

Pulmonary Embolism in a Patient with Antiphospholipid Syndrome and Graves' Disease

Antifosfolipid Sendromu ve Graves Hastalığı Bulunan Bir Olguda Pulmoner Emboli

Mustafa Cesur*, Neslihan Celik**, Meltem Aylı***

Ankara Güven Hospital, *Department of Endocrinology and Metabolic Disease, **Chest Diseases and ***Hematology, Ankara, Turkey

Abstract

Antiphospholipid syndrome (APS) is an autoimmune disease characterised by tendency to thrombosis, obstetrical and hematological complications. Patients with Graves' disease (GD) may have some abnormalities of blood coagulation due to endothelial dysfunction and decreased fibrinolytic activity with a higher thromboembolic potential. In some rare cases especially in severe thrombotic states; APS and GD may be present together. We describe a 44-year-old man with pulmonary embolism who had both APS and GD. Moreover thymic hyperplasia which is a seldom-recognized feature of GD was also established in computed tomography of the chest and thyroid stimulating hormone level was in the normal range probably due to antibody interference. *Turk Jem 2007; 11: 23-5*

Key words: Pulmonary embolism, antiphospholipid syndrome, Graves' disease, thymus hyperplasia, antibody interference

Özet

Antifosfolipid sendromu tromboza eğilim, obstetrik ve hematolojik komplikasyonlarla karakterize otoimmün bir hastalıktır. Graves hastalığı da endotel disfonksiyonu ve azalmış fibrinolitik aktivite nedeniyle bazı pıhtılaşma anormalliklerine sebep olabilir. Bazı nadir olgularda, özellikle ciddi trombotik durumlarda antifosfolipid sendromu ve Graves hastalığı birlikte görülebilmektedir. Burada antifosfolipid sendromu ve Graves hastalığının birlikte olduğu 44 yaşında bir pulmoner emboli olgusunu sunuyoruz. Daha önce literatürde bildirilmeyen bu olgunun ilk olduğunu düşünüyoruz. Bunun dışında olguda Graves hastalığının nadir rastlanan bir özelliği olan timik hiperplazi bilgisayarlı toraks tomografisinde tespit edildi. Ayrıca muhtemel bir antikor interferansı nedeniyle serbest T3 ve serbest T4 yüksek olarak bulunmasına rağmen TSH normal sınırlarda bulundu. *Turk Jem 2007; 11: 23-5*

Anahtar kelimeler: Pulmoner emboli, antifosfolipid sendromu, Graves hastalığı, timus hiperplazisi, antikor interferansı

Introduction

Autoimmune rheumatic diseases like rheumatoid arthritis, systemic lupus erythematosus, scleroderma are often accompanied by autoimmune thyroid disease (ATD) as Graves' disease (GD) or Hashimoto's thyroiditis, so physicians have to be in increased clinical alertness to the possibility of thyroid dysfunction if there is any rheumatic disease (1). Antiphospholipid syndrome (APS) is also an autoimmune disease characterised by tendency to thrombosis, obstetrical and hematological complications (2). There are some suspicious circumstances about the relation of ATD with APS for the existence of no enough evidence. Although Nabriski et al. reported increased prevalence of antiphospholipid antibodies (APLA) in patients with ATD, it may be attributed to be an epiphenomenon (3). However in some

rare cases, especially in severe thrombotic states; APS and GD may be present together (4).

Here we describe a pulmonary embolism which had occurred in a patient with both APS and GD. To our knowledge this hasn't been described in the literature previously.

Case Report

A 44-year-old man with three spontaneous deep venous thrombosis (DVT) history was admitted to the emergency department suffered from acute retrosternal chest pain and shortness of breath. In the physical examination he was found to be tachycardic and tachypneic. At admission the patient's blood pressure was 150/90 mmHg, heart rate was regular with 104 beats/min, and respiration rate was 24/min. On auscultation, no

