BMC Endocrine Disorders

CASE REPORT

Open Access

Postoperative pancytopenia in a patient with giant parathyroid adenoma and brown tumor: a case report

Wen-Ting Pan[1†], Zhi-Hong Zhao[1†], Kun Wang[1], Zhi-Yuan He[1] and Liang Ou[1*]

Abstract

Background Parathyroid adenoma is the primary cause of primary hyperparathyroidism, commonly presenting with elevated parathyroid hormone (PTH) and blood calcium levels. Chronic primary hyperparathyroidism often results in bone destruction, resulting in the formation of brown tumors. The preferred clinical treatment for parathyroid adenoma is parathyroidectomy. Postoperative pancytopenia, although rare, is a critical complication that warrants further investigation into its mechanisms and management strategies.

Case presentation We present a case of a 59-year-old female patient who was admitted due to nausea and vomiting. Positron emission tomography-computed tomography (PET-CT) revealed a mass posterior to the left thyroid lobe and multiple areas of fibrocystic osteitis throughout the body. Hematological tests showed elevated serum calcium and parathyroid hormone (PTH) levels. The patient subsequently underwent parathyroidectomy, and pathological examination confirmed the presence of a parathyroid adenoma. Postoperatively, the patient developed pancytopenia and received symptomatic treatment such as correction of anemia and elevation of white blood. At the two-month follow-up, all indicators had returned to normal.

Conclusions Pancytopenia is commonly seen in bone marrow diseases, infections and immune-related disorders, nutritional deficiencies, and metabolic diseases. This case confirms that pancytopenia can also occur postoperatively in patients with parathyroid adenoma. Therefore, Clinicians should be aware of the potential for postoperative pancytopenia following parathyroidectomy and the need for prompt management.

Keywords Primary hyperparathyroidism, Parathyroid adenoma, Pancytopenia, Brown tumor, Bone marrow fibrosis, Case report

†Wen-Ting Pan and Zhi-Hong Zhao contribute equally to this work and should be considered co-first authors.

*Correspondence:
Liang Ou
ouliang168@126.com
[1]Jiangsu University Affiliated Hospital Thyroid and Breast Surgery Department, Zhenjiang, China

Background

Primary hyperparathyroidism (PHPT) is an endocrine disorder characterized by abnormal regulation of parathyroid hormone secretion. Its etiology includes hyperplasia, adenoma, or carcinoma of the parathyroid glands. Among them, adenoma is the most common cause, accounting for the majority (80-85%) of PHPT cases, typically originating from a single parathyroid adenoma [1]. Parathyroidectomy is the preferred treatment for parathyroid adenomas [2]. There are some complications after parathyroidectomy, and several studies have shown that the postoperative incidence rates are high for hypocalcemia (4.1–21.3%) [3] and hypoparathyroidism (11.4%) [4]. Postoperative neurological damage (transient 10.6%, permanent 1.1%) and [5] infection (0.09–2.9%) are relatively rare [6]. According to literature review, there are few reports on the impact of PHPT on blood cell lines and the occurrence of pancytopenia after parathyroidectomy [7], and there have been no reports on the occurrence of pancytopenia after parathyroidectomy. Therefore, we present a case of pancytopenia following parathyroid surgery and discuss relevant literature regarding the relationship between the parathyroid gland and hematopoiesis. We emphasize the importance of considering parathyroidectomy in the context of pancytopenia.

Case presentation

A 59-year-old female was admitted to the hospital due to nausea and vomiting for one month. One month prior, an abdominal CT scan at another hospital revealed multiple soft tissue density lesions with bone destruction involving bilateral ribs, T12 vertebra, and right iliac bone, suspected to be metastatic tumors or multiple myeloma. Bilateral kidney stones were also noted (Fig. 1). Later, the patient presented to our hospital. Apart from nausea and vomiting, she had no other positive symptoms. Physical examination revealed skeletal deformities throughout the body, with no abdominal tenderness or

