Journal of Experimental and Clinical Medicine

Case Report

doi: 10.5835/jecm.omu.31.01.010

Thyrotropin-secreting pituitary macroadenoma presented with pulmonary embolism

Elif Kılıç Kan[a*], Gülçin Cengiz Ecemiş[a], Çiğdem Tura Bahadır[a], Hulusi Atmaca[a], Nurhan Köksal[b], Ayşegül Atmaca[a]

[a] *Department of Endocrinology and Metabolism, Faculty of Medicine, Ondokuz Mayis University, Samsun, Turkey*
[b] *Department of Pulmonary Diseases, Faculty of Medicine, Ondokuz Mayis University, Samsun, Turkey*

ARTICLE INFO

Article History
Received 08 / 01 / 2013
Accepted 29 / 07 / 2013

*** Correspondence to:**
Elif Kılıç Kan
Department of Endocrinology and Metabolism, Faculty of Medicine,
Ondokuz Mayis University,
Samsun, Turkey
e-mail: elifkilickan@yahoo.com

Keywords:
Hypercoagulability
Hyperthyroidism
Pulmonary embolism
Pituitary adenom

ABSTRACT

Although studies have indicated that hyperthyroidism is associated with pulmonary embolism, an association with thyroid stimulating hormone-producing pituitary adenoma (TSHoma) and pulmonary embolism has not been reported so far. A 43 year-old man hospitalized in the pulmonary diseases department with the diagnosis of pulmonary embolism. Thyroid function tests revealed increased thyroid hormone concentrations in the presence of inappropriately elevated serum TSH levels. Pituitary magnetic resonance imaging showed a 15 mm macroadenoma. Serum concentrations of the alpha-subunit of TSH (αTSH) and the αTSH/TSH molar ratio were 2.7 IU/L and 2.7, respectively. He underwent transsphenoidal adenomectomy with the diagnosis of TSHoma. Histopathological staining confirmed the diagnosis of TSHoma. We report an unusual case of pulmonary embolism accompanying TSHoma. TSHoma, like other causes of hyperthyroidism, may be associated with pulmonary embolism.

J. Exp. Clin. Med., 2014; 31:55-57

1. Introduction

Thyroid hormones are important mediators of some systems such as metabolism, embryonal development, cellular differentiation, and coagulation systems. Hyperthyroidism is a common endocrine disorder and various changes in the coagulation-fibrinolytic system have been described in patients with excess thyroid hormones. Hyperthyroid patients show tendency toward thromboembolic complications (Hofbauer and Heufelder, 1997). Patients with overt hyperthyroidism have prothrombotic abnormalities leading to increased risk of both arterial and venous thrombotic complications. It is showed increased risk of pulmonary embolism in hyperthyroidism (Lin et al., 2010).

Thyroid stimulating hormone-producing pituitary adenomas (TSHoma) are rare causes of hyperthyroidism. They account for less than one percent of all functioning pituitary tumors and much less than one percent of all cases of hyperthyroidism (Socin et al., 2003). We present a case with pulmonary embolism accompanying TSHoma.

2. Case

A 43-year old man admitted to pulmonary diseases department with chest pain, dyspnea and hemoptysis. He had no significant past medical history. The family history was also unremarkable for any medical problems, including thrombophilia. On physical examination, blood pressure was 110/64 mmHg, pulse was regular at 78 beats/min and respiratory rate was 20 breaths/min. There was no goitre on palpation and chest auscultation was normal. The oxygen saturation was 83% at room air. Electrocardiogram showed normal sinus rhythm. Chest computed tomography (CT) scan showed right pulmonary basal posterior and, left pulmonary basal lateral consolidation and infarct formation. In pulmonary CT angiography, embolism was detected in the branches of both pulmonary arteries. Transthoracic echocardiography was normal. Lower extremity Doppler ultrasonography did not reveal any venous thrombosis. After initial heparinization, treatment was continued with warfarin. On further questioning, he complained of unintentional weight loss, palpitations and heat in-

