



## Mediastinal parathyroid carcinoma: a case report

Rak przytarczycy w śródpiersiu: opis przypadku

Jacek Gawrychowski<sup>1</sup>, Andrzej Gabriel<sup>2</sup>, Ewa Kluczevska<sup>3</sup>, Grzegorz Buła<sup>1</sup>, Bożena Lackowska<sup>4</sup>

<sup>1</sup>Department of General Surgery, Silesian Medical University, Katowice, Poland

<sup>2</sup>Department of Pathology, Silesian Medical University, Katowice, Poland

<sup>3</sup>Department of Radiology, Silesian Medical University, Katowice, Poland

<sup>4</sup>Department of Cancer Pathology, Oncology Center, Krakow, Poland

### Abstract

A 72 year-old woman with primary hyperparathyroidism was operated for parathyroid crisis. PTH serum level was 808 pg/mL. During the operation, only two superior parathyroid glands were found. One was normal, and hypertrophy was revealed in the other. After the surgical procedure, PTH serum level was 726.5 pg/mL. Helical computer tomography examination showed a heterogeneous mass in the anterior mediastinum. The tumour was removed via a sternotomy approach. Histopathological examination revealed parathyroid carcinoma. PTH level dropped to 5.74 pg/mL. Cytofluorometric examination revealed diploidy (DI = 1) in both the hypertrophic and the unchanged upper glands, whereas parathyroid cancer was aneuploid. After the initial operation, the woman was discharged from the hospital on the 27th postoperative day. One year after surgical procedures, she is well. She has to take calcium. (*Pol J Endocrinol* 2012; 63 (2): 143–146)

**Key words:** mediastinal parathyroid carcinoma, DNA ploidy

### Streszczenie

Chora w wieku 72 lat była operowana z powodu zagrażającego przełomu przytarczycowego w przebiegu pierwotnej nadczynności przytarczyc. Przedoperacyjne stężenie PTH w surowicy krwi wynosiło 808 pg/ml. Śródoperacyjnie zlokalizowano jedynie dwie przytarczycy górne — jedną prawidłową i jedną w stanie rozrostu. Pooperacyjne stężenie PTH w surowicy krwi wynosiło 726,5 pg/ml. W badaniu TK w przednim śródpiersiu stwierdzono obecność heterogennego guza. Chorą operowano ponownie. Wykonano sternotomię pośrodkową górną, usuwając zmienioną ektopowo przytarczycę. W badaniu histopatologicznym rozpoznano raka przytarczycy. Uzyskano spadek stężenia PTH do wartości 5,74 pg/ml. Badanie cytofluorometryczne wykazało diploidę przytarczyc górnych, podczas gdy rak przytarczycy miał charakter aneuploidalny. Chora została wypisana z kliniki po 27 dniach od operacji; pozostaje pod kontrolą ambulatoryjną bez cech wznowy procesu nowotworowego i jest poddana substytucji preparatami wapnia. (*Endokrynol Pol* 2012; 63 (2): 143–146)

**Słowa kluczowe:** rak przytarczycy śródpiersia, ploidia DNA

### Introduction

Primary parathyroid cancers are rarely detected in the mediastinum. Their unusual occurrence is illustrated best by what is now the historical study performed by Nathaniels of Massachusetts General Hospital in 1970. His study group consisted of 84 patients with mediastinal parathyroid tumours, but there was only one case of parathyroid cancer among them [1]. Besides, there are still no clear criteria, either clinical or histopathological, enabling a definite differentiation between benign parathyroid hypertrophy and parathyroid adenoma or even cancer [2, 3].

This paper describes a female patient treated surgically for primary hyperparathyroidism (PHPT) in whom hypertrophy was detected in one of the three parathyroid glands, and cancer in another situated ectopically in the mediastinum.