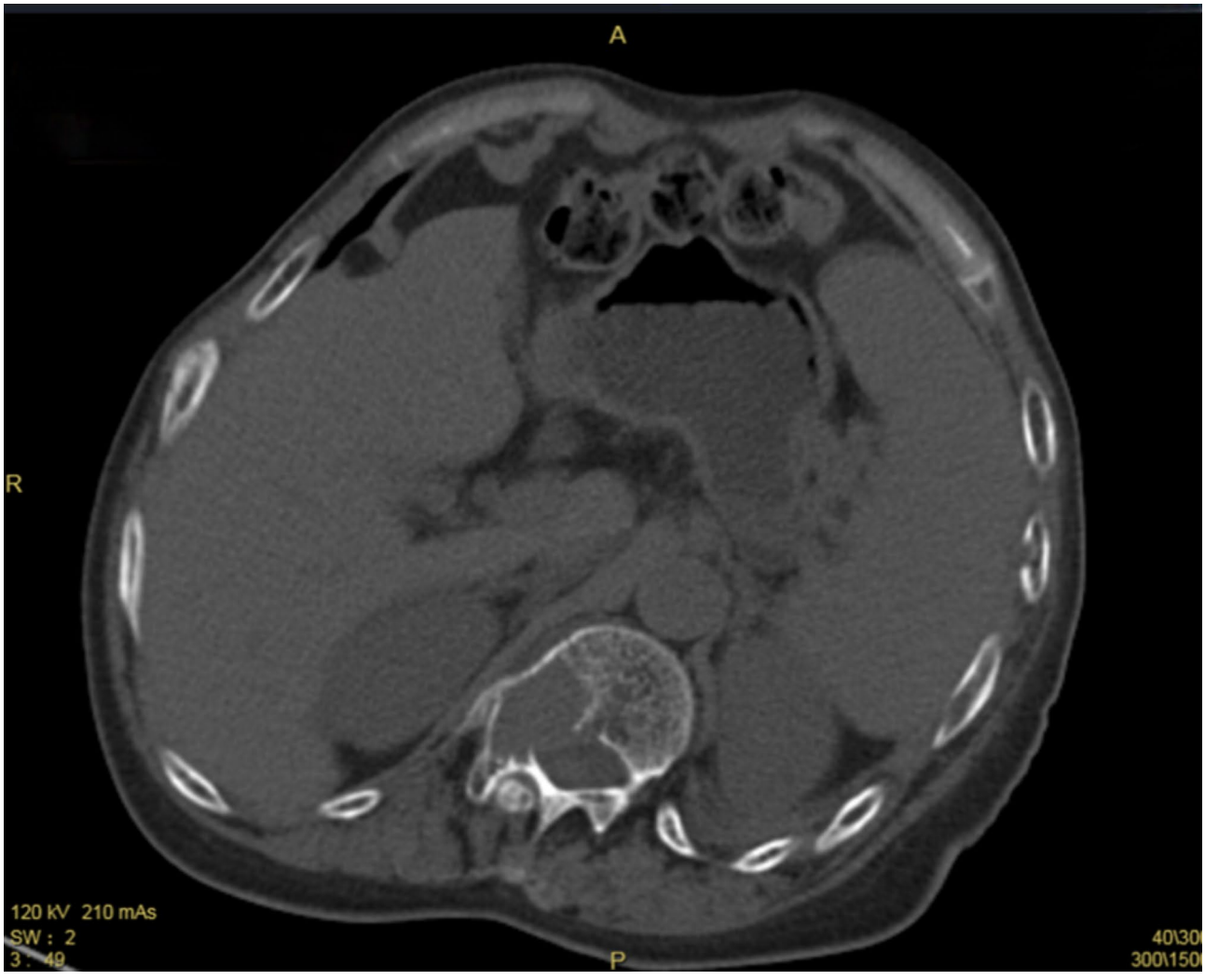

Fig. 1 Abdominal CT

rebound tenderness, and normal neurological examination. PET-CT scan shows a soft tissue mass below the left thyroid lobe, indicating the origin of parathyroid gland (parathyroid adenoma or other). Bone: Diffuse uneven decrease in bone density and bone destruction in multiple skeletal regions indicate fibrous dysplasia and osteoporosis. Kidney: bilateral kidney stones observed (Fig. 2). CT、 enhanced CT and thyroid ultrasound showed a mass in the posterior aspect of the left thyroid lobe (possibly parathyroid in origin), measuring approximately 45×28×26 mm, with relatively clear borders and irregular shape (Fig. 3). Laboratory tests revealed persistently elevated parathyroid hormone (PTH) levels, peaking at 1766 pg/ml (normal range: 12–88 pg/ml) (Fig. 4), fluctuating increase in serum calcium levels, peaking at 2.99 mmol/L (normal range: 2.08–2.60 mmol/L), and relatively low vitamin D levels at 7.62 ng/ml (normal range > 20 ng/ml). The preliminary diagnosis before surgery was a parathyroid tumor with a brown tumor. Intraoperatively, the lesion was found attached to the posterior aspect of the inferior pole of the left thyroid lobe, measuring approximately 3.5×3.5×2 cm (Fig. 5). Histopathological examination confirmed parathyroid adenomatous hyperplasia (left parathyroid gland) (Fig. 6). Postoperatively, PTH levels normalized (16.30 pg/ml), and serum total calcium levels decreased to 1.76 mmol/L. Additionally, the patient developed pancytopenia postoperatively (white blood cells: 1.6×10^9/L (N: 3.5–9.5×10^9/L), red blood cells: 2.49×10^12/L (N: 3.8–5.1×10^12/L), platelets: 84×10^9/L (N: 125–350×10^9/L)(Fig. 7), which was treated with correction of anemia and elevation of white blood. During the follow-up period of two months, the patient's PTH, serum calcium, and complete blood count parameters returned to normal, and there was some

