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# Adult Perithyroid and Cervical Thymus-Parathyroid Unit

## *Case Reports of a Rare Entity*

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**Abstract:** The thymus-parathyroid unit (TPU) occurring in adults is rare.

The main symptoms and important clinical findings are as follows: 2 patients presented with neomercazole-resistant Basedow–Graves disease. A third patient presented with thyroid nodules and a fourth patient with a neck mass after thyroid resection for medullary thyroid carcinoma.

The main diagnoses were those of thyroid nodules (either in the context of goiter, or not). In the fourth case the diagnosis was of thyroid medullary carcinoma recurrence in the neck.

Thyroidectomy was performed in the 2 cases of Basedow–Graves disease and in the third case (wherein selective neck dissection was also performed). In the fourth case, a neck dissection was performed for a possible medullary carcinoma recurrence.

A TPU was microscopically detected in 2 cases with perithyroid location, on thyroidectomies for Basedow–Graves disease and in the 2 other cases with neck soft tissue location (associated with thyroid papillary carcinoma and thyroid medullary carcinoma extension). Postsurgical hypocalcemia requiring treatment occurred in both patients with Basedow–Graves disease and in the fourth patient.

The presence of TPU should be acknowledged because such lesions can be misdiagnosed as suspect lymph nodes during thyroid surgery for malignant tumors.

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**Abbreviation**: TPU = thymus-parathyroid unit.

## INTRODUCTION

Thymus-parathyroid unit (TPU) (parathymus) occurring in adults is rare, reported in the perithyroid/thyroid and cervical location[1–10] when extrathoracic and extrathymic. Rare cases of parathyroid adenomas, in the context of parathyroid hyperfunction or thymic cyst, have been reported as developing in such units.[1,3,7,9] In the present study, we discuss the features observed in 2 cases where TPU was noted in the perithyroid site (diagnosed during thyroid surgery for Basedow–Graves disease), as well as 2 cases wherein TPU was located in the neck.

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## CASE REPORTS

Two patients (a woman and a man, aged 28 and 27 years, respectively) diagnosed with Basedow–Graves disease presented with perithyroid TPU. The Basedow–Graves disease was diagnosed at the age of 25 and 24 years, respectively; both patients showed tachycardia, loss of body weight, and bilateral exophtalmia. For the first patient (woman), the serum anti-TSH antibodies were 32.1 (positive, >1.5 UI/L), the antithyroperoxidase antibodies 123 UI/mL (normal, <34), and thyroid function tests showed <0.01 mU/L; 9.93 and 59 pmol/L for TSH, T3 and T4, respectively (normal ranges, 0.27–4.20 mU/L, 3.10–6.80 and 12–22 pmol/L, respectively). Ioduria was normal. This patient also showed persistent hypoleucocytemia with neutropenia (without positivity for HIV, viral hepatitis virus or tuberculosis tests) as well as a history of hyperprolactinemia in relation with a hypophysal microadenoma diagnosed on magnetic-resonance-imaging at the age of 25 and treated by cabergoline. Furthermore, ultrasound examination showed a normally sized thyroid with heterogeneous echogenicity and with several hypoechogenic nodules (2-mm). No jugulocarotid adenopathy was detected. For the second case, the serum levels of anti-TSH antibodies was 4.7 UI/L, of TSH were 0.04 mU/L, and of T4 were 18.7 pmol/L. The thyroid showed bilateral homogeneous goiter-like aspects. Both patients were treated by neomercazole (and propranolol for the female patient), but the anti-TSH antibodies remained high, although fluctuating. Both patients underwent total thyroidectomy. Macroscopic and microscopic features were consistent with Basedow–Graves disease; the thyroid parenchyma showed dystrophic vesicles, multifocal inflammation, fibrosis, and rare calcifications. A TPU consisting of parathyroid and thymic tissues was detected in the perithyroid fat. The parathyroid and the thymus were focally separated from the thyroid capsule by sparse adipocytes (Figure 1). The parathyroid tissue appeared normal and showed some adipocytes and chief cells (some with water-clear cytoplasm). The parathyroid, which was surrounded almost entirely by a capsule was focally in contact with the thymic tissue (Figure 1). In addition, the thymic tissue, which was also almost completely surrounded by a capsule appeared normal (with both cortical and medulla). Several Hassal corpuscles were noted, some of which were calcified. In one of the cases, one other parathyroid, (normal), was detected in the perithyroid adipose tissue at distance from the TPU. Postoperatively, both patients showed hypocalcemia (1.72 and 1.64 mmol/L, respectively) thereby requiring medication.

