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CASE REPORT

# Ectopic mediastinal parathyroid adenoma: a cause of acute pancreatitis

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**Abstract** A 38-year-old male was admitted to our hospital with epigastric pain, and he was confirmed to have acute exudative pancreatitis. After the episode of acute pancreatitis subsided, laboratory investigation revealed increased serum calcium (12.0 mg/dl), decreased serum phosphorus (2.7 mg/dl), and increased serum parathyroid hormone (intact) levels (131 pg/ml). A computed tomography (CT) scan of the neck did not reveal any mass lesions in the parathyroid gland. However, $^{99m}$Tc sestamibi scintigraphy revealed that there was one functioning parathyroid gland in the upper mediastinum. Combined $^{99m}$Tc sestamibi scintigraphy and CT scan confirmed the diagnosis of primary hyperparathyroidism in the mediastinum. Microscopic examination revealed the presence of a parathyroid adenoma ($1.3 \times 0.4$ cm$^2$) adjacent to the atrophic parathyroid gland in right thymus gland. We report the case of a patient diagnosed with primary hyperparathyroidism due to an ectopic mediastinal parathyroid adenoma. An ectopic mediastinal parathyroid adenoma may manifest as an episode of acute pancreatitis. Preoperative investigation to determine the exact location of an adenoma should include two types of imaging studies, preferably $^{99m}$Tc sestamibi scintigraphy and CT of the neck and chest.

**Keywords** Primary hyperparathyroidism · Pancreatitis · $^{99m}$Tc sestamibi scintigraphy · Computed tomography

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## Introduction

Primary hyperparathyroidism (PHP) is characterized by autonomous production of parathyroid hormone resulting in hypercalcemia. This is a common disease, occurring in approximately 1% of the adult population and approximately 2% of the population older than 55 years [1]. It occurs 2–3 times more frequently in women than in men. Adenomas were located in the neck in most cases. However, the incidence of ectopic parathyroid glands in healthy individuals was reported to be approximately 6% [2]. The most common ectopic location of the inferior parathyroid gland is within the thymic capsule or the superior mediastinum [3].

Primary hyperparathyroidism patients present with symptoms, such as urolithiasis, bone pain, and pathologic fractures, as well as nonspecific symptoms, such as depression, lethargy, and vague aches and pains. Since the advent of multichannel biochemical screening, however, patients frequently exhibit no symptoms after being incidentally detected with hypercalcemia by routine laboratory screening [4]. Primary hyperparathyroidism leads to hypercalcemia and subsequently renal-stone formation,

decreased bone mineral density, and gastric or duodenal ulcerations. Less often, PHP leads to acute pancreatitis. The occurrence of acute pancreatitis secondary to hypercalcemia is rare [5–7]. Here, we report a case of acute pancreatitis that occurred secondary to hypercalcemia due to an ectopic parathyroid adenoma in the mediastinum.

## Case report

A 38-year-old male was admitted with epigastric pain in August 2008. Blood tests revealed leukocytosis (11,500/$mm^3$) and increased serum levels of amylase (571 IU/l). A computed tomography (CT) scan of the abdomen confirmed the diagnosis of acute exudative pancreatitis. The patient was a chronic alcoholic, and he consumed 2 l of beer everyday. He had a history of urolithiasis. His family history was unremarkable in terms of any cancers or endocrine or renal disorders. After the acute pancreatitis episode subsided, laboratory investigation revealed increased serum calcium (12.0 mg/dl). He was referred to our endocrinology department because of this hypercalcemia. Other laboratory tests revealed decreased serum phosphorus (2.7 mg/dl), increased serum parathyroid hormone (intact) levels (131 pg/ml), and normal levels of serum-free triiodothyronine, free thyroxine, thyroid stimulating hormone, and intact parathyroid hormone-related protein. The bone mineral density, as assessed by double X-ray absorptiometry, was slightly decreased (T score: −1.1 at the L2 level). Ultrasonography of the thyroid and neck revealed that the appearance of the thyroid gland was normal, and no suspicious prevertebral masses were observed. A CT scan of the thorax and neck revealed a small mediastinal mass in close proximity to the thymus (Fig. 1). $^{99m}$Tc sestamibi scintigraphy revealed that there was one functioning parathyroid gland in the upper mediastinum. Combined $^{99m}$Tc sestamibi scintigraphy and CT confirmed the diagnosis of PHP in the mediastinum (Fig. 1).