Journal of Experimental and Clinical Medicine 31 (2014) 55-57

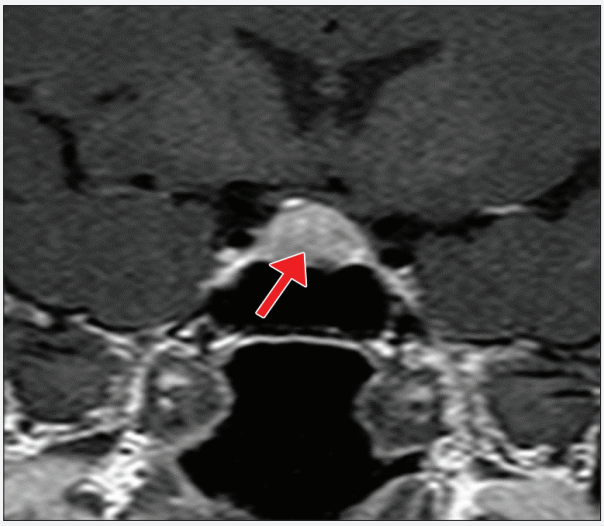

Fig. 1. Magnetic resonance imaging (MRI) showing a 15 mm pituitary macroadenoma.

tolerance which were present for several years. Laboratory measurements revealed high thyroid hormone concentrations [free T3: 5.7 pg/mL (normal range 2.0-4.4), free T4: 2.6 ng/dL (normal range 0.9-1.7 ng/dL)] in the presence of inappropriately elevated levels of serum TSH [TSH: 10.6 μIU/mL (normal range 0.27-4.2 μIU/mL)]. Anti-thyroglobulin and anti-thyroidperoxidase antibodies were below detection levels. Serum concentrations of the α-subunit of TSH (αTSH) and the αTSH/TSH molar ratio were 2.7 IU/L and 2.7 respectively. Serum luteinizing hormone (LH), follicle-stimulating hormone (FSH), adrenocorticotropic hormone (ACTH), prolactin, testosterone, cortisol and insulin-like growth factor-1 (IGF-1) were within the normal range. Magnetic resonance imaging (MRI) showed a 15 mm pituitary macroadenoma with suprasellar extension but without cavernous sinus invasion (Fig. 1). Visual field examination was normal. Based on these findings, a diagnosis of TSHoma was made. Preoperatively two doses of somatostatin analogues (octreotide LAR 30 mg intramuscular) monthly was administered. Two months later thyroid function tests normalized (TSH: 3 μIU/mL, free T3: 1.5 pg/mL, free T4: 0.9 ng/dL). Six months later, after the resolution of pulmonary embolism transsphenoidal surgery was performed. Histopathological examination revealed a TSHoma with strong positive TSH staining. Two months after the surgery, TSH, free T3 and free T4 were 7.3 μIU/mL, 5.9 pg/mL and 2.3 ng/dL, respectively. Postoperative pituitary MRI showed a six mm left sided residual adenoma. After initiation of somatostatin analogue, the patient remained euthyroid and asymptomatic.

3. Discussion

The presence of high serum T4 and T3 concentrations and normal or high serum TSH concentrations in the presence of anatomic evidence of a pituitary tumor by MRI constitute very strong evidence that the patient has a TSHoma. Patients with TSHomas and hyperthyroidism must be distinguished from those with the syndrome of resistance to thyroid hormone (RTH) (Paolo et al., 2009). In addition to the described findings, high molar ratio of serum alpha-subunit to TSH, strongly positive TSH staining of the tumor and a good response to octreotide indicate presence of TSHoma in this patient.

It is well known that excess or deficit of thyroid hormones interact with coagulation-fibrinolytic system causing a hypercoagulability in the state of hyperthyroidism and vice versa (Squizzato et al., 2007). TSH-secreting adenomas secrete biologically active thyrotropin in an autonomous fashion. Most patients have typical symptoms of hyperthyroidism. Various factors contribute to hypercoagulability in hyperthyroidism such as increased hepatic protein synthesis, acute phase reactants, plasma thrombin and plasmin activity and increased tissue factor, one of the major triggers for the extrinsic pathway of coagulation (Erem, 2001). A systematic analysis supports an increased risk of venous thrombotic complications, including cerebral venous thrombosis, deep vein thrombosis and pulmonary embolism in patients with hyperthyroidism (Franchini et al., 2011). In a retrospective case-controlled study pulmonary embolism was found 2.3 times greater for hyperthyroid patients than control group after adjustment for the risk factors which could be interfering with thrombosis (Lin et al., 2010).

