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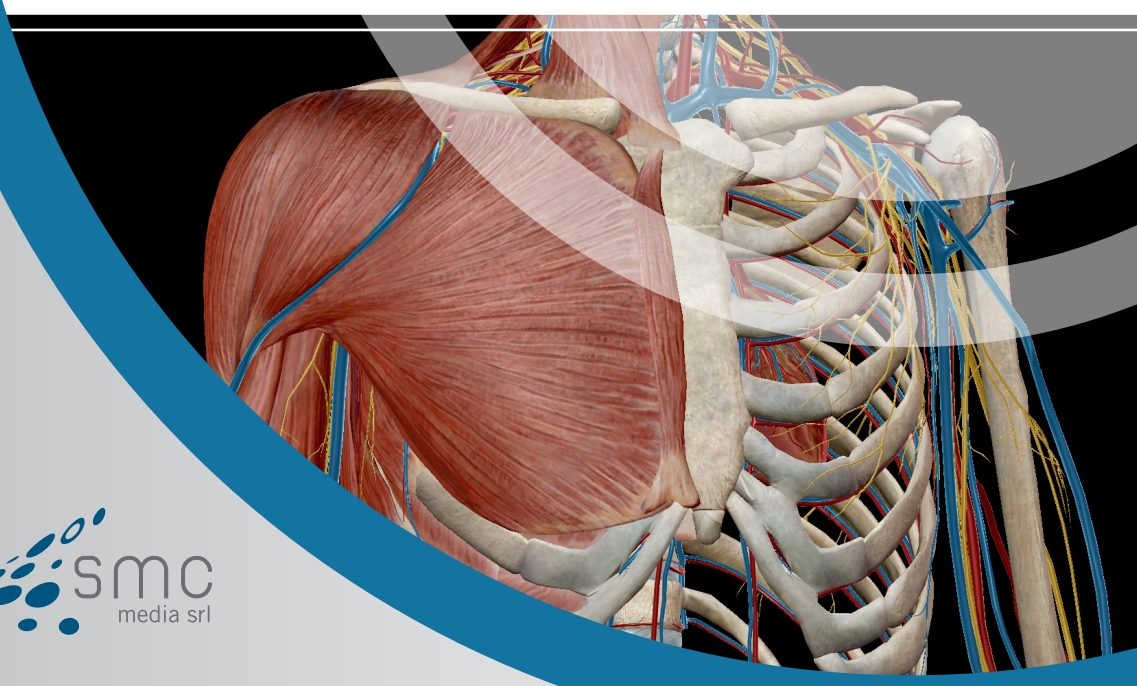

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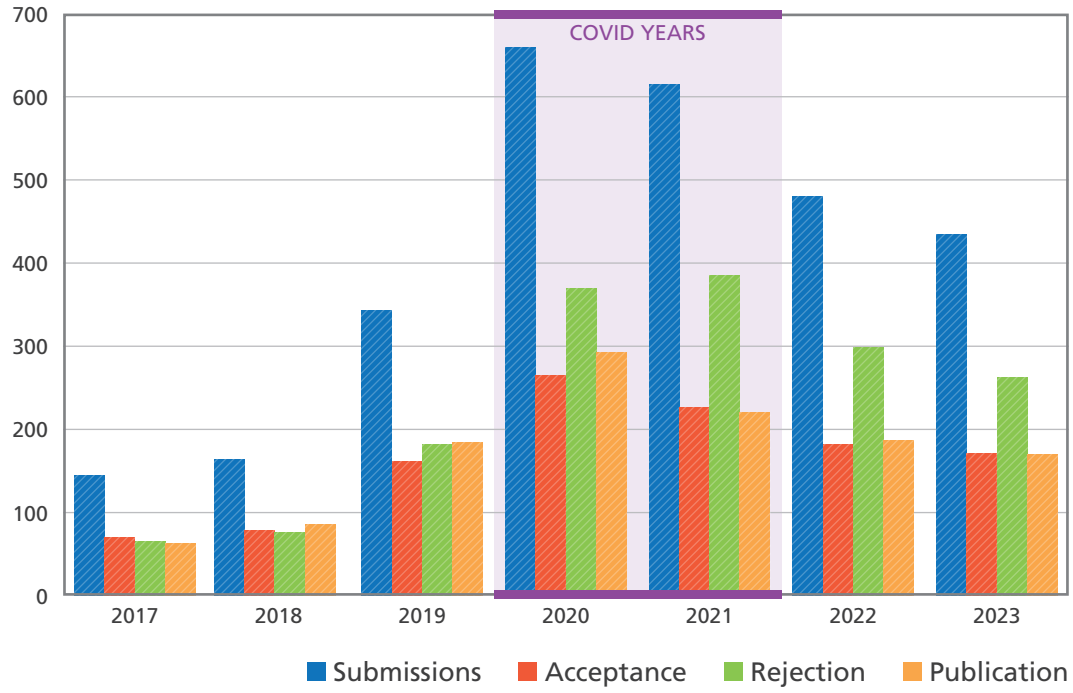