For the other 2 cases, the TPU was observed on the central neck dissection specimen, which was performed in the third case during thyroidectomy for thyroid papillary carcinoma (woman, 42-years) and in the fourth, for thyroid medullary carcinoma extension.[3] For the third case, the ultrasound-examination showed a homogeneous right thyroid lobe and 2 adjacent hypoechogenic nodules (3 and 1.6-cm) with microcysts,

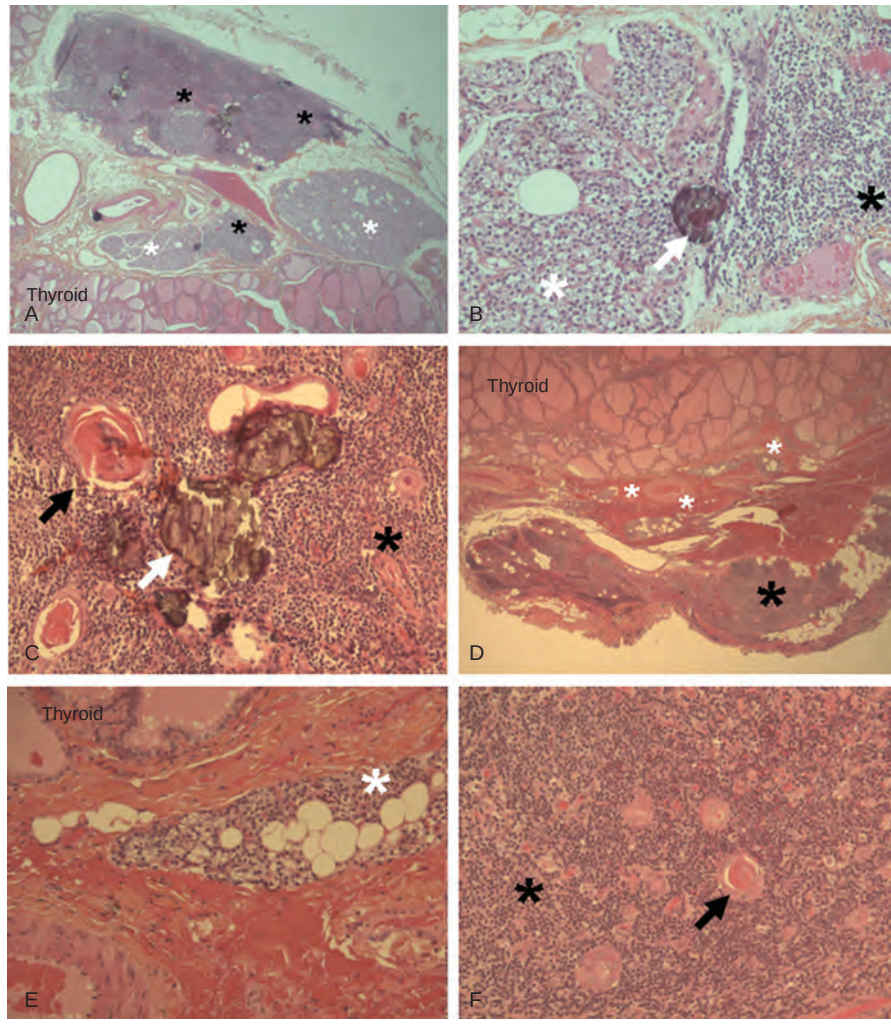


**FIGURE 1.** In the 2 cases of perithyroid TPU (cases 1 and 2) (A, B, C, and D, E, F, respectively), the thymic tissue was situated in the perithyroid tissue, focally separated either by parathyroid tissue or by fibroadipose tissue (A and D, respectively). Thymic and parathyroid tissues were focally separated by an inconspicuous fibrous layer or a calcified Hassal corpuscle (B) or adipose tissue (D and E). The thymic tissue contains several Hassal corpuscles, some of them calcified (A, B, C, and F). The thyroid tissue showed enlarged vesicles (A, D, and E). The white asterisks indicate the parathyroid, the black asterisks the thymic tissue. The white arrows indicate Hassal corpuscles (calcified), the black arrows uncalcified Hassal corpuscles. Hematoxylin-and-eosin stain, original magnification×2.5 (A and D) and ×20 (B, C, E, and F). TPU = thymus-parathyroid unit.