Hypercoagulation, endothelial dysfunction and hemodynamic changes are the important pathophysiological factors for thrombosis.It is demonstrated shortened activated thromboplastin time and higher fibrinogen levels in hyperthyroid patients when compared with euthyroid patients (Lippi et al., 2009). In our patient, activated thromboplastin time was found to be normal. In one study including 41 patients with overt hyperthyroidism compared with euthyroid controls, patients with hyperthyroidism had increased levels of plasma fibrinogen, factor IX, von Willebrand factor (VWF), antithrombin and plasminogen activator inhibitor (PAI-1), along with decreased levels of factor X and tissue plasminogen activator (t-PA), thus suggesting a globally reduced plasma fibrinolytic activity (Erem et al., 2002). These parameters were not investigated in our patient since anticoagulation therapy was already started.

It has been suggested that thrombophilia screening is controversial, except in patients with first venous thrombosis at young age and/or a strong family history of venous thrombosis (Lijfering et al., 2009). In our patient, personal and family medical history were unremarkable. In addition, no other risk factors for thrombosis were detected.

Octretoide is an effective treatment option for TSHomas, especially for inoperable and incompletely removed tumors (Socin et al., 2003). The excellent response to somatostatin analogues in TSHomas may also prevent the risk of pulmonary embolism in such patients.

To our knowledge this is the first reported case of pulmonary embolism accompanying TSHoma. TSHoma, like other causes of hyperthyroidism, may be associated with pulmonary embolism.

REFERENCES

Erem, C., 2001. Thyroid disorders and hypercoagulability. Semin. Thromb. Hemost. 37, 17-26. doi:10.1055/s-0030-1270067.
Erem, C., Ersoz, H.O., Karti, S.S., Ukinç, K., Hacihasanoglu, A., Deger, O., Telatar, M., 2002. Blood coagulation and fibrinolysis in patients with

hyperthyroidism. J. Endocrinol. Invest. 25, 345-350.
Franchini, M., Lippi, G., Targher, G., 2011. Hyperthyroidism and venous thrombosis: A casual or causal association? A systematic literature review. Clin. Appl. Thromb. Hemost. 17, 387-392. doi:10.1177/1076029610364521.
Hofbauer, L.C., Heufelder, A.E., 1997. Coagulation disorders in thyroid diseases. Eur. J. Endocrinol. 136, 1-7. doi:10.1530/eje.0.1360001.
Lijfering, W.M., Brouwer, J.L., Veeger, N.J., Bank, I., Coppens, M., Middeldorp, S., Hamulyak, K., Prins, M.H., Büller, H.R., Van der Meer, J., 2009. Selective testing for thrombophilia in patients with first venous thrombosis: Results from a retrospective family cohort study on absolute thrombotic risk for currently known thrombophilic defects in 2479 relatives. Blood. 113, 5314-5322. doi: 10.1182/blood-2008-10-184879.
Lin, H.C., Yang, L.Y., Kang, J.H., 2010. Increased risk of pulmonary embolism among patients with hyperthyroidism: A 5-year follow-up study. J. Thromb. Haemost. 8, 2176-2181. doi:10.1111/j.1538-7836.2010.03993.x.
Lippi, G., Franchini, M., Targher, G., Montagnana, M., Salvagno, G.L., Guidi, G.C., Favaloro, E.J., 2009. Hyperthyroidism is associated with shortened APTT and increased fibrinogen values in a general population of unselected outpatients. J. Thromb. Thrombolysis. 28, 362-365. doi:10.1007/s11239-008-0269-z.
Paolo, B., Persani, L., Mannavola, D., Campi, I., 2009. TSH-secreting adenomas. Best. Pract. Res. Clin. Endocrin. Metab. 23, 597-606.
Socin, H.V., Chanson, P., Delemer, B., Tabarin, A., Rohmer, V., Mockel, J., Stevenaert A, Beckers, A., 2003. The changing spectrum of TSH-secreting pituitary adenomas: diagnosis and management in 43 patients. Eur. J. Endocrinol. 148, 433-442. doi:10.1530/eje.0.1480433.
Squizzato, A., Romualdi, E., Büller, H.R,, Gerdes, V.E., 2007. Clinical review: Thyroid dysfunction and effects on coagulation and fibrinolysis: A systematic review. J. Clin. Endocrinol. Metab. 92, 2415-2420. doi:http://dx.doi.org/10.1210/jc.2007-0199.