Original Research Article

Analysis of common etiology between Takayasu's Arteritis and Hyperthyroidism in a middle aged female in Eastern part of India

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Abstract

Takayasu's arteritis is a chronic, progressive, granulomatous vasculitis involving large arteries especially aorta and its branches. Hyperthyroidism is a condition which involves excess synthesis and secretion of thyroid hormones by the thyroid gland. A 36 year old female patient presented at the General Medicine Outdoor of a tertiary-care hospital situated in the Eastern part of India with clinical features and laboratory reports suggestive of hyperthyroidism. There was also history of ischemic stroke 8 years back leading to right sided weakness in this patient. On careful physical examination left sided radial, brachial, femoral and dorsalis pedis arterial pulses were found to be impalpable. Digital subtraction angiography of aorta and its branches revealed narrowing of left common carotid and left subclavian artery suggestive of Takayasu's arteritis. This existence of Takayasu's arteritis and hyperthyroidism may not be just fortuitous. An underlying autoimmune mechanism might be a possible explanation.

Key words

Analysis of etiology, Takayasu's arteritis, Hyperthyroidism.

Introduction

Takayasu's arteritis is defined as "granulomatous inflammation of the aorta and its major branches" by the Chapel Hill Consensus Conference on the Nomenclature of systemic vasculitis [1]. It is commonly reported among young women of 20-40 years age group mainly of Eastern and Southeast Asian countries [2]. Vessel wall inflammation Takayasu's arteritis is characterized by panarteritis involving all the three layers of the blood vessel namely tunica intima, tunica media and tunica adventitia. There is extensive infiltration of vessel wall by mononuclear cells and occasional giant cells leading to thickening, which along with intimal infiltration leads to narrowing or stenosis and sometimes complete obliteration of the artery. This explains the "pulseless" nature of the disease. Sometimes acute inflammation may lead to dilatation and aneurysm formation of the affected vessel [3]. Though the exact etiopathogenesis of Takayasu's arteritis is still left to be determined, immune mechanisms are thought to play a major role in the disease process [4, 5].

Hyperthyroidism, defined as a state of excessive thyroid gland function has multiple causes. Grave's disease happens to be the most common cause of hyperthyroidism. In Grave's disease thyroid stimulating immunoglobulins (TSI) bind to and activate the G-protein-coupled thyrotropin receptors leading to increased hormone production [6]. Biochemically there is suppression of Thyroid Stimulating Hormone (TSH) level and increase in the level of total and unbound thyroid hormones. Anti-thyroid peroxidase (anti-TPO) antibody is present in 80% cases and serves as a ready marker of autoimmunity [7]. The hallmark of the disease is ophthalmopathy distinguished by the variable degrees of ophthalmoplegia, proptosis and periorbital swelling.

Simultaneous presence of the two diseases, Takayasu's arteritis and hyperthyroidism, in the same individual might explain the common autoimmune process involved in both the diseases.

Materials and methods

A 36 year old female patient from Chinsurah, Hooghly in the state of West Bengal, situated in the Eastern part of India, presented to the out-patient department of a tertiary care hospital with the chief complaints of gradual enlargement of both eyes for the past 3 months along with palpitation and tremors for the same duration. On further interrogation she also gave history of easy fatigability, insomnia and heat intolerance for the past 6 months. There was no history of any neck swelling. There was past history of stroke 8 years back leading to the weakness of the right side of her body for which she is on regular physiotherapy regimen. She also gave history of claudication of left upper and lower limbs for last 10-12 years. Drug history included intake of Aspirin 75 mg, Atorvastatin 10 mg, Pantoprazole 40 mg for last 8 years. No history of any addiction.