microcalcifications, and hypervascularisation. There was no jugulocarotid adenopathies. Further, in the fourth case, the follow-up positron-emission-computed-tomography showed 3 hypermetabolic foci of paratracheal and right hilar, subcarina location. Postoperatively, hypocalcemia occurred in case 4, requiring treatment.

In both cases, the neck resection specimen did not show thyroid tissue. The parathyroid tissue, which was situated between the thymic lobules (Figure 2), showed an incomplete capsule and comprised chief cells and focally oncocytic cells. Sparse adipocytes were also seen. The thymic lobules showed Hassal corpuscles (some with calcifications). In addition, an epithelial microcyst was found in the fourth case and another parathyroid.[3] In the other case, parathyroid cells, some of which had clarified cytoplasm, were focally found in direct contact with or intermingled within the thymus (Figure 2).

## DISCUSSION

Here we report the features observed for 2 cases of TPU at a perithyroid location, both of which were incidentally diagnosed upon the inspection of thyroidectomy specimens obtained for Basedow–Graves disease. Features were similar to those previously observed in the cases reported in 1928 and in 2001,[2,10] occurring in the context of Basedow disease and lymphocytic thyroiditis with adenoma. However, in one of the cases presented here, both parathyroid and thymic tissues were observed in direct proximity to the thyroid capsule. The 2 cases showing perithyroid thymus were both young adults and had been diagnosed with Basedow–Graves thyroiditis. In the report of a large series of patients with Basedow–Graves disease,[11] ectopic thymus was observed in 1.8% of patients but at a cervical location. The pathogenesis of the perithyroid thymus, is not completely elucidated. One hypothesis suggests

