
CASE REPORT

Paraparesis and Bipolar Affective Disorder Episodes of Depression in Graves' Disease with Thyroid Cancer Patient

Yohana Prima Ceria Anindita^{1*}, Zaki Mita Kusumaadhi¹, Tania Tedjo Minuljo¹, K. Heri Nugroho HS¹, Suryadi², Alifiati Fitrikasari³, Subiyakto⁴, Dik Puspasari⁵

- 1 Division of Metabolic Endocrine, Department of Internal Medicine, Faculty of Medicine, RSUP Dr. Kariadi/Universitas Diponegoro
- 2 Department of Neurology, Faculty of Medicine, RSUP Dr. Kariadi/Universitas Diponegoro
- 3 Department of Psychiatry, Faculty of Medicine, RSUP Dr. Kariadi/Universitas Diponegoro
- 4 Division of Surgical Oncology, Department of Surgery, Faculty of Medicine, RSUP Dr. Kariadi/Universitas Diponegoro
- 5 Department of Anatomical Pathology Faculty of Medicine, RSUP Dr. Kariadi/Universitas Diponegoro

*Corresponding author:

Yohana Prima Ceria Anindita, MD.

Division of Metabolic Endocrine, Department of Internal Medicine, RSUP Dr. Kariadi/Fakultas Kedokteran Universitas Diponegoro, Semarang, Jawa Tengah, Indonesia.

Email: ceriaanindita@gmail.com

ABSTRACT

Thyroid nodules in Graves' disease raise awareness of thyroid cancer. Thyrotoxicosis in patients with thyroid cancer suggests extensive metastases or large tumours. Hyperthyroidism or thyrotoxicosis can exacerbate symptoms of anxiety, depression, mood lability, and insomnia in patients with bipolar disorder. We present a rare case, a 29-year-old woman with a history of Graves' variant nodule and bipolar affective disorder since the age of 17, was admitted to the hospital for paraparesis within a month. Patients also complain of sleeplessness, hopelessness, and fatigue. The patient has been taking Thiamazole 10 mg twice daily, Propranolol 20 mg twice daily, Alprazolam 0.5 mg trice daily, Haloperidol 5 mg nightly, Trihexyphenidyl 2 mg daily, Lamotrigine 100 mg twice daily but not routinely. History of partial thyroidectomy 10 years ago with pathology results was said to be benign. Neurological examination: bilateral lower extremity motor weakness with a value of 2/5 muscle function. MRI of the spine with contrast: changes in signal intensity in the vertebral bodies C.2, C.4, C.5, Th.2 - tend to bone metastases. Thyrotoxicosis thyroid function test results (free T₄ = 66.71 pmol/L (N = 10.6 - 19.4); TSHs < 0.05 uIU/mL (0.51 - 4.94 uIU/mL) and thyroid scintigraphy showed toxic multinodular goiter (cold nodule) with high thyroid uptake. A total thyroidectomy was performed, and the pathology result revealed papillary thyroid cancer. Thyroid cancer can occur together with Graves' disease. Graves' disease-associated cancers were more often metastatic to distant sites such as spinal metastases that significantly increases morbidity and mortality. Thyrotoxicosis was associated with regional metabolic changes of limbic structures that mediate affect in patients with bipolar affective disorder.

Keywords: Graves' disease, thyroid cancer, bipolar disorder

INTRODUCTION

Thyroid nodules are frequently found in patients with Graves' disease. The presence of these nodules raises concern about co-existent thyroid carcinoma.¹ The reported incidence of nodules in Graves' disease varies from 12,8% to 33.6%. Around 10-15% of nodules associated with Graves' disease are reported to be thyroid cancers with papillary thyroid cancer being the commonest histopathology.¹ During the past few years, there has been growing recognition that thyroid-stimulating antibodies (TSABs) may enhance the growth and function of differentiated malignant thyroid cells.² Increased aggressiveness of thyroid cancers in patients with coexistent Graves' disease and suggested that, in these patients, monitoring (and attempting to lower) TSABs may be as important as suppressing the release of thyrotropin by the pituitary.^{2,3}

Thyrotoxicosis in patients with thyroid cancer was of patients with extensive metastatic involvement or a large tumor. The bone is the second most common location to which thyroid cancer is known to metastasize, affecting 3% of patients with thyroid cancer.⁴ Neuropsychiatric symptoms, such as mood disturbances and cognitive impairment, are very common among patients with thyroid disorders.⁵ Hyperthyroidism or thyrotoxicosis is usually associated with symptoms such as anxiety, depression, mood lability, and insomnia in patients with bipolar disorder. However, overt psychiatric disorder is rare and occurs in only about 10% of the patients.⁶

