had decreased in size since initial imaging; volumetric segmentation performed on the CT showed that the mass had decreased in volume from 53 cc to 35 cc. Cinematic rendering of the mass from the CT data set provided a photorealistic evaluation of the mass, nicely demonstrating the internal architecture with interspersed fat and soft tissue elements, and non-invasive relationship with the adjacent anatomy (Fig. 3). MRI of the mediastinal mass with chemical shift imaging showed the mass contained microscopic fat, with a signal intensity index of 67% consistent with benign thymic hyperplasia (Fig. 4) [1]. In summary, the imaging

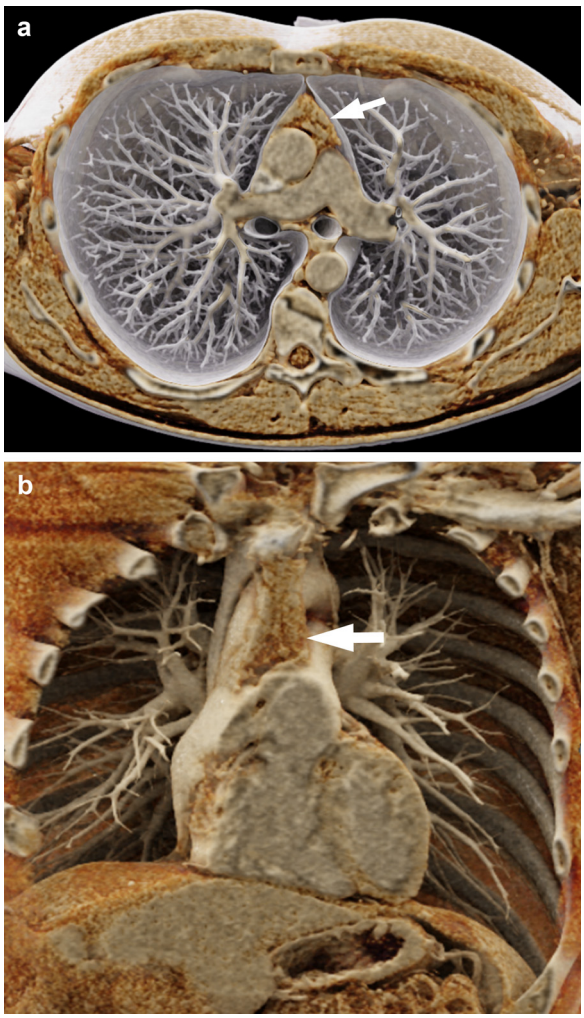

Fig. 3 – (A) Axial and (B) coronal cinematic rendered CT show triangular shaped anterior mediastinal mass (white arrow) with smooth contours and internal architecture consistent with thymic hyperplasia. The additional detail provided by the cinematic rendering provides depth perception to visualize the internal architecture as well as excellent definition of adjacent vascular and pulmonary anatomy.

findings of this mass were consistent with thymic hyperplasia, and the thymic hyperplasia decreased following treatment of his acromegaly.

Discussion

Here we present a case of thymic hyperplasia due to excess growth hormone stimulation in the setting of acromegaly. Thymic hyperplasia initially simulated a thymic tumor or lymphoma in the setting of the patient's complex constellation of symptoms, however, the shape and texture of the thymus reinforced the diagnosis of thymic hyperplasia.

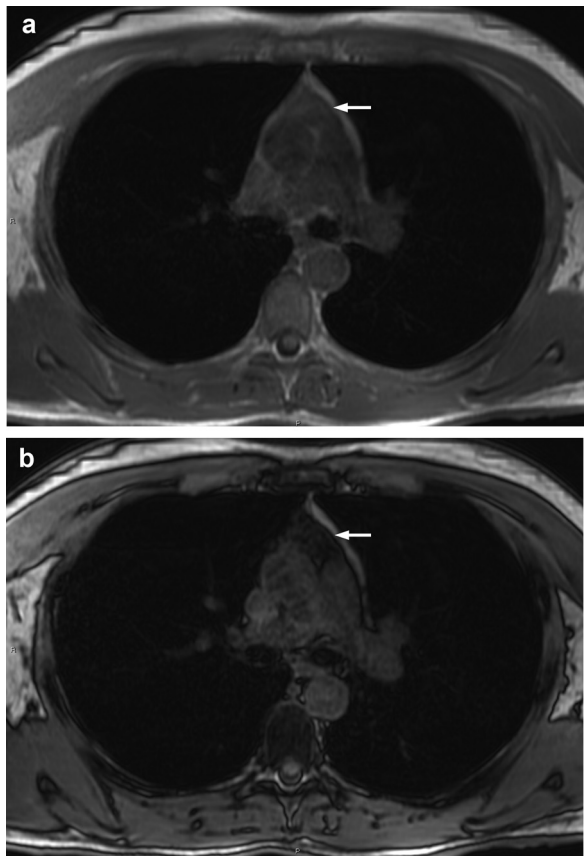

Fig. 4 – Axial dual-echo imaging shows clear signal drop-out in the anterior mediastinal mass (white arrow) from the (A) in-phase image to the (B) out-of-phase image. Calculated Signal Intensity Index using ROIs placed in the mass was 67%, consistent with thymic hyperplasia.

Acromegaly is an uncommon disorder of excess growth hormone production usually caused by a pituitary adenoma. Acromegaly has a prevalence of 60 cases per million [2]. Most cases of acromegaly are caused by benign somatotroph pituitary adenomas, and of those 70% are macroadenomas at the time of presentation [2]. Manifestations of acromegaly may be due multisystemic effects from growth hormone excess and associated endocrine abnormalities, or due to direct mass effect from the pituitary adenoma. While acral overgrowth and coarsened facial features are classic for acromegaly, they are often insidious onset and not the reason for presentation [3]. Presentation is more often due to the systemic complications like those in our patient who complained of neuropsychiatric effects, arthralgias, hyperhydrosis, and respiratory complications like upper airway obstruction [3].

The effect of GH excess on the thymus is of particular interest in our case. The thymus is a known target organ for GH [4]. Thymocytes and thymic epithelial cells express GH receptors. In vitro studies show that GH increases thymic epithelial cell proliferation and assists in stimulation of thymocyte proliferation. In vivo animal studies show that transgenic mice with overexpression of GH or GH-release hormone

demonstrate thymic overgrowth [4]. For these reasons, GH has been explored as a potential therapy to induce T-cell production in the setting of immunodeficiency. For example, in a small randomized prospective study of HIV-1 infected adults, administration of GH induced increased thymic mass and increased circulating CD4+ T-cells [5,6].

To our knowledge, this is only the second reported case of thymic hyperplasia in the setting of acromegaly [7]. Thymic hyperplasia has also been reported in a pediatric patient receiving GH replacement therapy [8]. Our patient displayed classic imaging features of thymic hyperplasia on CT and MRI. It is most likely that our patient's thymic hyperplasia was due to GH excess given the evidence of the effect of GH on the thymus, and our patient's decreasing thymic hyperplasia following treatment of his acromegaly.

Conclusion

Endogenous or exogenous growth hormone excess may cause thymic hyperplasia. Knowledge of this association may increase radiologists' confidence in identifying thymic hyperplasia in this clinical setting in which a patient's presentation may mimic systemic malignancy or infection, and help avoid unnecessary additional testing or biopsy.

Patient Consent Statement

The IRB at our institution does not require IRB approval of patient consent for case reports. No protected health information is shown in this case report.

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