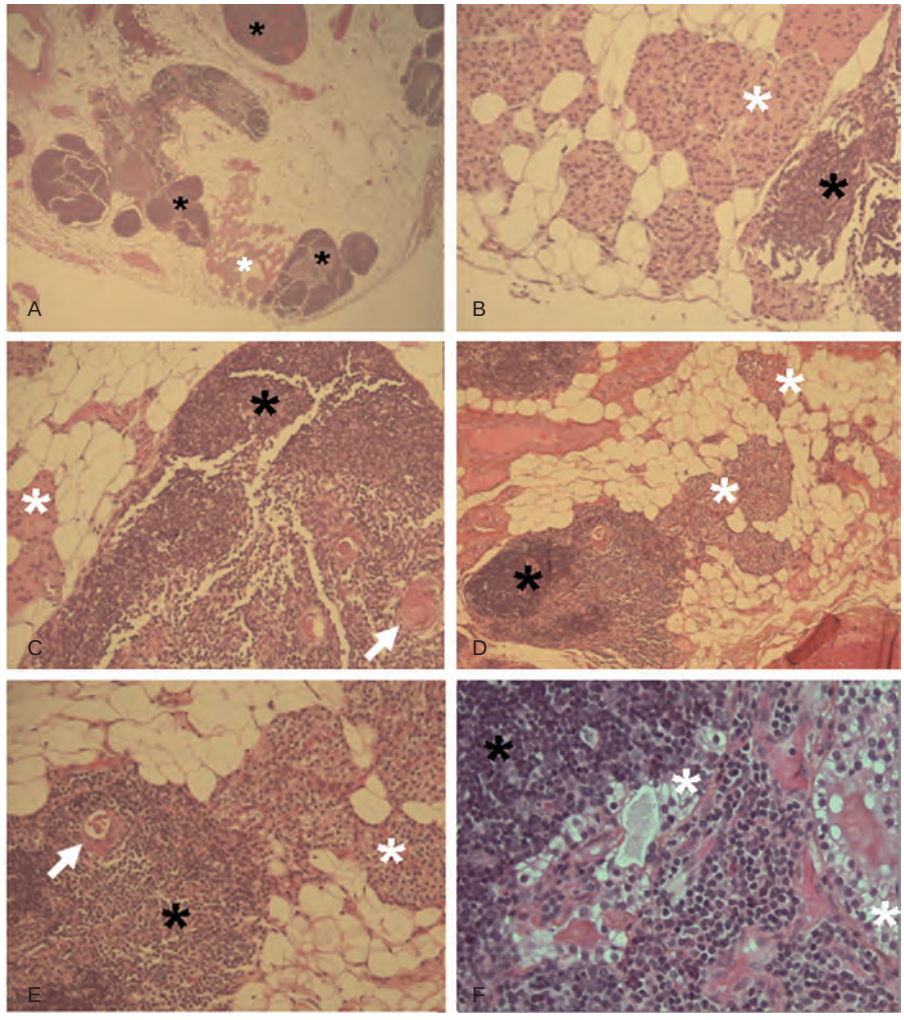


**FIGURE 2.** In the 2 cases of cervical TPU (cases 3 and 4) (A, B, C and D, E, F, respectively), the parathyroid tissue was situated between thymic lobules (A–F), separated either by a thin fibrous capsule, or at contact or intermingled with thymic tissue (B, C, E, and F). The thymic tissue contained several Hassal corpuscles (C and D). The white asterisks indicate the parathyroid, the black asterisks the thymic tissue. The white arrows indicate Hassal corpuscles (uncalcified), hematoxylin-and-eosin stain, original magnification×2.5 (A), ×5 (D), ×20 (B, C, and E), and ×40 (F). TPU = thymus-parathyroid unit.

that the incomplete migration of the thymus during embryogenesis results in its ectopic presence within the perithyroid tissue, along with the parathyroid.[2,10,12] Furthermore, the fact that the TPU may occur in adults in the neck at a distance from the thyroid (as observed in 2 cases), in addition to the presence of intermingled parathyroid cells in the thymic lobule, also favors the hypothesis of developmental abnormalities of the third and/or fourth pharyngeal pouches. A direct fusion of thymus and parathyroid has been reported in 65-mm-fetus and older fetus, being known as the parathymus.[13,14] Water-clear cell buds, similar to the clear cells we observed in the cervical thymus of patient 3, were already mentioned in 1937 as rudiments present in the embryofetal life.[13] Moreover, the coexistence of thymic and parathyroid tissues has been reported in the subangulomaxillary region,[4] incidentally, or in the context of hyperparathyroidism in esophageal and jaw sites, in association or not with the adenomatous parathyroid.[7,9] However, one may question whether metabolic factors related to iodine intake could also be involved in the development of abnormal perithyroid thymus because increased iodine has been reported to result in perithyroid thymic tissue occurrence as demonstrated in rat models wherein the perithyroid/thyroid lymphoid tissue with thymus-like CD4/CD8/Tdt immunophenotype and without Hassal corpuscles appeared more frequently after consuming enriched-iodine than after normal-iodine or low-iodine diets.[15] Iodine intake is difficult to retrospectively evaluate. The presence of a normal ioduria in one patient, with Basedow–Graves disease, in which this analysis was performed, does not favor the hypothesis of iodine-induced thymic tissue. However, the finding of high levels of anti-TSH antibodies in both patients could be representative of an increased tolerance toward thyroid autoantigens, including during neomercazole treatment. Moreover, the presence of persistent neuropenia may suggest a specific immunological profile with regard to the evolution of the disease and response type to treatments.

The clinical significance of TPU diagnosed on thyroidectomy specimens performed for a benign inflammatory, autoimmune disease is limited except the postsurgical

hypocalcemia, which may occur similarly to patients having the cervical unit and which may require treatment. However, the differential diagnosis with perithyroid lymph node metastases of thyroid tumors, such as papillary or medullary carcinomas may rise as thymic Hassal corpuscles may also show calcifications on imaging procedures. Although rare, the presence of parathyroid cells intermingled with thymic tissue (as we have observed in one of the cervical units) warrants further interest because of eventual abnormalities related to an parathyroid hormone secretion or, to a lesser extent, immunological disturbances, since in adults.

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