CASE PRESENTATION

A 29-year-old woman was admitted to the hospital complaining of progressive loss of muscle strength in the lower limbs. Within a month of evolution, this case had recently been followed by paraparesis. The patient already partially cared dependent. Patients also complain of sleeplessness, hopelessness, and fatigue. Her past medical history was Graves' variant nodule and bipolar affective disorder since the age of 17. The patient has been taking Thiamazole 10 mg twice daily, Propranolol 20

mg twice daily, Alprazolam 0.5 mg trice daily, Haloperidol 5 mg nightly, Trihexyphenidyl 2 mg daily, Lamotrigine 100 mg twice daily but not routinely. History of partial thyroidectomy 10 years ago with pathology results was said to be benign.

On neurological examination, there was bilateral lower extremity motor weakness with a value of 2/5 muscle function. On mental status examination determined that she was alert and oriented, fairly groomed in an appropriate dress with good eye contact, and polite and cooperative with the interview and exam. Her speech was not pressured, loud, or rapid. She denied auditory and visual hallucinations, suicidal ideation and homicidal ideation. However, she did sleeplessness, hopelessness, and fatigue. Her thought processes were linear, no looseness of associations or ideas of reference. Her cognition and memory were intact. It was established the diagnosis of bipolar affective disorder episodes of depression and the patient received treatment with Alprazolam 0,5 mg twice daily and Lamogritine 100 mg nightly. An MRI of the spine with contrast was performed and revealed changes in signal intensity in the vertebral bodies C.2, C.4, C.5, Th.2 - tend to bone metastases (Figure. 1).



Figure 1. Spinal MRI - notice changes signal intensity

Thyrotoxicosis thyroid function test results (free T4 = 66.71 pmol/L (N = 10.6 - 19.4); TSHs < 0.05 uIU/mL (0.51 - 4.94)) and thyroid scintigraphy showed toxic multinodular goiter (cold nodule) with high thyroid uptake. The patient was then referred to the Division of Oncology Surgery. Interdisciplinary consultation recommended total thyroidectomy as a therapeutic approach. The patient was prepared psychologically for the accomplishment of total thyroidectomy with full acceptance. During the surgical procedure, it was noticed that the lobes had an irregular shape and had a multinodular structure (Figure. 2). Thyroid pathological examination revealed a papillary thyroid carcinoma.



Figure 2. Macroscopic aspect of thyroid after excision - irregular shape and a multinodular structure.

DISCUSSION

The only clinical feature that initially distinguished this patient's thyroid from that of Graves' disease was the firm nodule within the right and left thyroid gland. Thyrotoxicosis in patients with thyroid cancer were of patients with extensive metastatic involvement or a large tumor. These tumors have almost always been follicular carcinomas or occult papillary carcinoma.⁷ Thyroid cancer was detected in patients with Graves' disease with a frequency 2.5-fold that among patients with autonomous thyroid nodules, and the Graves' disease associated cancers were more often multifocal, locally invasive, and metastatic to lymph nodes or distant sites (10-fold) than were the cancers in patients with autonomous thyroid nodules.⁸ We suspect that the growth and function of the tumor in our patient were modulated by thyroid-stimulating autoantibodies.

Among all the variants of thyroid carcinomas, follicular thyroid carcinoma (FTC) is the most likely to present with distant metastasis or metastasize during the disease.⁹ It is estimated that metastatic disease develops in 7-23% of FTC cases and its initial presentation occurs in 1-4%. When present, it normally leads to a worse prognosis and constitutes the main mortality factor.⁹ Bone and lung are the most likely locations for metastatic disease in FTC.¹⁰ In a series of 444 patients with thyroid carcinoma and distant metastasis, 44% of them had bone involvement, and among these, 36% were diagnosed with FTC. According to the literature, over 80% of bone metastasis of all tumors are mainly located in the axial skeleton, namely vertebrae, ribs and basin.¹¹ Metastasis of thyroid carcinomas is preferentially osteolytic, being in pain is the most common manifestation found at its presentation, followed by pathological fractures¹¹, and rarely, medullary compression symptoms¹², as in this clinical case.