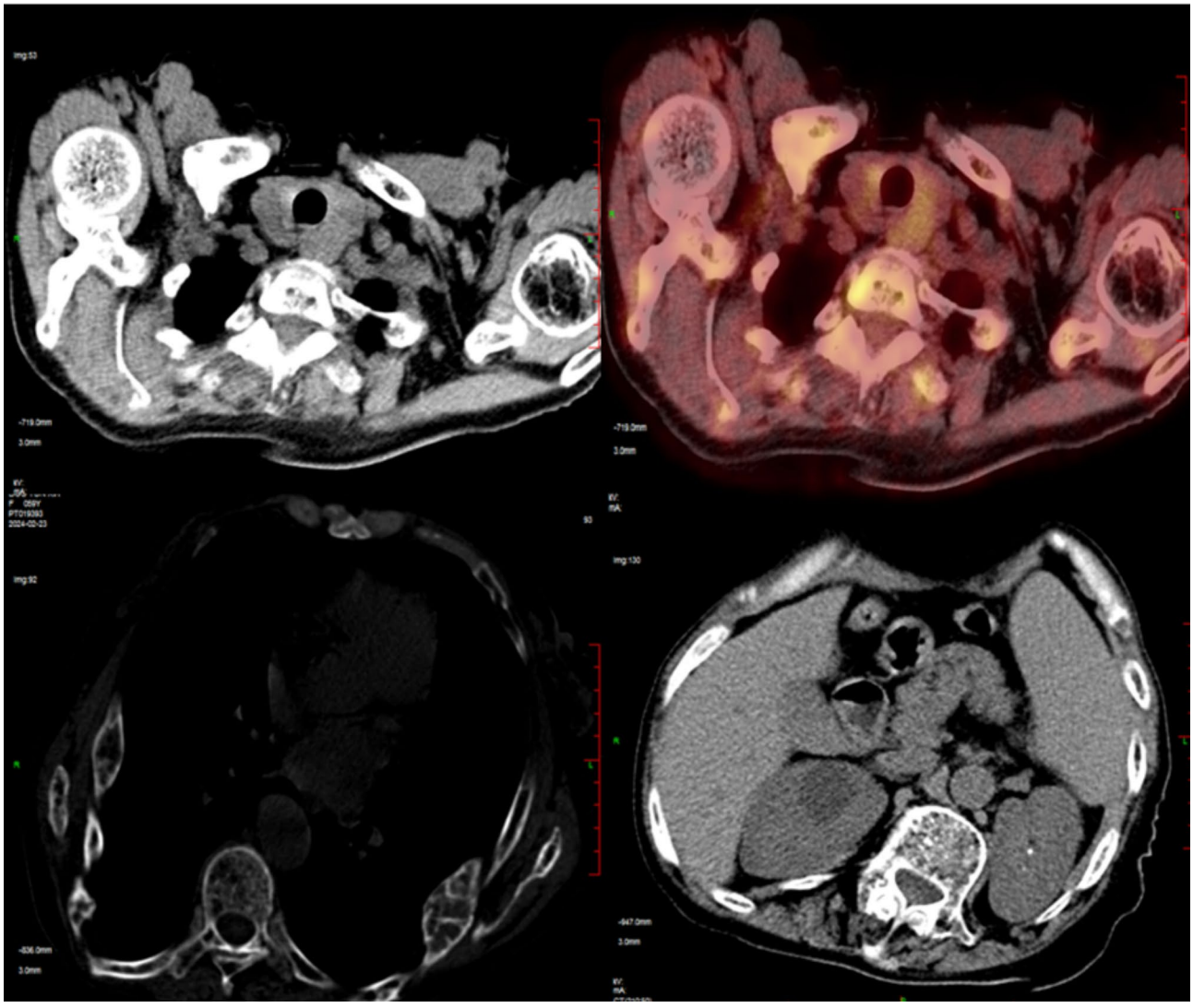

Fig. 2 PET-CT

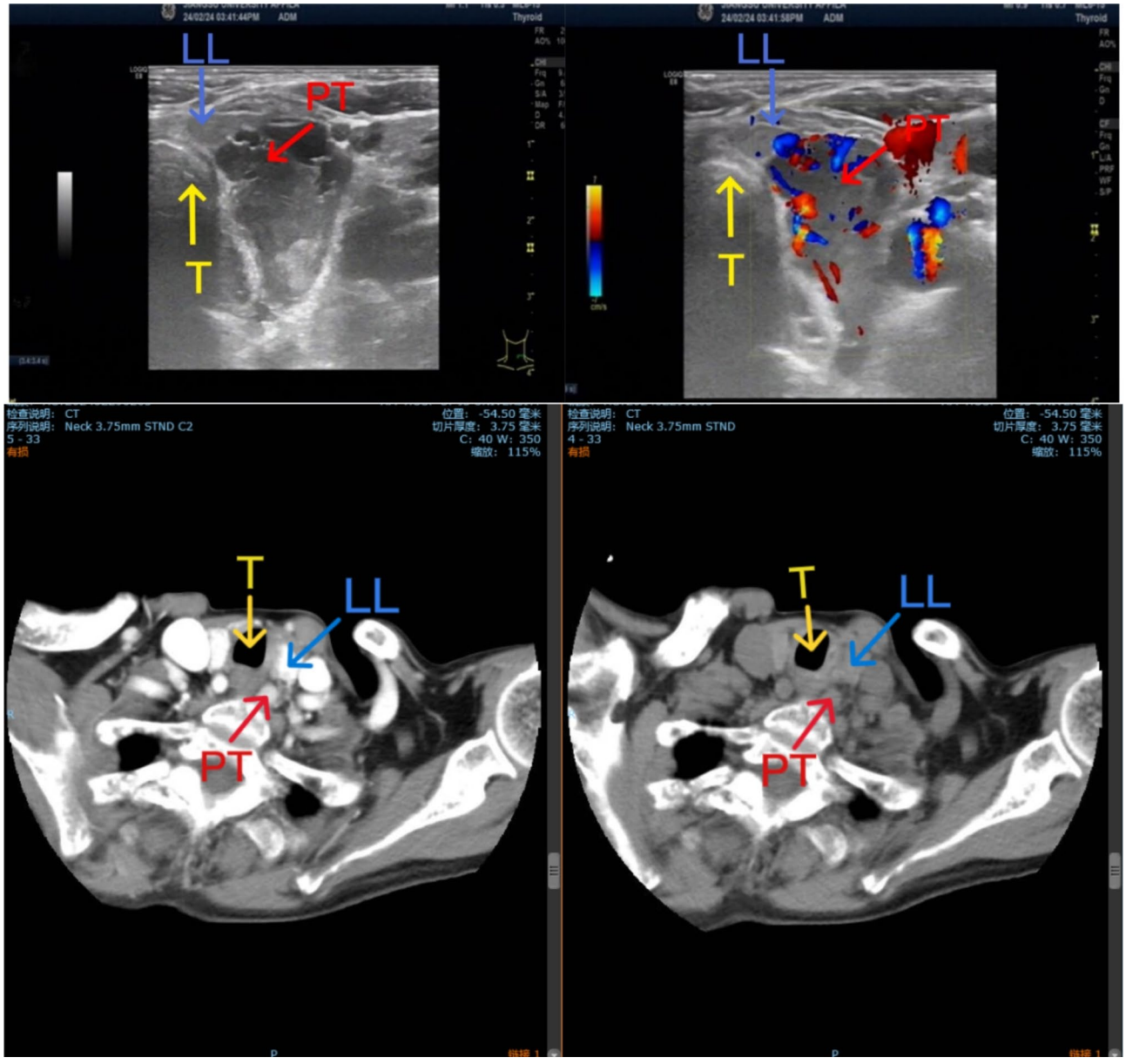

Fig. 3 Neck CT, Enhanced CT, and Ultrasound (T: Trachea, LL: Left lobe of the thyroid gland, PT: Parathyroid Adenoma)

improvement in the degree of bone destruction compared to before surgery.

Discussion

The most common cause of primary hyperparathyroidism is parathyroid adenoma. Its clinical manifestations include gastrointestinal symptoms (nausea, vomiting, peptic ulcers), kidney stones, osteoporosis with fractures, and changes in mental status [8]. Brown tumors result from excessive activity of osteoclasts induced by parathyroid hormone. They can affect any part of the skeleton, including the skull (usually the jawbone), cranium, clavicles, ribs, pelvic bones, femurs, and spine. They present as osteoporosis with localized bone resorption accompanied by fibrous tissue proliferation, cyst formation, increased osteoclasts, and bone marrow fibrosis. They are named "brown tumors" because the cysts contain brown fluid [9]. It is closely associated with primary hyperparathyroidism, occurring in approximately 3% of patients with this condition [10]. In addition, primary hyperparathyroidism (PHPT) with fibrous cystic bone disease is more likely to result in bone marrow fibrosis compared to other presentations of PHPT [11]. The patient, in this case, has a history of poliomyelitis since childhood and reports low physical activity. Physical examination revealed multiple skeletal deformities throughout the body and a history of left femoral fracture. The PET-CT report indicated a mass of parathyroid

Test	Preoperative	Postoperative	Reference Interval
Total Calcium(mmol/L)	2.99	1.76	2.00-2.50
25-OH VitaminD(ng/ml)	7.62	14.30	>20
PTH (pg/ml)	1766	16.30	12-88
Phosphate(mmol/L)	0.57	0.68	0.90-1.34
Leukocyte(10^9/L)	3.8	1.6	3.5-9.5
Erythrocyte(10^{12}/L)	3.75	2.49	3.8-5.1
Platelet(10^9/L)	155	84	125-350