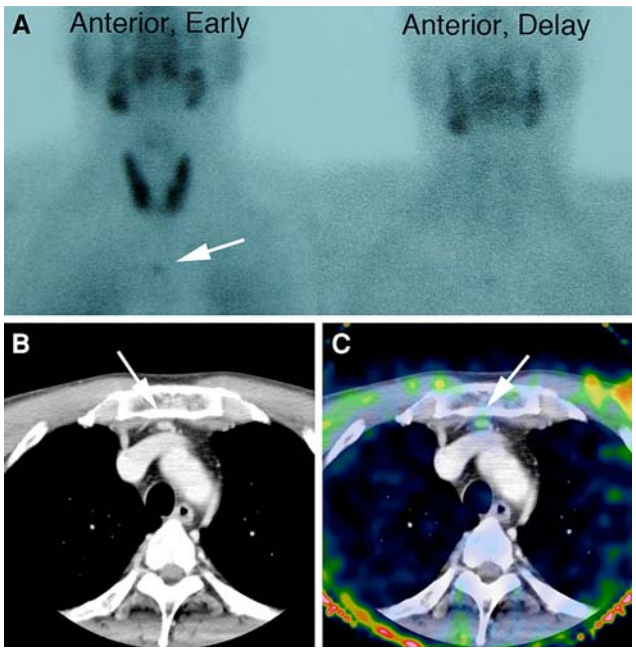


**Fig. 1** Localization of the functioning parathyroid tissue. **a** $^{99m}$Tc sestamibi scintigraphy shows the accumulation of parathyroid tissue in the upper mediastinum. **b** CT scan shows a mass in the upper anterior mediastinum. **c** Combined $^{99m}$Tc-sestamibi and CT scan reveal the ectopic functioning parathyroid tissue in the mediastinum

After diagnosis of PHP, the mediastinal mass and thymus glands were resected. The calcium and parathyroid hormone levels in the serum returned to normal within 3 h of completing the operation. Slight serum hypocalcaemia was observed over the subsequent days, and the patient received oral therapy with calcium and 1α,25-(OH)2 vitamin D3 to restore the serum calcium level to a value within the normal range. Microscopic examination revealed the presence of a parathyroid adenoma (1.3 × 0.4 $cm^2$) adjacent to the atrophic parathyroid gland in right thymus gland. Another atrophic parathyroid gland was identified in the right thymus gland (Fig. 2).

## Discussion

Acute pancreatitis secondary to hypercalcemia is an uncommon presentation of PHP [5]. Acute pancreatitis was reported to be associated with PHP in 1–7% of cases in a large series of cases. Sporadically reported cases of acute pancreatitis induced by PHP suggest that the relationship between the two clinical conditions is not incidental [8–10]. Carnaille et al. found significantly elevated serum calcium levels to be of major importance in the development of pancreatitis in patients with PHP [11]. However, more recent report indicated that the estimated hazard ratio of acute pancreatitis for PHP relative to the control subjects was 0.84 ($P = 0.89$) [12]. Primary hyperparathyroidism should be suspected if increased levels of serum calcium are detected during the first episode of acute pancreatitis. In patients with a history of alcohol consumption (as in the present case), where the main cause of an episode of acute pancreatitis is long-term alcohol intake, PHP can go undiagnosed if serum calcium levels are within the normal range.

The parathyroid glands develop during the sixth week of gestation. The superior glands develop from the fourth branchial pouch, along with the ultimobranchial bodies, which eventually develop into the C cells of the thyroid gland [13]. Inferior parathyroid glands develop from the third branchial pouch, along with the thymus. A common