In this case, the patient was diagnosed with bipolar affective disorder episodes of depression. Hyperthyroidism is frequently associated with irritability, insomnia, anxiety, restlessness, fatigue, and impairment in

concentrating and memory, these symptoms can be episodic or may develop into mania and depression.¹³ However, overt psychiatric disorder is rare and occurs in only about 10% of the patients.¹⁴ Thyrotoxicosis and attendant psychological symptoms were associated with regional metabolic changes of limbic structures that mediate affect. Psychiatric symptoms in hyperthyroidism, such as anxiety or mania, appear to be mediated by beta-adrenergic hyperactivity.¹⁵

CONCLUSION

Thyroid neoplasms usually have an indolent behavior and patients are commonly asymptomatic. Metastatic disease is uncommon as an initial manifestation but, when present, it assumes a later stage of the disease along with a worse prognosis. Paraparesis is a rare form of presentation of thyroid carcinoma. Hyperthyroidism or thyrotoxicosis is usually associated with symptoms such as anxiety, depression, mood lability, and insomnia in patients with bipolar disorder; early treatment of the hormone or metabolic alteration can minimize the morbidity of a secondary psychopathology.

REFERENCES

1. Khan SH, Rather TA, Makhdoomi R, Malik D. Nodular Graves' disease with medullary thyroid cancer. *Indian J Nucl Med.* 2015 ;30(4):341-4.
2. Li C, Yu W, Fan J, Li G, Tao X, Feng Y, Sun R. Thyroid functional parameters and correlative autoantibodies as prognostic factors for differentiated thyroid cancers. *Oncotarget.* 2016;7(31):49930-8.
3. Yoon JH, Jin M, Kim M, Hong AR, Kim HK, Kim BH, Kim WB, Shong YK, Jeon MJ, Kang HC. Clinical Characteristics and Prognosis of Coexisting Thyroid Cancer in Patients with Graves' Disease: A Retrospective Multicenter Study. *Endocrinol Metab (Seoul).* 2021;36(6):1268-76.
4. Fu H, Cheng L, Jin Y, Chen L. Thyrotoxicosis with concomitant thyroid cancer. *Endocr Relat Cancer.* 2019;26(7):R395-R413.
5. Lekurwale V, Acharya S, Shukla S, Kumar S. Neuropsychiatric Manifestations of Thyroid Diseases. *Cureus.* 2023;15(1):e33987.
6. Chakrabarti S. Thyroid functions and bipolar affective disorder. *J Thyroid Res.* 2011;2011:306367.
7. Ono Y, Ono S, Yasunaga H, Matsui H, Fushimi K, Tanaka Y. Factors Associated With Mortality of Thyroid Storm: Analysis Using a National Inpatient Database in Japan. *Medicine (Baltimore).* 2016;95(7):e2848.
8. Keskin C, Sahin M, Hasanov R, Aydogan BI, Demir O, Emral R, Gullu S, Erdogan MF, Gedik V, Uysal AR, Baskal N, Corapcioglu D. Frequency of thyroid nodules and thyroid cancer in thyroidectomized patients with Graves' disease. *Arch Med Sci.* 2019;16(2):302-7.
9. Parameswaran R, Shulin Hu J, Min En N, Tan WB, Yuan NK. Patterns of metastasis in follicular thyroid carcinoma and the difference between early and delayed presentation. *Ann R Coll Surg Engl.* 2017;99(2):151-4.
10. Matta-Coelho C, Simões-Pereira J, Vilar H, Leite V. Bone Metastases from Thyroid Carcinoma of Follicular Origin: A Single Institutional Experience. *Eur Thyroid J.* 2019;8(2):96-101.
11. Baião JM, Guimarães A, Moreira N, Correia JG, Rosenvinge CU, Gonçalves D, Calvo MA. Acute paraparesis as presentation of an occult follicular thyroid carcinoma: A case report. *Int J Surg Case Rep.* 2017;41:498-501.
12. Iñiguez-Ariza NM, Bible KC, Clarke BL. Bone metastases in thyroid cancer. *J Bone Oncol.* 2020;21:100282.
13. Li L, Zhi M, Hou Z, Zhang Y, Yue Y, Yuan Y. Abnormal brain functional connectivity leads to impaired mood and cognition in hyperthyroidism: a resting-state functional MRI study. *Oncotarget.* 2017;8(4):6283-94.

14. Zimmerman M, Morgan TA, Stanton K. The severity of psychiatric disorders. *World Psychiatry*. 2018;17(3):258-75.
15. Göbel A, Heldmann M, Göttlich M, Dirk AL, Brabant G, Münte TF. Effect of Mild Thyrotoxicosis on Performance and Brain Activations in a Working Memory Task. *PLoS One*. 2016;11(8):e0161552.