Fig. 4 Preoperative and postoperative laboratory test results

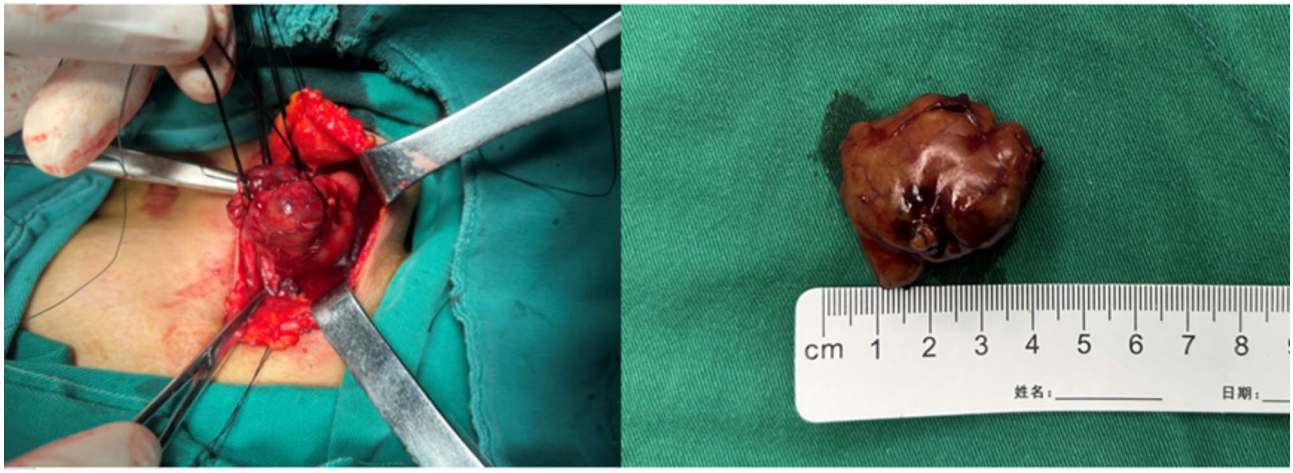

Fig. 5 Parathyroid adenoma specimen after excision

origin, multiple bone lesions with bone destruction, local thickening, and expansion changes in the bones, suggesting fibrous cystic bone disease. Bilateral renal stones and osteoporosis were also observed. Considering the elevated levels of serum PTH and calcium, along with decreased phosphate levels, the diagnosis was concluded as a brown tumor secondary to hyperparathyroidism [12]. The three-month postoperative CT re-examination revealed an improvement in the systemic osteolytic lesions compared to before, further confirming the diagnosis of parathyroid adenoma combined with brown tumor in the patient.

The histological morphology of parathyroid adenoma is typically small, usually between 3 and 5 millimeters in size, with an average weight of less than 1 gram. The diagnostic criteria for giant parathyroid adenoma include a weight exceeding 3.5 g, a length greater than 2 centimeters, and concurrent manifestations of hyperparathyroidism [13]. The specimen removed in this case measured 3.5×3.5×2 cm and weighed 10.0 g, meeting the diagnostic criteria for giant parathyroid adenoma. The preferred treatment for parathyroid adenoma is parathyroidectomy [2]. Hypocalcemia, hypoparathyroidism, recurrent laryngeal nerve injury, infection, and thyroid dysfunction are potential complications following surgical treatment for parathyroid adenoma. In patients whose serum calcium levels remain below 2.1 mmol/L for more than four days after thyroid or parathyroidectomy, hungry bone syndrome (HBS) should be considered [14]. In this case, the patient experienced persistent hypocalcemia postoperatively, with the lowest serum total calcium level reaching 1.76 mmol/L (normal range: 2.08–2.60 mmol/L), consistent with HBS. Treatment included oral chewable calcium carbonate tablets (1.5 g twice daily), alfacalcidol tablets (1.5ug once daily), and intravenous calcium gluconate infusion. One month after surgery, the patient's serum calcium levels normalized upon outpatient follow-up.

