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Collective Ectopia of All Four Ectopic Parathyroid Adenomas Clustered in the Right Cervicomediastinum: A Rare Case Report

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Case Report

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Abstract

Introduction:

Primary hyperparathyroidism (PHPT) typically results from a solitary parathyroid adenoma. Multiple parathyroid adenomas are rare and four parathyroid adenomas clustered in a single ectopic region has never been reported.

Case presentation:

A 32-year-old male patient with ongoing PHPT after resection of a right inferior parathyroid adenoma was referred to our center. Upon admission, reoperative exploration revealed no parathyroid tissue in any of the four normal anatomical locations. Instead, three ectopic parathyroid adenomas were discovered as a single, continuous cluster in the medial side of the right carotid sheath at the thoracic inlet level, extending into the superior posterior mediastinum. After complete excision of these three lesions, the patient developed permanent hypoparathyroidism.

Conclusion:

This first report of collective ectopia of all four parathyroid adenomas in the cervicomediastinum, suggesting an extreme failure of embryonic migration. Surgeons should be aware that an ectopic adenoma may represent only the tip of a contiguous iceberg.

Introduction

Primary hyperparathyroidism (PHPT) most commonly results from a solitary parathyroid adenoma, comprising about 80–85% of cases.[1] Precise surgical identification and removal of the lesion is the most effective way to achieve biochemical cure.[2] However, surgical failure occurs in 3–5% of initial explorations, and most of these failures are attributable to ectopic gland location or multiglandular disease.[3] Ectopic parathyroids, resulting from aberrant embryonic migration, are found in 6–22% of persistent PHPT, with common locations including the thymus, anterior mediastinum, carotid sheath and retroesophageal space.[2, 4] Multiple gland disease—such as double adenomas (2–15% of cases) or hyperplasia—poses an additional challenge, as incomplete resection is more likely.[5]

However, the simultaneous occurrence of extreme ectopia and multiglandular disease is exceptionally rare. To our knowledge, the presence of all four parathyroid adenomas forming a single continuous cluster in an ectopic location has never been reported. In this report, we present an unprecedented case of collective ectopia of all four parathyroid adenomas as a continuous mass from the right lower neck into the superior posterior mediastinum. We propose a potential embryologic mechanism for this extreme migration defect and discuss its surgical implications for reoperative parathyroidectomy.

Case presentation

A male patient aged 32 years was admitted to an outside institution for hypertension, where further evaluation led to an incidental diagnosis of primary hyperparathyroidism secondary to a parathyroid adenoma. Laboratory and imaging findings showed elevated PTH (459.31 pg/mL) (SI: 48.67 pmol/L) (reference range: 12–88 pg/mL [1.27–9.33 pmol/L]), and serum calcium (14.24 mg/dL) (SI: 3.56 mmol/L) (reference range: 8.45–10.08 mg/dL [2.11–2.52 mmol/L]), as well as renal stones, bone loss, and osteitis fibrosa cystica. The patient denied any discomfort or family history of endocrine disorders. Preoperative single photon emission CT (SPECT) and Tc-99m sestamibi imaging (MIBI) demonstrated a clumped tracer concentration located posteroinferior to the inferior pole of the right thyroid lobe, extending into the mediastinum (Fig. 1). Therefore, a unilateral cervical exploration was performed, and a 3cm×1.8cm adenoma located in right inferior parathyroid was easily identified and resected. However, the postoperative levels of PTH (233.35 pg/mL) (SI: 24.74 pmol/L) and serum calcium (10.96 mg/dL) (SI: 2.74 mmol/L) remained elevated. Due to persistent elevated postoperative PTH and serum calcium levels, the patient was referred to our hospital after 4 months.

Upon referral, we conducted a comprehensive re-evaluation. Cervical ultrasound revealed that there were hypoechoic lesions located posterior to the lower poles of bilateral thyroid gland. MIBI demonstrated an area of high tracer uptake in the inferior posterior to the lower right thyroid gland extending to the superior posterior mediastinum (Fig. 2). To rule out multiple neuroendocrine tumor disease, adrenal function assessment, sex hormone, adrenal ultrasound and CT scan, pituitary MRI, thyroid ultrasound, calcitonin and CEA levels, genetic testing (MEN1) were conducted, but without any positive findings. Consequently, the patient underwent a second bilateral cervical exploration via the initial cervical incision. Intraoperatively, in the expected anatomical regions of bilateral superior parathyroid glands and the left inferior parathyroid gland, no parathyroid gland was detected. After cautiously exploring the area, three enlarged parathyroid glands were discovered. Crucially, these three lesions formed a single, continuous, grape-like cluster that originated from the region medial to the right carotid sheath at the thoracic inlet level, passed beyond the posterior aspect of the brachiocephalic artery and extended into the superior posterior mediastinum (Fig. 3). Three lesions were removed successfully and confirmed the diagnosis of ectopic parathyroid adenoma by postoperative pathology.