### Case report

The patient, aged 72, was referred on 4 May 2009 from the Department of Nephrology, Endocrinology and Metabolic Diseases to be treated surgically as an urgent case because of the risk of parathyroid crisis primary hyperparathyroidism. Concomitant conditions were insulin-dependent diabetes, generalised atherosclerosis, and osteoporosis.

Upon admission, the patient complained of general weakness, ostealgia and arthralgia, in particular in the region of the vertebral column and pelvic girdle, all of them having worsened in the previous six months. Laboratory tests revealed: serum of ionised calcium level 1.63 mmol/L (N 1 — 1.28 mmol/L), glucose 189.4 mg/dL, sodium 4.94 mmol/L, creatinine 0.53 mg/dL and PTH level 808 pg/mL (N 15 — 65 pg/mL).



Prof. Jacek Gawrychowski MD, PhD, Katedra i Oddział Kliniczny Chirurgii Ogólnej, Śląski Uniwersytet Medyczny w Katowicach, Szpital Specjalistyczny nr 2, ul. Stefana Batorego 15, 41-902 Bytom, e-mail: jacekgaw@o2.pl

Ultrasonography of thyroid and parathyroid glands, carried out on 20 April 2009, revealed: thyroid gland — multinodular structure, left upper parathyroid gland — enlarged, 11 × 7 mm.

After preparation, the patient was operated on 7 May 2009. Both upper parathyroid glands were removed. Lower parathyroid glands were not visible. For this reason, and also because of nodular goitre detected intraoperatively, it was decided that near total removal of both thyroid lobes should be performed.

Histopathological findings were as follows: right upper parathyroid gland (0.4 cm) — no changes, left upper parathyroid gland (0.9 cm) — hyperplasia. No parathyroid pattern was found within the removed thyroid lobes.

Serum of ionised calcium level was 1.494 mmol/L six hours after the operation, and 1.56 mmol/L on 8 May 2009. PTH level was 726.5 pg/mL.

Helical computer tomography of the neck and mediastinum revealed a mass 3 cm × 2 cm × 2 cm looking like an enlarged lymph node or persistent thymus. Pathological fracture Th8-Th9 was also visible.

After preparation, the patient was reoperated on 15 May 2009 through longitudinal upper sternotomy. A tumour 3 cm × 2 cm × 2 cm connecting with the lower thymic corner was detected intraoperatively. The lesion was removed totally, together with the persistent thymus. Histopathological finding: carcinoma glandulae parathyreoideae (2.5 cm).

Six hours after the operation, serum of ionised calcium had dropped to 1.36 mmol/L.

On 16 May, the serum of ionised calcium level was 1.32 mmol/L, and on 20 May, it was 1.05 mmol/L. Serum PTH level was 5.74 pg/mL.