murmur was heard. Respiratory sounds had decreased bilaterally with widespread crepitant rales in both but more in the left lung field. Other systemic examinations showed no pathology. Hypoxemia and hypocapnia were seen in the arterial blood gas examination (pH = 7.45, partial pressure of oxygen (pO₂) = 68 mmHg, partial pressure of carbon dioxide (pCO₂) = 28 mmHg, oxygen saturation (SO₂) = 95%, bicarbonate (HCO₃) = 21.6 mmol/L, Base excess = -4.2 mmol/L). In his complete blood counts; leukocyte count was 11 700 u/L, hemoglobin level was 13.2 g/dL, and platelet count was 277 000 u/L. Erythrocyte sedimentation rate and C-reactive protein levels were higher (respectively 68 mm/h, 192.6 mg/L). In his biochemical tests, only liver function tests were higher (aspartate aminotransferase: 87 U/L, alanine aminotransferase: 106 U/L, gamma-glutamyltranspeptidase: 71 U/L) while there was no viral or autoimmune hepatitis. Lactate dehydrogenase, alkaline phosphatase and the other biochemical parameters were in reference range. D-dimer was found to be elevated to 2028 ng/ml. Thyroid stimulating hormone (TSH) level was found to be 0.402 mIU/mL, in normal but near to basal range (normal range, 0.270-4.20). Free triiodothyronine (FT3) and free thyroxine (FT4) were not studied. There was no sign of cardiac ischemia as electrocardiogram presented only sinus tachycardia and serum creatine kinase (CK), CK-MB isoenzyme, and troponin-T levels were in normal range. Doppler echocardiography was found to be normal. There were some findings on posterior-anterior chest radiography; right costophrenic sinus was obliterated and there was an infiltrative field at lower right lobe of the lung. On the computed tomography (CT) of the chest, consolidation and atelectasia areas were seen at the right lower lobe of postero-lateral segment, and right hemidiaphragm was elevated. Minimally subpleural consolidation was seen at the left lower lobe of postero-lateral segment. Pulmonary embolism (PE) and pneumonia weren't ruled out, so the patient was treated with enoxaparin, sulbactam/ampicillin and clarithromycin therapy. Ventilation/perfusion (V/Q) lung scintigraphy showed right anterolaterally basal segment perfusion defect whereas ventilation defect was also seen at the same area. Although V/Q lung scintigraphy presented low probability of PE, the patient was accepted PE. Because he had been operated for his DVT seven years ago, and it was repeated two times which the last was one month ago. Moreover he had been taken no warfarin sodium since the last attack, only acetylsalicylic acid and pentoxifylline were given. Screening studies revealed the positivity of the lupus anticoagulant (LAC), factor V Leiden and MTHFR heterozygote mutations in the patient while the other thrombotic factors were negative. After the patient's recovery, he was discharged with still higher liver function tests on his seventh day after admittance. In the control examination he was suffered from fatigue, palpitation, excessive sweating, weight loss, emotional liability and insomnia. Pulmonary CT angiography was performed. Pleural based consolidation was seen at the anterior basal segment of the right lower lobe and triangle shaped consolidation was seen at the posterior basal segment of the same lobe. These findings were concordant with old pulmonary infarction (Figure 1). It was also found normally triangle shaped thymus hyperplasia at the anterior mediasten (Figure 2) and enlarged thyroid gland at CT

scan. Thyroid function studies revealed a normal TSH of 0.399 mIU/mL and elevated FT4 of 111.8 pmol/L (normal range, 10.3-24.5), and FT3 of 51.4 pmol/L (normal range, 2.3-7.1). Anti-thyroglobulin antibody (anti-Tg) titer was elevated to 144.9 IU/mL (normal range, 0-115). Anti-thyroid peroxidase antibody (anti-TPO) titer was found to be 30.2 IU/mL (normal range, 0-34). Circulating TSH receptor antibody (TRAb) level was elevated to 25 U/L (normal range, 0-10). The thyroid ultrasound showed diffuse heterogenous enlargement of the thyroid gland. Thyroid scan with Tc-99m showed an enlarged thyroid gland with diffuse uptake. I-131 uptake was 63% at 4 hours (normal,



Figure 1. Pleural based consolidation was seen at the anterior basal segment of the right lower lobe and triangle shaped consolidation was seen at the posterior basal segment of the same lobe

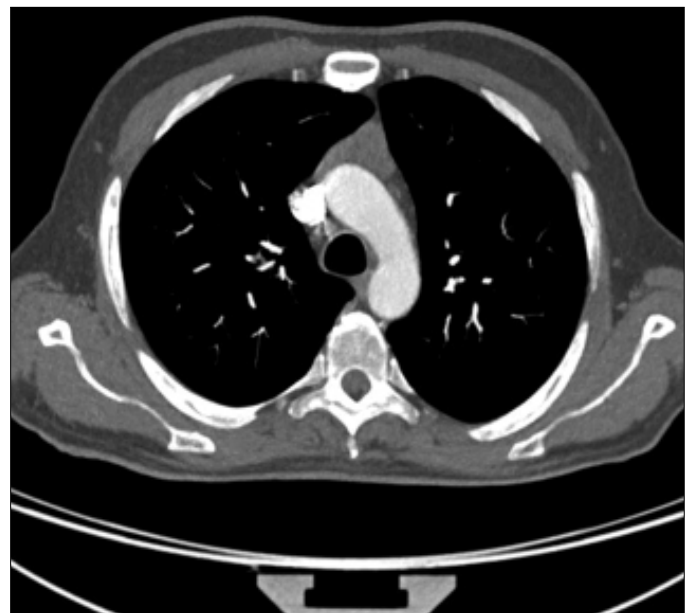


Figure 2. Normally triangle shaped thymus hyperplasia in the anterior mediastinum

4-36%) and 58% at 24 hours (normal, 19-51%). Thyroid function, thyroid autoantibodies, thyroid ultrasound and a thyroid scan findings were consistent with the diagnosis of Graves' disease. To rule out a TSH secreting pituitary adenoma, alpha subunit and dynamic magnetic resonance imaging of hypophysis were performed. Alpha subunit was found to be in normal limits (0.30 mIU/mL- normal range, 0-0.80) and no pituitary adenoma was screened.