On postoperative day 1, PTH dropped to 6.25 pg/mL (SI: 0.66 pmol/L) and serum calcium decreased to 8.84 mg/dL (SI: 2.21 mmol/L). During six months of follow-up, the patient developed permanent hypoparathyroidism with low levels of PTH and serum calcium (Fig. 4). After discharge, the patient developed recurrent cramping episodes, which were relieved by calcium administration via the intravenous route. At six months after reoperation, PTH levels remained low, suggesting the development of permanent hypoparathyroidism.

From the patient’s perspective, persistent postoperative elevation of parathyroid hormone and serum calcium after primary resection left his underlying disease unresolved, causing significant anxiety amid continuous risks of skeletal and renal damage. He expresses sincere and profound gratitude to our medical team for accurately recognizing his rare condition of clustered ectopic parathyroid lesions, which was undiagnosed in the initial surgery. Through meticulous exploration and precise revision

surgery, the residual ectopic adenoma lesions were completely resected. The patient experienced an immediate substantial decline in postoperative PTH and serum calcium levels on the first day after reoperation. Though he ultimately developed permanent hypoparathyroidism requiring long-term calcium supplementation during follow-up, the precise identification and resection of his rare clustered ectopic lesions addressed his treatment-refractory hyperparathyroidism. The patient highly acknowledges our center's professional diagnostic expertise and meticulous clinical care for managing his complex condition.

Discussion

The parathyroid glands have an embryologic origin in the third and fourth pharyngeal pouches. The inferior parathyroids (third pouch) descend with the thymus to the thyroid lower pole, while the superior parathyroids (fourth pouch) descend a shorter distance to the cricothyroid junction.[6, 7] The inferior parathyroids exhibit greater variability because of their prolonged embryologic descent, and they may commonly be found ectopically within anterior mediastinum, thymus, or retroesophageal space; the superior parathyroids are more constant but may occasionally be found in posterior mediastinum or tracheoesophageal groove.[8, 9] Although parathyroid ectopia is relatively common (16%), typically involving one or two glands, and simultaneous ectopia of all four parathyroid glands is extremely rare.[9, 10]

In this case, the preoperative MIBI obtained before the first surgery demonstrated a clustered and fused tracer uptake in the right lower neck and mediastinum, without any discrete solitary lesion. Therefore, we consider that the right inferior parathyroid adenoma resected during the first operation and the three adenomas subsequently removed in our reoperation were all part of the same ectopic complex. Due to insufficient thorough exploration, only the most cephalad portion of this complex was removed during the first surgery. These four parathyroid adenomas formed a single, continuous, grape-like cluster in the right cervicomediastinum—making all four glands ectopic and adenomatous.

What embryologic mechanism could explain this extreme anomaly? We hypothesize that during 5 to 8 weeks of gestation, all four parathyroid primordia failed to segregate from one another and from the descending thymus, instead forming a single migratory complex that descended a masses into the right cervicomediastinum—a phenomenon we term "collective ectopia".

The second notable feature is that all four ectopic glands were adenomas. Accounting for only 2–15% of PHPT cases, multiple parathyroid adenomas are considered uncommon, and involvement of all four glands as adenomas is exceptionally rare.[5, 11] When four or more glands are involved, an underlying hereditary syndrome should be considered, particularly multiple endocrine neoplasia (MEN).[12] However, comprehensive evaluation in our patient, including MEN1 genetic testing, normal calcitonin, normal metanephrines, normal prolactin, unremarkable adrenal and pituitary imaging, and without any similar family history, revealed no evidence of MEN. Nevertheless, parathyroid involvement in MEN

syndromes may be asymmetrical and asynchronous.[13] Therefore, while no genetic syndrome is currently confirmed, the possibility cannot be completely excluded, and long-term follow-up is warranted.