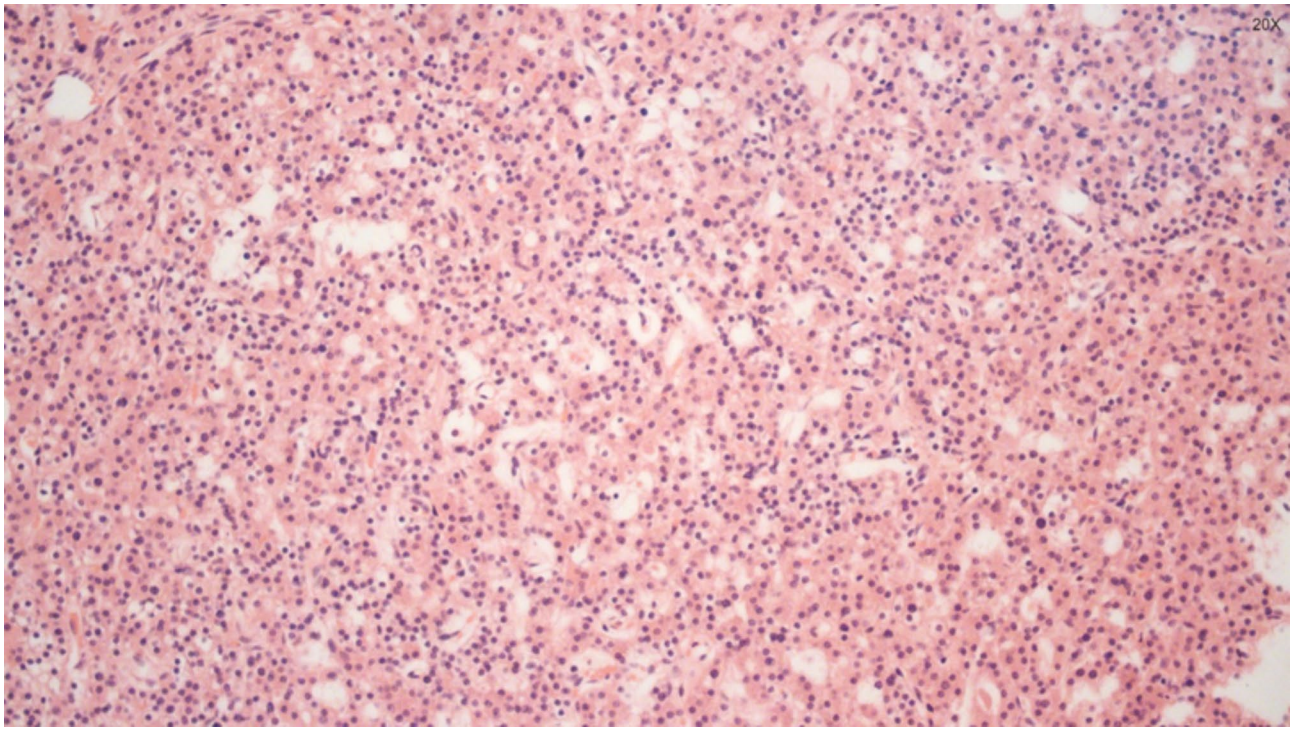

Fig. 6 Adenoma of parathyroid gland HE-staining, 20× magnification

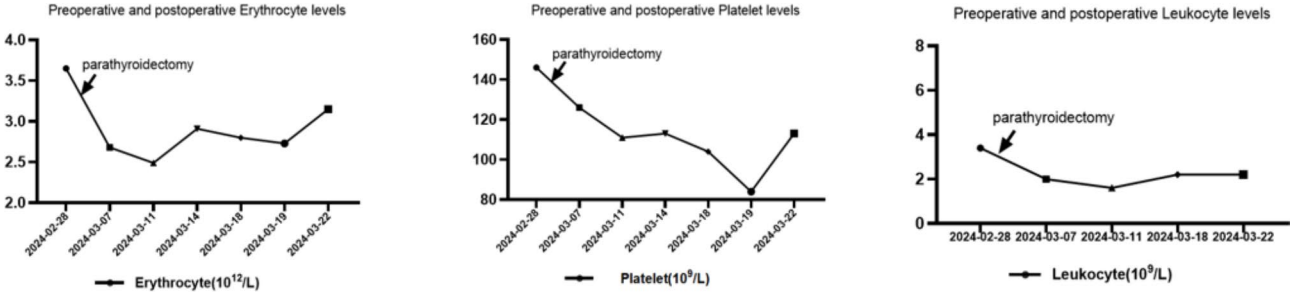

Fig. 7 Preoperative and postoperative complete blood cell counts

Currently, there are no reports of decreased whole blood cells after parathyroidectomy. In the case reported in this article, the patient was diagnosed with parathyroid adenoma combined with brown tumor, and postoperative pancytopenia occurred. Although the patient's complete blood cell count eventually returned to normal during follow-up, it is important to actively investigate the root cause of postoperative complete blood cell reduction to guide prevention and treatment strategies and improve prognosis.