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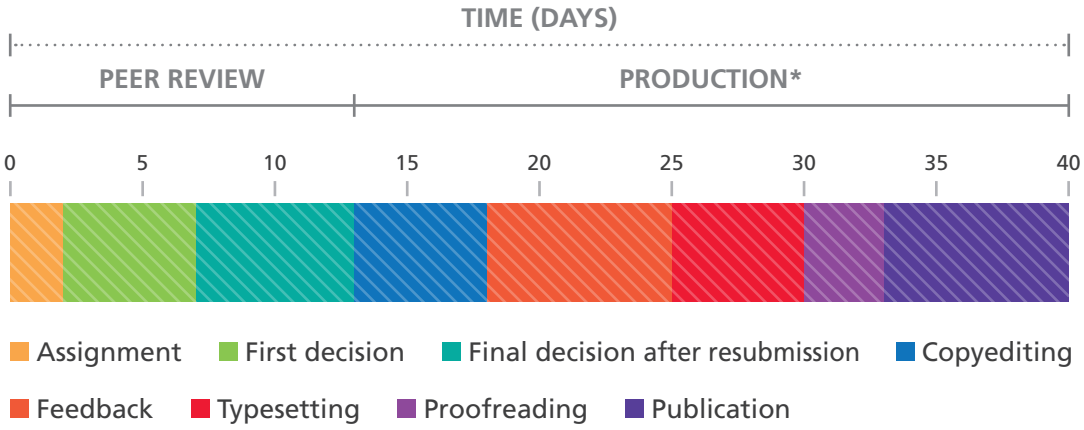

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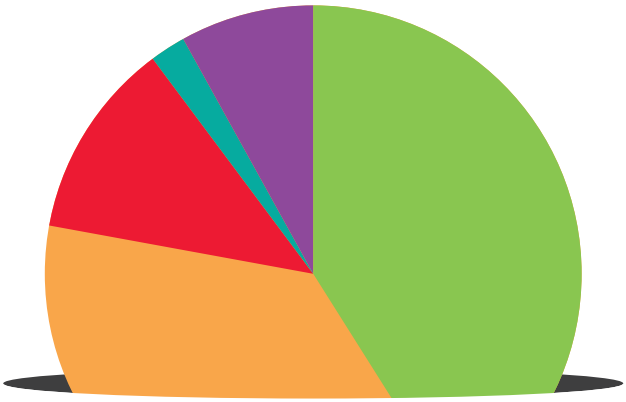

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THYROTROPIN SECRETING PITUITARY ADENOMA: A CLINICAL CASE OF POSTOPERATIVE RE-ONSET THYROTOXICOSIS WITH ADENOMA RECURRENCE

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ABSTRACT

We report a case of a 19-year-old young male presenting with thyrotoxicosis with inappropriately elevated TSH. Magnetic resonance imaging revealed a pituitary adenoma (8.2 x 9.7 mm), TRH stimulation test showed abnormal blunted TSH response, and serum glycoprotein hormone alpha-sub-unit was elevated. He had no family history of thyroid disease and TRβ genetic testing excluded resistance to thyroid hormone action. The diagnosis of thyrotropin-secreting pituitary adenoma (TSHoma) was presumed and long-acting somatostatin analogue was promptly initiated. After two months of octreotide treatment, serum TSH and FT3 returned to within normal ranges. Tumour resection by transsphenoidal surgery was performed and, ten days after surgery, clinical hypothyroidism was achieved, despite detectable TSH levels (TSH 1.02 µU/ml[RR 0.27-4.2]). Although the patient remained euthyroid for the following three years, there was a gradual biochemical elevation in the levels of TSH, FT4, and FT3 over time, reaching serum values above the normal limit in the third year after surgery. Imaging did not show neoplasm recurrence at this point. After two years, the patient presented with clinical manifestations of re-onset thyrotoxicosis, with MRI revealing a T2 hypersignal oval area compatible with a pituitary adenoma. Adenectomy was performed. Histopathological and immunohistochemical analyses revealed a pituitary adenoma with transcription factor PIT1 expression and positivity for TSH and PRL. TSHoma treatment may not be always effective in the first therapeutic approach and recurrences are a possibility, making follow-up essential. The present case highlights the heterogeneity of post-treatment cure criteria and their limitations.