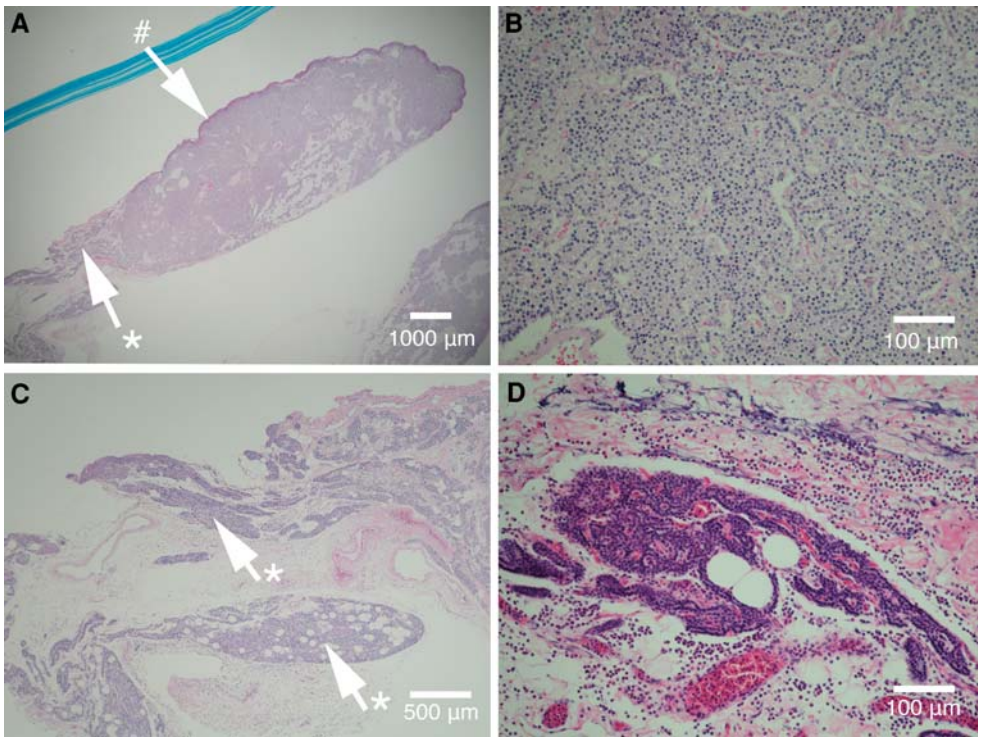


**Fig. 2** Histology of the parathyroid adenoma. **a** The tumor is surrounded by connective tissue (#) and an atrophic parathyroid gland (*). **b** The tumor cells with vacuolated cytoplasm and round nuclei show solid sheet to trabecular and acinar pattern. **c** The atrophic parathyroid gland is located adjacent to the adenoma (*). **d** Another atrophic parathyroid in the right thymus gland

cause of persistent PHP is an unidentified parathyroid gland or glands at ectopicpositions [1]. The incidence of ectopic parathyroid glands in healthy individuals is reported to be approximately 6% [1]. Previous reports have indicated that 5–10% of the parathyroid glands were located in the posterior mediastinum, 20% were substernally located within the thymic tissue in the anterior mediastinum (1–2%), 1% of the glands were located in the carotid sheath, and 5% were located within the thyroid gland [14]. Other rare sites of ectopic parathyroid tissue occurrence are the vagus nerve sheath, thyrothymic ligament, and pericardium [15]. Parathyroid glands have recently been identified with increasing frequency in the visceral compartment of the mediastinum (aortopulmonary window and right pulmonary artery, in close proximity to the tracheal bifurcation) because of the improvement in imaging techniques ($^{99m}$Tc sestamibi scintigraphy). Currently, the frequency of ectopic parathyroid tissue occurrence is uncertain [14].

Regardless of the technique used, the sensitivity of sestamibi scanning as a single modality for identifying adenomas was reported to be 54–100%, with a sensitivity of 80–90% in most cases. The sensitivity of ultrasound alone as a single modality for the identification of adenomas was reported to be of 27–89%. In several series of cases, a combined sensitivity in the range 78–96% was reported [4, 16]. When localizing studies are undertaken, a sestamibi scan is frequently used in conjunction with some type of anatomic imaging, either ultrasound, CT, or magnetic resonance imaging (MRI). Of these anatomic imaging modalities, the use of ultrasound has the most advantages as it does not involve ionizing radiation and is the least expensive; furthermore, it is the most frequently used imaging modality in this setting. It is, however, highly user dependant and does not permit retromanubrial or mediastinal visualization. Invasive localization studies, such as angiography and the selective venous PTH assay, are now rarely used because of the high success rate of noninvasive approaches. Recently, several studies have reported the use of single-photon emission computed tomography/CT for localization studies in patients with previously untreated PHP. The results were variable, with some studies demonstrating improved sensitivity and a positive predictive value, resulting in a change in therapeutic management, whereas others reported a limited clinical value when evaluating patients with previously untreated PHP [17].