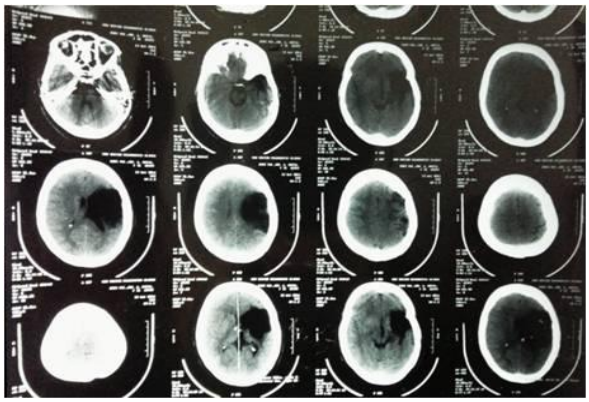
On examination, peripheral pulses were found to be absent in the left-sided radial, brachial, femoral, poplitial and dorsalis pedis artery. On right side all the peripheral pulses could be palpated, the pulse was of low volume with a rate of 108 per minute. Also blood pressure could not be recorded in her left hand. In right upper limb the brachial pressure was 110/70 mm of Hg. There was no visible or palpable neck swelling. The patient had a typical stare look, with exophthalmos and a positive Joffroy's sign which indicates the loss of wrinkling of forehead on looking up. On neurological examination the tone of her right upper and lower limbs was found to be increased, with power diminished compared to the left side. No audible bruit was heard over the thyroid, carotids or in the abdomen.

Results

Complete hemogram, blood urea nitrogen, creatinine, serum electrolytes, liver function test and lipid profile were found to be within the

normal range. Erythrocyte sedimentation rate was elevated. C-reactive protein was marginally raised. Serum Thyroid Stimulating Hormone (TSH) level was found to be 0.01 microIU/ml (0.27- 4.20), serum free T4 level was 3.05 ng/dl (0.93- 1.70) and serum free T3 level was 7.31 pg/ml (2.0- 4.4). Anti-thyroid peroxidise antibodies (Anti-TPO) level was 195 (>60 is positive). 2D ECHO revealed normal study. Ultrasonography of neck revealed both lobes of thyroid to be heterogenous with few cystic areas. A tiny calcification noted in right lobe of thyroid. CT scan of brain revealed a large hypodense area in the left temporo-parietal lobes consistent with a porencephalic cyst. (**Figure - 1**)

Figure – 1: CT scan brain showing a large hypodense area in the left temporo-parietal lobes consistent with a porencephalic cyst.



Digital subtraction angiography of the arch of aorta and its branches revealed narrowing of left common carotid and left subclavian artery with occlusion noted in the left subclavian artery at the 1st rib, suggestive of inflammatory arteritis most probably Takayasu's disease. (**Figure - 2**)

A Thyroid scan (TcO4-) was done which showed normal sized thyroid gland with increased trapping function of thyroid gland. (**Figure - 3**)

Discussion

According to the American College of Rheumatology Classification Criteria, 1990 for Takayasu's Arteritis [8], our patient fulfils five out of the six criteria mentioned. The presence of palpitation, tremors, heat intolerance, with the typical eye signs of hyperthyroidism, along with the biochemical findings of thyroid function test, presence of Anti-TPO antibodies in blood and good trapping function of the thyroid gland on Thyroid scan confirms the presence of Grave's disease in this patient. The patient was administered Carbimazole, B-blocker in the form of Propranolol, Oral steroids, Cilastazole. She was discharged and advised to follow-up in our out-patient department. Presently she is doing well.

Figure – 2: Digital subtraction angiography images of arch of aorta and its branches.

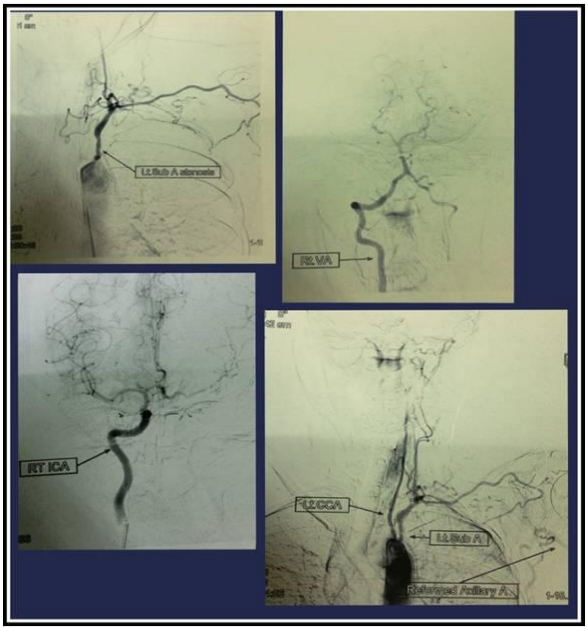
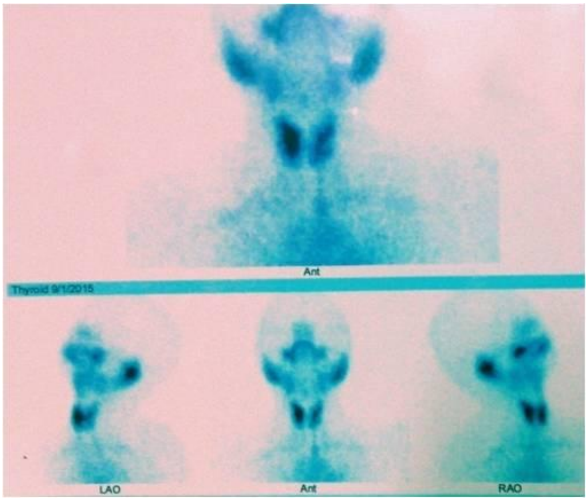