In this case, the lowest recorded postoperative red blood cell count for the patient was 2.49×10^12/L (normal range: 3.8–5.1×10^12/L), white blood cell count was 1.6×10^9/L (normal range: 3.5–9.5×10^9/L), and platelet count was 84×10^9/L (normal range: 125–350×10^9/L). Given these findings, clinical doctors may initially suspect it to be a hematological disorder. However, further laboratory tests, including anemia, blood slide examination, immunofixation electrophoresis, complement immunoglobulin, etc., did not show any significant abnormalities, ruling out hematological disorders. Another factor to consider is that liver and spleen diseases lead to a decrease in whole blood cells [15], but the patient's abdominal ultrasound, CT examination, and related experimental indicators did not diagnose obvious liver and spleen diseases, so this possibility was ruled out. According to the patient's medical history, it was found that no medication affecting the hematopoietic system was taken, and the factor of medication influence was excluded. Finally, it is speculated that the postoperative decrease in blood cell counts in this patient may be attributed to the stimulation of hematopoiesis by parathyroid hormone and the development of bone marrow fibrosis caused by elevated parathyroid hormone levels,

disrupting the balance between hematopoietic factors and resulting in decreased blood cell counts. According to relevant literature, the stimulation of hematopoiesis by parathyroid hormone may occur through various mechanisms, including increasing the number of hematopoietic stem cells via parathyroid hormone receptor 1 (PTHR1) [16]. Parathyroid hormone may also stimulate hematopoiesis by upregulating the expression of CDH11 in bone marrow stromal stem cells [17]. Therefore, parathyroid adenoma-induced elevation of parathyroid hormone promotes hematopoiesis, leading to an increase in blood cell count. Meanwhile, studies suggest that the most likely mechanism by which primary hyperparathyroidism (PHPT) causes anemia is through bone marrow fibrosis. PTH stimulates bone marrow fibroblasts, resulting in bone marrow fibrosis, which leads to a reduction in hematopoietic factors and consequently causes a decrease in blood cell count [7]. In addition, elevated levels of PTH can stimulate osteoclasts to release cytokines, which affect bone marrow fibrosis and bone loss [18]. The patient's preoperative elevated levels of parathyroid hormone (PTH) continuously stimulated hematopoietic stem cells to produce blood cells. The increased PTH levels further exacerbated bone marrow fibrosis, leading to suppression of the release of hematopoietic factors. The balance between these two factors maintained the patient's preoperative blood cell counts within normal levels. However, after the parathyroid adenoma resection surgery, PTH levels quickly returned to normal, resulting in a decline in hematopoietic activity. Despite this, bone marrow fibrosis could not be completely reversed in the short term, leading to persistent suppression of hematopoiesis postoperatively, thereby causing the patient to exhibit a period of decreased blood cell counts after surgery. With the patient's postoperative PTH levels consistently within the normal range, bone marrow fibrosis gradually improved, and the blood cell count steadily increased. Eventually, during follow-up, the blood cell count returned to normal range.

Based on the patient's case, it has prompted us to consider whether there is a correlation between parathyroidectomy and the hematopoietic system. Based on existing literature, we speculate that the occurrence of pancytopenia after parathyroid adenoma resection may be due to the disruption of pathological balance. Elevated parathyroid hormone not only stimulates hematopoiesis but also accelerates bone marrow fibrosis to suppress hematopoiesis, reaching a pathological balance between the two. The emergence of parathyroidectomy breaks this balance, leading to the occurrence of temporary pancytopenia. However, the specific mechanisms involved urgently require further research and confirmation.

Conclusion

Postoperative pancytopenia can be caused by various factors. This case report describes a rare occurrence of postoperative pancytopenia in a patient with a giant parathyroid adenoma combined with multiple brown tumors. This article discusses the possible mechanism of pancytopenia after parathyroidectomy based on existing literature. It emphasizes the importance of closely monitoring blood cell counts in patients with parathyroid adenoma combined with brown tumors after surgery. Further research on the relationship between parathyroidectomy and hematopoietic complications is crucial for the prevention and management of pancytopenia.

Acknowledgements
The authors express sincere gratitude to the patients who consented to participate in this study.

Author contributions
PWT conceptualized the manuscript, interpreted the data, and revised the manuscript. OL revised the draft and analyzed specific diagnostic correlations. ZZH performed the diagnosis, surgery, and follow-up for the patient. WK engaged in the case discussion and helped with manuscript revisions. HZY participated in the case discussion. All authors have reviewed and endorsed the final manuscript.

Funding
All funding for the report research comes from a project in Zhenjiang City, Zhi-Hong Zhao, Affiliated Hospital of Jiangsu University, with project number SH2016030/SH2020062.

Data availability
The data used and analyzed in the current study are provided in the manuscript and are available upon reasonable request from the corresponding author.

Declarations

Ethics approval and consent to participate
Ethics Committee of Jiangsu University Affiliated Hospital. Committee's reference number: KY2023K1105.

Consent for publication
The patient provided written informed consent for the publication of this case report and any accompanying images. A copy of the written consent form is available for review by the series editor of this journal.

Competing interests
The authors declare no competing interests.