Discussion

In our case, true pulmonary embolism had occurred in a patient with both Antiphospholipid syndrome (APS) and Graves' disease (GD). Pulmonary embolism (PE) was seen in thorax CT scan. Patients with GD may have some abnormalities of blood coagulation due to endothelial dysfunction and decreased fibrinolytic activity with a higher thromboembolic potential (5). Therefore severe thrombotic complications may be seen in thyrotoxic states (6). In contrast, symptoms of PE can be mimicked in patients with GD, without PE (7). Thus, physicians should evaluate such cases deeply.

Interestingly, thymic hyperplasia which is a seldom-recognized feature of GD was also established in CT scan of the patient. The pathophysiology of thymic hyperplasia is not well understood, but immunological aspects seem to play a predominant role as TSH receptors have been identified in the human thymic gland (8). Furthermore recently thymus enlargement was suggested to be in a pathogenetic role in some autoimmune rheumatic diseases mostly in systemic sclerosis (8). For that reason this kind of togetherness must not be thought just like an epiphenomenon. There must be further investigations to clear this subject.

In our case; the patient had positive antiphospholipid antibodies (APLA) which is a thrombotic factor with together factor V Leiden and MTHFR mutations which are also thrombotic factors (9). Although his early repeated deep venous thrombosis story, these thrombotic factors were misdiagnosed because of never screened. Our case shows the importance of detection of APLA and maybe the other thrombotic factors when there was a tendency to thrombosis. Moreover it seems to be the necessity of detecting autoimmune thyroid pathology especially while there is APLA positivity.

Another interesting part of our case is unsuppressed TSH of the patient which caused delayed diagnosis of thyrotoxicosis. Sometimes, despite "normal" serum TSH value, the patient may be in thyrotoxic state. Antibody interference may be the reason of this kind of false estimation (10). This case show us the necessity of analysing FT3 and FT4 in such cases which prone to have different antibodies.

In conclusion, true pulmonary embolism may be seen in patients with together antiphospholipid syndrome and Graves' disease. Thymic hyperplasia is a seldom-recognized feature of GD and this may not be only an epiphenomenon. In some cases, despite normal levels of serum TSH values, the GD patients may be in thyrotoxic state. Antibody interference may be responsible from this kind of false estimation.

References

1. Lockshin MD. Endocrine origins of rheumatic disease. Diagnostic clues to interrelated syndromes. *Postgrad Med* 2002; 111: 87-8, 91-2.
2. Soy M, Oktun MT, Tuncbilek N, Ermantas N, Okten O, Altinay G, Turgut B. Nocardiosis in a patient with primary anti-phospholipid syndrome. *Rheumatol Int* 2006; 26: 461-4.
3. Nabriski D, Ellis M, Ness-Abramof R, Shapiro M, Shenkman L. Autoimmune thyroid disease and antiphospholipid antibodies. *Am J Hematol* 2000; 64: 73-5.
4. Takahashi A, Tamura A, Ishikawa O. Antiphospholipid antibody syndrome complicated by Grave's disease. *J Dermatol* 2002; 29: 776-80.
5. Erem C, Ersoz HO, Karti SS, Ukinc K, Hacıhasanoglu A, Deger O, Telatar M. Blood coagulation and fibrinolysis in patients with hyperthyroidism. *J Endocrinol Invest* 2002; 25: 345-50.
6. Mouton S, Nighoghossian N, Berruyer M, Derex L, Philippeau F, Cakmak S, Honnorat J, Hermier M, Trouillas P. Hyperthyroidism and cerebral venous thrombosis. *Eur Neurol* 2005; 54: 78-80.
7. van Nieuwkoop C, Bolk JH. A mediastinal mass: Graves' disease related thymic hyperplasia. *Eur J Intern Med* 2005; 16: 606-7.
8. Ferri C, Colaci M, Battolla L, Giuggioli D, Sebastiani M. Thymus alterations and systemic sclerosis. *Rheumatology* 2006; 45: 72-5.
9. Bick RL, Hoppensteadt D. Recurrent miscarriage syndrome and infertility due to blood coagulation protein/platelet defects: a review and update. *Clin Appl Thromb Hemost* 2005; 11: 1-13.
10. Toshima K, Momotani N, Shimizu K, Saito H, Hisaoka T, Yoshimura H, Ishikawa N, Ito K, Shoji T. Cases of Graves' disease with falsely high TSH values due to interfering substances which cross-link with mouse monoclonal antibodies in the TSH assay kits. *Nippon Naibunpi Gakkai Zasshi* 1993; 69: 1083-91.