KEYWORDS

Pituitary adenoma, thyrotoxicosis, hyperthyroidism, thyrotropin, neurosurgery

LEARNING POINTS

- Thyrotropin-secreting pituitary adenomas are rare benign tumours. Proper diagnosis can be challenging, requiring TSH autonomous production and differentiation from resistance to thyroid hormone action (RTH).
- Undetectable TSH levels one week after surgery and/or positive T3 suppression test or no response to TRH stimulation test seem to be the criteria with the best prognostic value post-treatment.
- Close clinical, biochemical and imaging follow-up is crucial to detect TSHoma recurrence.

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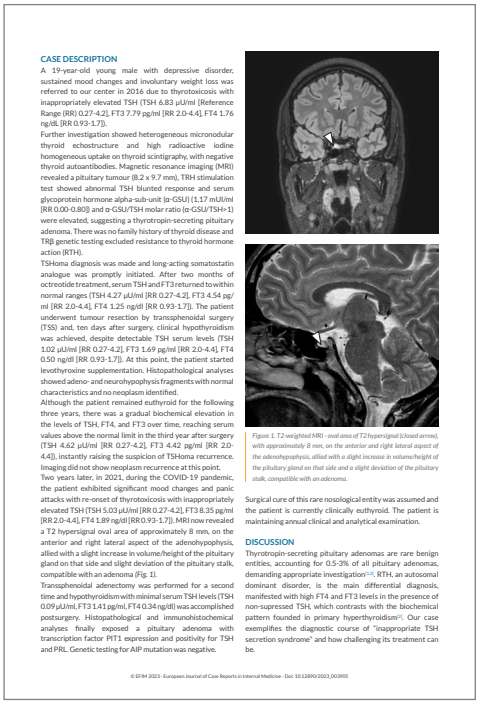

CASE DESCRIPTION

A 19-year-old young male with depressive disorder, sustained mood changes and involuntary weight loss was referred to our center in 2016 due to thyrotoxicosis with inappropriately elevated TSH (TSH 6.83 µU/ml [Reference Range (RR) 0.27-4.2], FT3 7.79 pg/ml [RR 2.0-4.4], FT4 1.76 ng/dL [RR 0.93-1.7]).

Further investigation showed heterogeneous micronodular thyroid echostructure and high radioactive iodine homogeneous uptake on thyroid scintigraphy, with negative thyroid autoantibodies. Magnetic resonance imaging (MRI) revealed a pituitary tumour (8.2 x 9.7 mm). TRH stimulation test showed abnormal TSH blunted response and serum glycoprotein hormone alpha-sub-unit (α-GSU) (1.17 uUI/ml [RR 0.00-0.80]) and α-GSU/TSH molar ratio (α-GSU/TSH×1) were elevated, suggesting a thyrotropin-secreting pituitary adenoma. There was no family history of thyroid disease and TRβ genetic testing excluded resistance to thyroid hormone action (RTH).

TSHoma diagnosis was made and long-acting somatostatin analogue was promptly initiated. After two months of octreotide treatment, serum TSH and FT3 returned to within normal ranges (TSH 4.27 µU/ml [RR 0.27-4.2], FT3 4.54 pg/ml [RR 2.0-4.4], FT4 1.25 ng/dl [RR 0.93-1.7]). The patient underwent tumour resection by transsphenoidal surgery (TSS) and, ten days after surgery, clinical hypothyroidism was achieved, despite detectable TSH serum levels (TSH 1.02 µU/ml [RR 0.27-4.2], FT3 1.69 pg/ml [RR 2.0-4.4], FT4 0.50 ng/dl [RR 0.93-1.7]). At this point, the patient started levothyroxine supplementation. Histopathological analyses showed adeno- and neurohypophysis fragments with normal characteristics and no neoplasm identified.

Although the patient remained euthyroid for the following three years, there was a gradual biochemical elevation in the levels of TSH, FT4, and FT3 over time, reaching serum values above the normal limit in the third year after surgery (TSH 4.62 µU/ml [RR 0.27-4.2], FT3 4.42 pg/ml [RR 2.0-4.4]), instantly raising the suspicion of TSHoma recurrence. Imaging did not show neoplasm recurrence at this point.

Two years later, in 2021, during the COVID-19 pandemic, the patient exhibited significant mood changes and panic attacks with re-onset of thyrotoxicosis with inappropriately elevated TSH (TSH 5.03 µU/ml [RR 0.27-4.2], FT3 8.35 pg/ml [RR 2.0-4.4], FT4 1.89 ng/dl [RR 0.93-1.7]). MRI now revealed a T2 hypersignal oval area of approximately 8 mm, on the anterior and right lateral aspect of the adenohypophysis, allied with a slight increase in volume/height of the pituitary gland on that side and slight deviation of the pituitary stalk, compatible with an adenoma (Fig. 1).