There are three mechanisms described for the development of acute pancreatitis in patients with PHP. One explanation is that hypercalcemia from PHP leads to de novo activation of trypsinogen to trypsin, resulting in autodigestion of the pancreas and subsequent pancreatitis. Another possibility is that hypercalcemia leads to formation of pancreatic calculi, ductal obstruction, and subsequent attacks of acute or chronic pancreatitis. Finally, factors other than calcium, such as genetic risk factors, may predispose patients with PHP to acute pancreatitis [18]. In our case, the patient is a chronic alcoholic. Alcohol consumption has long been associated with cell damage, and it is thought that it is involved in approximately 40% of cases

of acute pancreatitis. The risk of developing alcoholic pancreatitis increases in a linear fashion with increasing alcoholic consumption, indicating that there are constant toxic effects of alcohol on the gland [19]. Alcohol abuse may be one of the trigger factors in this patient. In this patient, there was little change in bone mineral density. Recent report indicated that bone disease was seen in significantly more cases (81%) in patients with PHP without chronic pancreatitis (CP), when compared to PHP group (44%). Probably, patients with CP have abdominal pain and hence seek medical evaluation early, during which parathyroid adenoma is detected and excised [20]. This may be a reason to prevent the progression of the disease to the bones in our case.

Here, we reported the case of a patient diagnosed with PHP due to an ectopic mediastinal parathyroid adenoma. An ectopic mediastinal parathyroid adenoma may manifest as an episode of acute pancreatitis. Preoperative investigation to determine the exact location of an adenoma should include two imaging studies, preferably $^{99m}$Tc sestamibi scintigraphy and a CT scan of the neck and chest.

## References


1. G.B. Melton, H. Somervell, K.P. Friedman, M.A. Zeiger, C.A. Cahid, Nucl. Med. Commun. **26**, 633–638 (2005)
2. N.B. Ravipati, E.C. McLemore, R.T. Schlinkert, R. Argueta, Am. J. Surg. **195**, 799–802 (2008)
3. F.E. Nwariaku, W.H. Snyder, S.H. Burkey, L. Watumull, D. Mathews, World J. Surg. **29**, 491–494 (2005)
4. C.R. McHenry, J. Am. Coll. Surg. **195**, 364–371 (2002)
5. J.P. Bilezikian, S.J. Silverberg, N. Engl. J. Med. **350**, 1746–1751 (2004)
6. J. Egea Valenzuela, E. Belchí Segura, A. Sánchez Torres, F. Carballo Alvarez, Rev. Esp. Enferm. Dig. **101**, 65–69 (2009)
7. U.P. Phatak, A.J. Park, S.U. Latif, G. Bultron, D.S. Pashankar, S.Z. Husain, J. Pediatr. Endocrinol. Metab. **21**, 1191–1194 (2008)
8. A. Agarwal, R.K. George, S.K. Gupta, S.K. Mishra, Indian J. Gastroenterol. **22**, 224–225 (2003)
9. J.J. Shepherd, Aust. N. Z. J. Surg. **66**, 85–87 (1996)
10. J.J. Jacob, M. John, N. Thomas, A. Chacko, R. Cherian, B. Selvan, A. Nair, M. Seshadri, Aust. N. Z. J. Surg. **76**, 740–744 (2006)
11. B. Carnaille, C. Oudar, F. Pattou, F. Combamale, J. Rocha, C. Proye, Aust. N. Z. J. Surg. **68**, 117–119 (1998)
12. T.K. Khoo, S.S. Vege, H.S. Abu-Lebdeh, E. Ryu, S. Nadeem, R.A. Wermers, J. Clin. Endocrinol. Metab. **94**, 2115–2118 (2009)
13. B.L. Judson, A.R. Shaha, J. Nucl. Med. **49**, 1813–1818 (2008)
14. M.L. Richards, A.G. Bondeson, N.W. Thompson, in *General Thoracic Surgery*, ed. by T.W. Shields, J. LoCicero III, R.B. Ponn (Lippincott Williams and Wilkins, Philadelphia, 2000)
15. B.D. Nguyen, Radiographics **19**, 601–614 (1999)
16. K. Friedman, H. Somervell, P. Patel, G.B. Melton, E. Garrett-Mayer, A.P. Dackiw, A.C. Civelek, M.A. Zeiger, Surgery **136**, 1199–1204 (2004)
17. C.J. Palestro, M.B. Tomas, G.G. Tronco, Semin. Nucl. Med. **35**, 266–276 (2005)
18. A. Vonlaufen, J.S. Wilson, M.V. Apte, J. Gastroenterol. Hepatol. **23**, 1339–1348 (2008)
19. A. González, J.A. Pariente, G.M. Salido, Alcohol **42**, 565–573 (2008)
20. S.K. Bhadada, H.P. Udawat, A. Bhansali, S.S. Rana, S.K. Sinha, D.K. Bhasin, J. Gastroenterol. Hepatol. **23**, 959–964 (2008)