This case offers several practical lessons. When preoperative imaging shows clustered or fused tracer uptake forming a continuous lesion rather than a discrete solitary focus, a contiguous ectopic complex should be suspected. The first ectopic adenoma encountered during surgical exploration may be only the tip of a contiguous iceberg—failure to recognize this can lead to persistent disease. Given the diversity and complexity of ectopic parathyroid locations, when no parathyroid tissue is found in normal anatomical regions, a thorough exploration of the bilateral cervical area and even the superior mediastinum should be performed. In such complex reoperative settings, intraoperative PTH monitoring is particularly valuable; the rapid post-excision drop confirmed complete resection in this case and can help reduce the incidence of reoperation.

Conclusion

This case raises the possibility of an unprecedented embryologic phenomenon—collective ectopia—in which all four parathyroid adenomas may have descended en masse as a single continuous cervicomediastinal cluster. If confirmed, this finding will challenge the conventional view of independent glandular migration and carries a practical warning: when imaging shows clustered tracer uptake, a contiguous ectopic complex should be suspected, and the first gland encountered may be only the tip of an iceberg.

Abbreviations

Abbreviation	Full Name
PHPT	Primary hyperparathyroidism
SPECT	single photon emission CT
MIBI	Tc-99m sestamibi imaging
MEN	multiple endocrine neoplasia

Declarations

Ethical Approval

The patient agreed to participate in the study and provided consent in written form.

Consent for publication

The patient has provided written informed consent for the publication of his clinical data and relevant case details in this report. All identifying personal information has been appropriately anonymized to protect patient privacy.

Conflicts of Interest

The authors state that they have no conflicts of interest to disclose.

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Author Contribution

Liu Y: Conceptualization, Writing – Review & Editing, Writing – original draft. Dai Y: Writing – original draft, Investigation, Data Curation. Ai G: Writing – original draft, Visualization, Data Curation. Mu G: Conceptualization, Writing – Review & Editing, Supervision, Funding acquisition.

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Not applicable.

Data Availability

The datasets supporting the conclusions of this article can be obtained from the corresponding author following a reasonable request.

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Figures

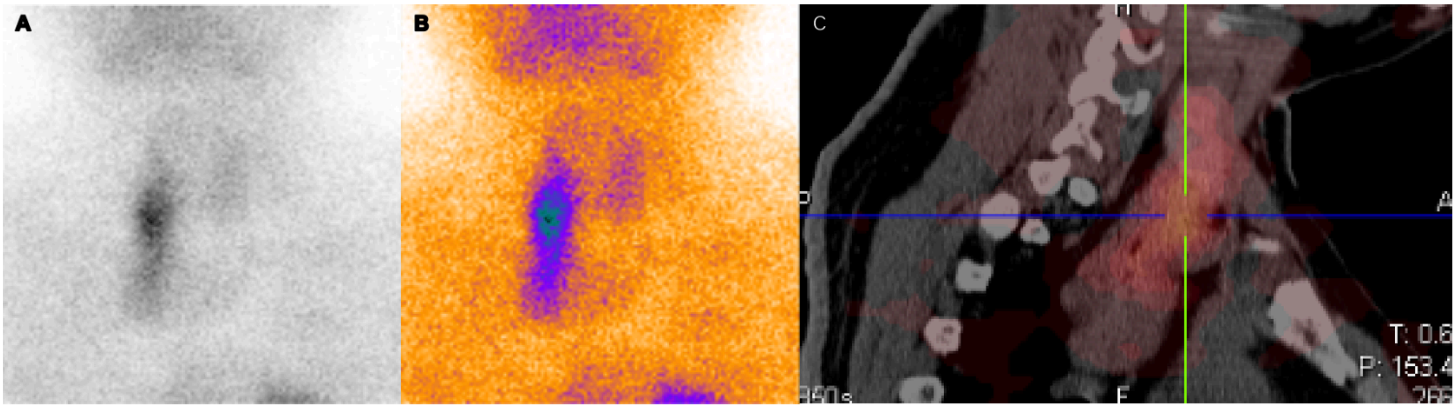


Figure 1

MIBI (A, B) and SPECT (C) showing a clumped tracer concentration located in the right cervicomediastinum before the first operation.