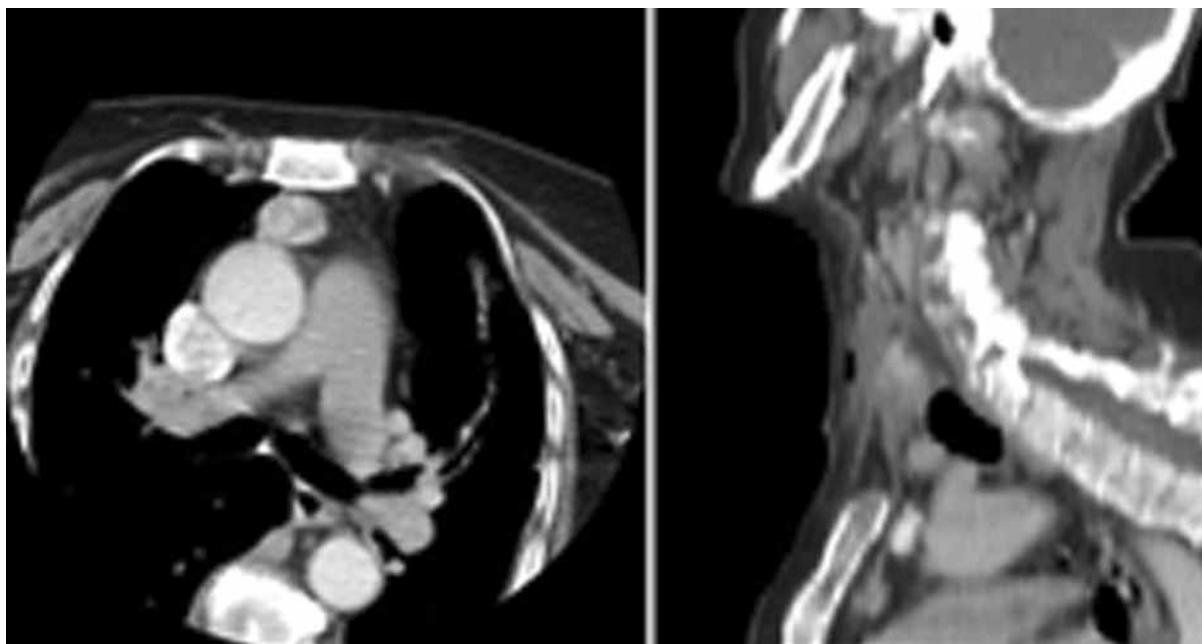
The postoperative period was complicated with bilateral pneumonia and quite serious hypocalcaemia, the latter requiring both oral and intravenous doses of calcium (approx. 14 g/24 h).

On day 27, the patient was referred back in good general condition to her previous hospital, where she stayed for another 16 days and was finally discharged with a recommendation to take calcium orally.

Cytofluorometric examinations [4] revealed that both the hypertrophic changes in the upper left parathyroid gland and the unchanged upper right parathyroid gland had diploid pattern (DI = 1; CV = 4.99), whereas parathyroid cancer had aneuploid. There were four cell lines within the tumour: diploid, tetraploid (DI = 2.0, CV = 5.94) and two aneuploid (DI = 1.62, CV = 4.0 and 1.36; CV = 1.02) (Figures 1, 2 A–D). Total percentage of S phase cells was 7.62%.

