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-
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 lutetinizing 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 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 (Fracchini 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), anti-thrombin 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.

Octreotide 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