Transsphenoidal adenectomy was performed for a second time and hypothyroidism with minimal serum TSH levels (TSH 0.09 µU/ml, FT3 1.41 pg/ml, FT4 0.34 ng/dl) was accomplished postsurgery. Histopathological and immunohistochemical analyses finally exposed a pituitary adenoma with transcription factor PIT1 expression and positivity for TSH and PRL. Genetic testing for AIP mutation was negative.

Figure 1. T2-weighted MRI - oval area of T2 hypersignal (closed arrow), with approximately 8 mm, on the anterior and right lateral aspect of the adenohypophysis, allied with a slight increase in volume/height of the pituitary gland on that side and a slight deviation of the pituitary stalk, compatible with an adenoma.

Surgical cure of this rare nosological entity was assumed and the patient is currently clinically euthyroid. The patient is maintaining annual clinical and analytical examination.

DISCUSSION

Thyrotropin-secreting pituitary adenomas are rare benign entities, accounting for 0.5-3% of all pituitary adenomas, demanding appropriate investigation[1,2]. RTH, an autosomal dominant disorder, is the main differential diagnosis, manifested with high FT4 and FT3 levels in the presence of non-supressed TSH, which contrasts with the biochemical pattern founded in primary hyperthyroidism[2]. Our case exemplifies the diagnostic course of "inappropriate TSH secretion syndrome" and how challenging its treatment can be.

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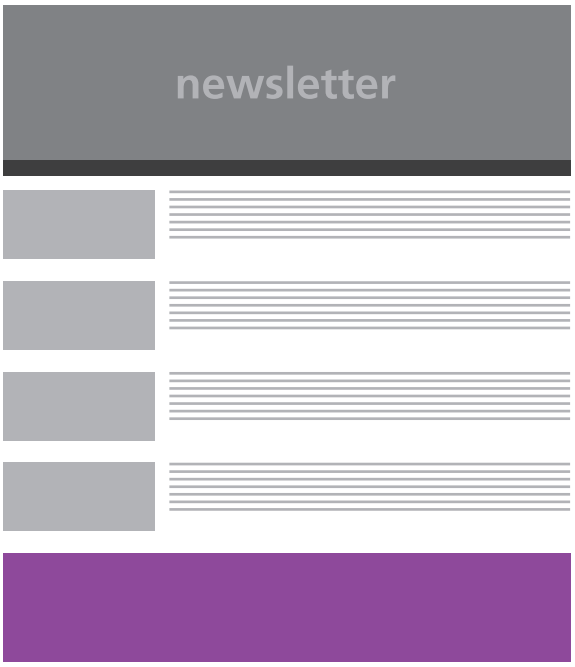

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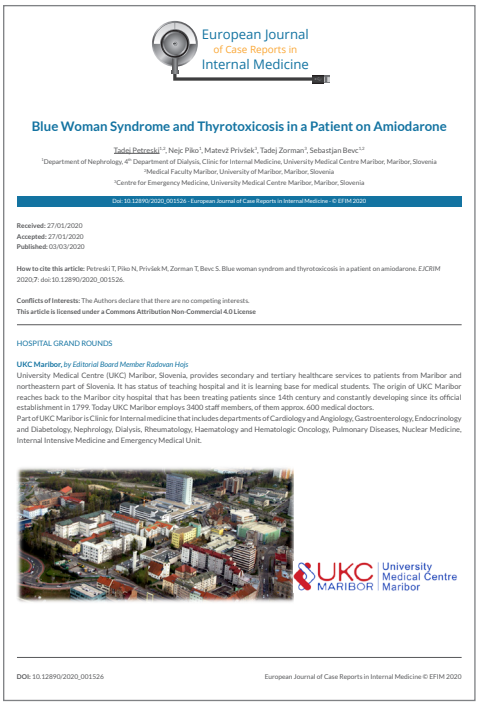

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Blue Woman Syndrome and Thyrotoxicosis in a Patient on Amiodarone

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A 28-Year-Old Woman with Ascites and Multiple Focal Spleen Lesions

Alice Pirovano[1], Erica Matino[1], Erika Zecca[1], Martina Costanzo[1], Alessandro Croce[1], Monica Leutner[2], Raffaele Romito[2], Mario Pirisi[1,2]

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Public University Hospital Maggiore della Carità, Novara, Italy *by Editorial Board Member, Prof. Ettore Bartoli*

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