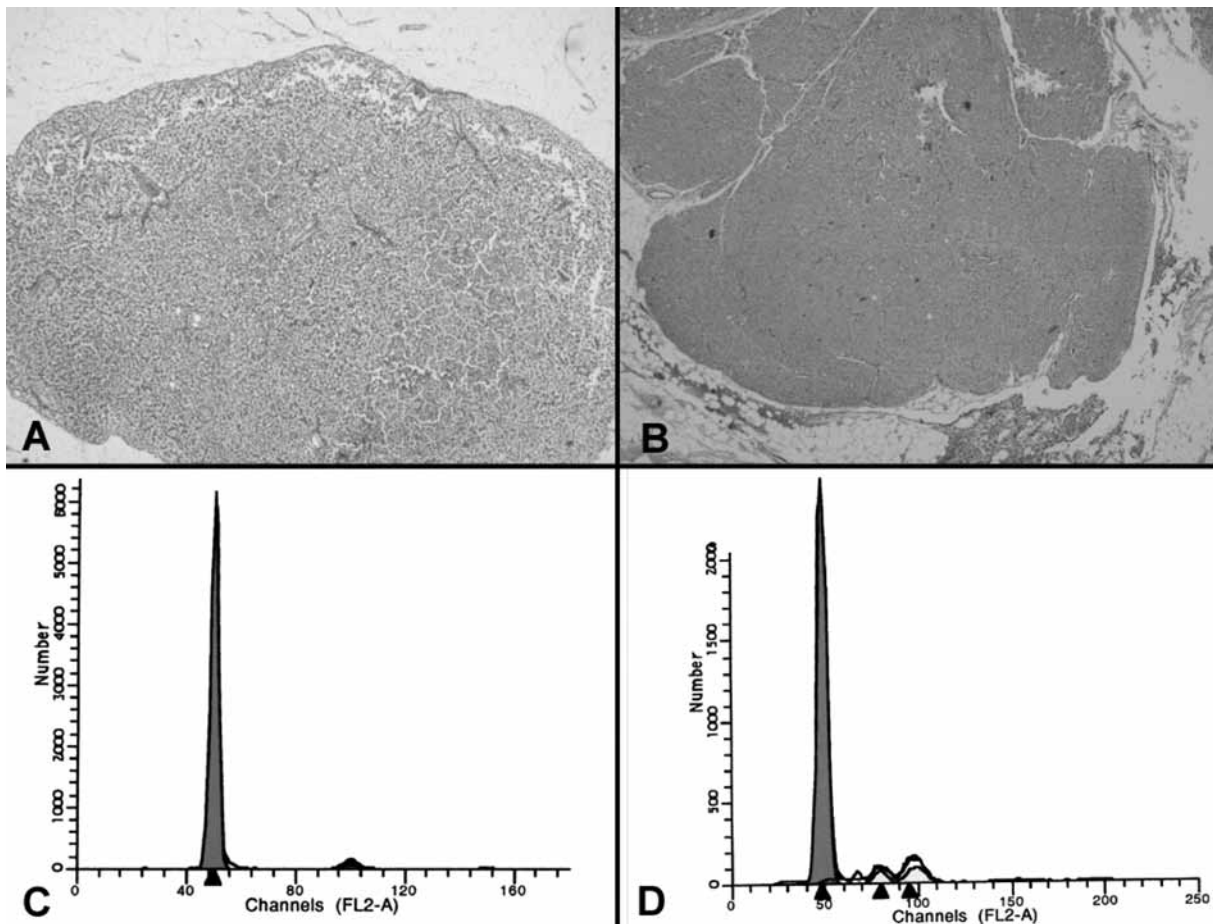
## Discussion

Approximately 20% of adenomas causing primary hyperparathyroidism are situated ectopically in the mediastinum [5]. However, most of them can be removed via a classical neck approach. Only 1–2% of patients require sternotomy (as in our case) or thoracotomy, often accompanied by low-invasive techniques [6]. It could be argued whether or not the ultrasonography was a sufficient method to diagnose enlargement of



**Figure 1.** CT scans of parathyroid cancer in the anterior mediastinum

**Rycina 1.** Tomografia komputerowa przedniego śródpiersia: rak przytarczycy



**Figure 2** **A.** Parathyroid hyperplasia circumscribed by the delicate fibrous capsule of the gland. Cell proliferation arranged in solid sheets and cords, focal oxyphilic cells may be present (200 ×); **B.** Irregular contour, lack of distinct encapsulation. Trabecular growth of the cells in the parathyroid carcinoma, fibrous bands dissecting through the tumour (100 ×); **C.** Parathyroid hyperplasia. Histogram has a diploid DNA distribution pattern; **D.** Parathyroid carcinoma. Histogram has an aneuploid DNA distribution pattern

**Rycina 2** **A.** Rozrost przytarczyc ograniczony przez delikatną otoczkę włóknistą. Rozrost komórek grupujących się w płaciki i sznury, możliwa obecność ognisk komórek oksyfilnych (200 ×). **B.** Nieregularny obrys, brak wyraźnego otorebkowania. Bełczkowaty wzrost komórek w raku przytarczyc, pasy włókniste wnikające w guz (100 ×); **C.** Rozrost przytarczyc. Histiogram posiadający diploidalny wzór rozdziału DNA; **D.** Rak przytarczyc. Histiogram posiadający aneuploidalny wzór rozdziału DNA

the upper left parathyroid gland, but the patient was in a bad general condition with an increasing threat of hypercalcaemic crisis, and therefore the decision to operate was taken quickly [7].