Received: 8 August 2024 / Accepted: 25 September 2024
Published online: 30 September 2024

References

1. Abshirini H, Heidari M, Fahimi A, Ghorbani P, Ghadirzadeh E, Shafiei S. Giant parathyroid adenoma presenting with multiple pathologic fractures: a case report. Clin Case Rep 2023, 11(6).
2. Papanikos V, Papadodima E, Bantouna D, Paparodis RD, Livadas S, Angelopoulos N, Karvounis E. Hypercalcemic Crisis due to a giant Intrathyroidal parathyroid adenoma, with postsurgical severe hypocalcemia and hungry bone syndrome: a Case Report. Clin Pract. 2024;14(1):179–87.
3. Mu Y, Zhao Y, Zhao J, Zhao Q, Zhang Y, Li Y, Kou J, Dionigi G, Bian X, Sun H. Factors influencing serum calcium levels and the incidence of hypocalcemia

after parathyroidectomy in primary hyperparathyroidism patients. Front Endocrinol. 2023;14:1276992.
4. Unsal IO, Calapkulu M, Sencar ME, Hepsen S, Sakiz D, Ozbek M, Cakal E. Preoperative Vitamin D Levels as a predictor of transient hypocalcemia and Hypoparathyroidism after Parathyroidectomy. Sci Rep. 2020;10(1):9895.
5. Joliat GR, Guarnero V, Demartines N, Schweizer V, Matter M. Recurrent laryngeal nerve injury after thyroid and parathyroid surgery: incidence and postoperative evolution assessment. Medicine. 2017;96(17):e6674.
6. Polistena A, Prete FP, Avenia S, Cavallaro G, Di Meo G, Pasculli A, Rondelli F, Sanguinetti A, Sgaramella LI, Avenia N et al. Effect of antibiotic Prophylaxis on Surgical Site infection in thyroid and parathyroid surgery: a systematic review and Meta-analysis. Antibiot (Basel Switzerland) 2022, 11(3).
7. Rajan R, Paul I, Cherian KE, Korula A, Hephzibah J, Manipadam MT, Abraham DT, Kapoor N, Paul TV. Myelofibrosis and Pancytopenia Associated with primary hyperparathyroidism. AACE Clin case Rep. 2021;7(1):69–71.
8. Aygün N, Uludağ M. Surgical Treatment of primary hyperparathyroidism: which therapy to whom? Sisli Etfal Hastanesi tip Bulteni. 2019;53(3):201–14.
9. Hoshi M, Takami M, Kajikawa M, Teramura K, Okamoto T, Yanagida I, Matsumura A. A case of multiple skeletal lesions of brown tumors, mimicking carcinoma metastases. Arch Orthop Trauma Surg. 2008;128(2):149–54.
10. Ergen FB, Ayvaz M, Yildiz AE, Aydingoz U, Gedikoglu G. Brown tumour presenting as a soft-tissue mass. Clin Radiol. 2012;67(3):286–9.
11. Hunter D, Turnbull HM. Hyperparathyroidism: generalized osteitis fibrosa. Br J Surg. 1931;19(74):486.
12. Majic Tengg A, Cigrovski Berkovic M, Zajc I, Salaric I, Müller D, Markota I. Expect the unexpected: Brown tumor of the mandible as the first manifestation of primary hyperparathyroidism. World J Clin Cases. 2024;12(7):1200–4.
13. Matías-García B, Mendoza-Moreno F, Díez-Alonso M, Ovejero-Merino E, Vera-Mansilla C, Blázquez-Martín A, Quiroga-Valcárcel A, Jiménez-Martín R, D'Amico R, Lasa-Unzúe I, et al. Spontaneous cervical hematoma caused by giant parathyroid adenoma in an elderly patient: a case report. Med Int. 2024;4(1):1.
14. Aw MNE, Ml N. The role of intra-operative parathyroid hormone assay in non-localized adenoma. Pakistan J Med Sci. 2022;38(8):2376–9.
15. Gonzalez-Casas R, Jones EA, Moreno-Otero R. Spectrum of anemia associated with chronic liver disease. World J Gastroenterol. 2009;15(37):4653–8.
16. Calvi LM. Osteoblastic activation in the hematopoietic stem cell niche. Ann N Y Acad Sci. 2006;1068:477–88.
17. Yao H, Miura Y, Yoshioka S, Miura M, Hayashi Y, Tamura A, Iwasa M, Sato A, Hishita T, Higashi Y, et al. Parathyroid hormone enhances hematopoietic expansion via upregulation of cadherin-11 in bone marrow mesenchymal stromal cells. Stem Cells. 2014;32(8):2245–55.
18. Bhadada SK, Sridhar S, Ahluwalia J, Bhansali A, Malhotra P, Behera A, Mittal BR. Anemia and thrombocytopenia improves after curative parathyroidectomy in a patient of primary hyperparathyroidism (PHPT). J Clin Endocrinol Metab. 2012;97(5):1420–2.

Publisher's note