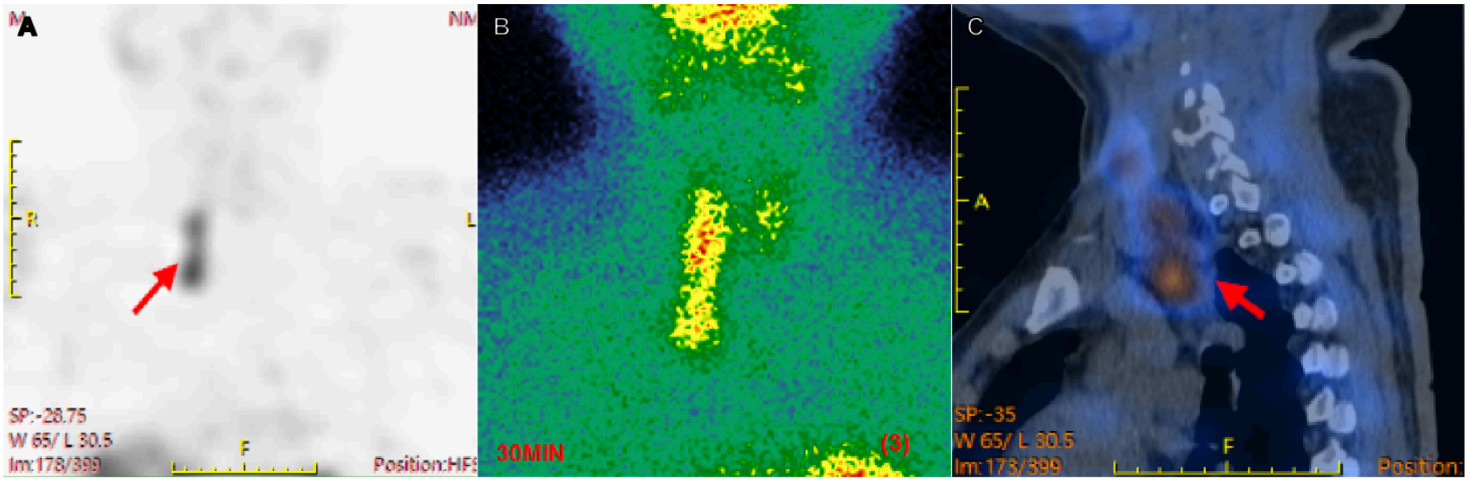


Figure 2

The MIBI (A, B) and SPECT (C) showing a clumped tracer concentration located in the right cervicomediastinum before re-operation.