In cases of problems regarding identification of changed parathyroid glands, intraoperative ultrasonography may be useful. A successful operation will be confirmed by a noticeable decrease in PTH level. The patient was identified using macroscopy to have a changed parathyroid gland i.e. the left upper one. This was confirmed in the histopathology exam. A few symptoms causing the disease, poor condition, and lack of intraoperative macroscopy changes in parathyroid glands during neck exploration, as well as a lack of technical possibilities in intraoperative parathyroid gland ultrasonography helped make the decision to finish the operation. After the operation, an absence of

decreased PTH level in serum qualified the patient to immediate reoperation.

There is a hope, based on the Tana report on immunohistochemical reaction with parafibromin, that differential diagnostics for parathyroid lesions will become much improved. As far as parathyroid cancer is concerned, research has demonstrated 96% sensitivity and 99% specificity [8]. Besides, it is still a matter of debate as to how valuable DNA ploidy can be as a malignancy indicator in parathyroid lesions [9].

The presence of hypertrophy in one parathyroid gland and cancer in another at the same time has an appearance similar to a number of disorders connected with primary hyperparathyroidism (e.g. multinodular hypertrophy, multinodular syndromes [MEN] or family hyperparathyroidism [HPT]).

The heterogeneity of the tumour can be demonstrated through assessment of cell ploidy if differences in DNA content between cell clones cover at least 4% of the tested cells [4]. Examinations of both removed lesions indicated that the neck parathyroid adenoma had diploid character. On the other hand, the cancer showed four different cell lines i.e. diploid, tetraploid and two typical aneuploid.

It is also interesting to note that only three parathyroid glands were seen in the patient, and such a situation occurs in less than 3% of patients. Although authors have different opinions as to the usefulness of cytofluorometry in distinguishing between benign lesions and cancers, it is accepted that aneuploidy involves malignant conditions, and this was confirmed by our case. A benign lesion may suggest the presence of at least a pre-cancerous condition if the lesion is found to have aneuploid character, and regular follow-up examinations are necessary for many years [9, 10].

We are aware that further research is needed regarding this aspect, but as the case described above was

unusual and specific, we would like to make it a topic for debate.

## References

1. Nathaniels EK, Nathaniels AM, Wang CA. Mediastinal parathyroid tumors: a clinical and pathological study of 84 cases. *Ann Surg* 1970; 171: 165–170.
2. Ippolito G, Palazzo FF, Sebag F, De Micho C, Henry JF. Intraoperative diagnosis and treatment of parathyroid cancer and atypical parathyroid adenoma. *Br J Surg* 2007; 94: 566–570.
3. Shane E. Clinical review of 122 parathyroid carcinoma. *J Clin Endocrinol Metab* 2001; 86: 485–493.
4. Shankey TW, Rabinovitch PS, Bagwell B et al. Guidelines for implementation of clinical DNA cytometry. *Cytometry* 1993; 14: 472–477.
5. Conn JM, Goncalves MA, Mansour KA, McGrity WC. The mediastinal parathyroid. *Am Surg* 1991; 57: 62–66.
6. Prinz RA, Lonchyna V, Carnaille B, Wurtz A, Proye C. Thoracoscopic excision of enlarged mediastinal parathyroid glands. *Surgery* 1994; 116: 999–1005.
7. Huppert BJ, Reading CC. Parathyroid sonography: Imaging and intervention. *J Clin Ultrasound* 2007; 35: 144–155.
8. Tan MH, Morrison C, Wang P et al. Loss of parafibromin immunoreactivity is a distinguishing feature of parathyroid carcinoma. *Clin Cancer Res* 2004; 10: 6629–6637.
9. Obara T, Fujimoto Y, Hirayama A et al. Flow cytometric DNA analysis of parathyroid tumors with special reference to its diagnostic and prognostic value in parathyroid carcinoma. *Cancer* 1990; 65: 1789–1793.
10. Bowlby LS, DeBault LE, Abraham SR. Flow cytometric DNA analysis of parathyroid glands. Relationship between nuclear and pathologic classifications. *Am J Pathol* 1987; 128: 338–344.