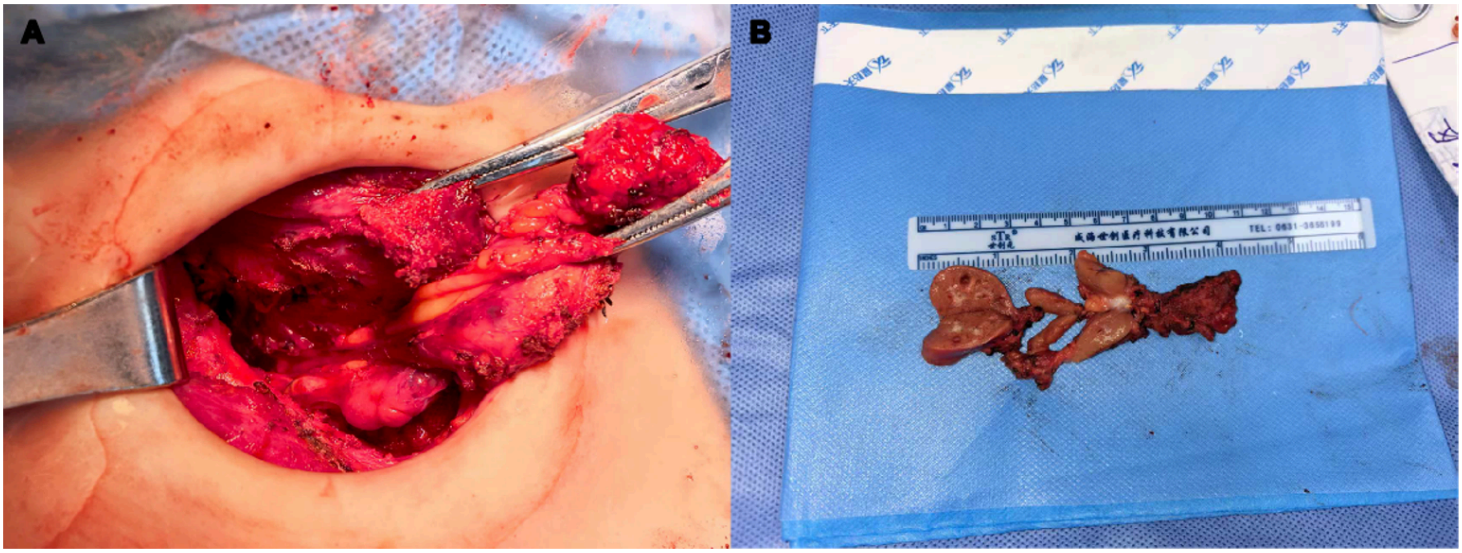


Figure 3

Intraoperative findings (A) and gross pathology (B) show three enlarged parathyroid glands forming a single, continuous, grape-like cluster in the cervicomediastinum.

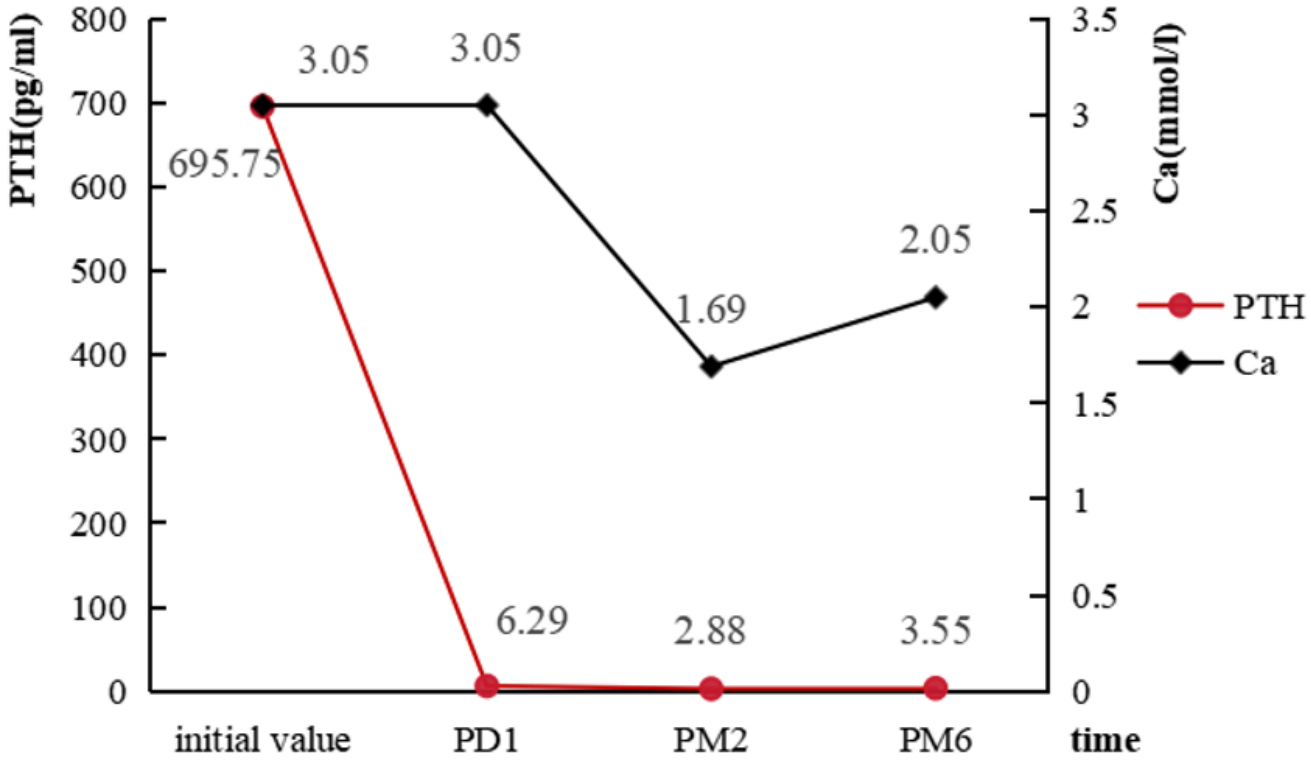


Figure 4

The changes in PTH and serum calcium levels during hospitalization and follow-up (PD1, Postoperative Day 1; PM2, Postoperative Month 2; PM6, Postoperative Month 6).