Figure – 3: Thyroid scan (TcO4-) showing normal sized thyroid gland with good trapping function of thyroid gland.



Yoshihiro Sato and colleagues in 1980 published a case of aortitis syndrome and hyperthyroidism [9]. They also conducted a literature review which revealed 14 other cases with aortitis syndrome and hyperthyroidism in Japan, implicating a strong role of immune system in the pathogenesis of aortitis syndrome. Ashraf M, et al. [10] published a rare case of Takayasu's arteritis with hyperthyroidism where a 23 year old female patient was found to have absent pulses in the upper limbs, with elevated acute phase reactants, diffuse goitre on USG neck and elevated thyroglobulin antibody levels. MDCT findings included diffuse stenosis in bilateral subclavian artery, an aberrant right subclavian artery, the narrowing of left vertebral, celiac and the superior mesenteric arteries and multiple chest wall and intra-abdominal collaterals. The patient later on developed renovascular hypertension and required an angioplasty of the right subclavian and both the renal arteries.

Kettaneh A, et al. [11] reported hyperthyroidism in two patients with Crohn's disease and Takayasu's arteritis. The authors have tried to highlight the genetic predisposing factors and disease-related iodine deficiency both involving the nuclear factor kappa B pathway as the possible explanation for the simultaneous manifestation of the three diseases in the same individual. Similarly Umh [12] and colleagues had isolated a case of pulmonary Takayasu's Arteritis combined with pulmonary thromboembolism and hyperthyroidism in Korea.

Takayasu's arteritis is a very rare form of vasculitis affecting aorta and its branches. Recently many susceptibility genes and human leukocyte antigen (HLA) alleles have been identified which explains the auto-immune nature of the disease [13]. However no serum auto-antibodies have been identified till date. Pentraxin-3, a novel biomarker has recently been shown to be useful to assess the disease activity in patients with Takayasu arteritis [14]. The Indian Takayasu's arteritis consortium has proposed Indian Takayasu Clinical Activity score (ITAS2010), to assess disease activity and is one of the largest study following patients of Takayasu's arteritis [15, 16].

Auto-immune thyroid disease (AITD) which includes both Hashimoto's thyroiditis and Grave's disease, have auto-antibodies directed against the thyroid gland. Different linkage and association studies in AITD have identified many thyroid specific genes (thyroglobulin (Tg) and thyroid stimulating hormone receptor (TSHR)) and immune regulatory genes. These immune regulatory genes were found to be associated with other autoimmune diseases also [17].

The role of human leukocyte antigen (HLA) has been investigated in both the diseases. HLA B52 and HLA B39 haplotypes have been found to be closely associated with Takayasu's arteritis in the Japanese population. Another study conducted by Takamura C., et al. [18] published in 2012 revealed a strong association of HLA B67 with Takayasu arteritis in the Japanese population. Although its prevalence was lower compared to HLA B52, its Odds ratio was higher.

Similarly HLA genes have been found to play a major role in orchestrating the pathophysiology of Grave's disease, with different alleles in different populations. HLA-B8 and HLA-DR3 are found to be strongly associated with Grave's disease. Sequencing the DR beta chain has revealed a strong association between the presence of arginine at position 74 of the DR beta chain and Grave's disease in Caucasians [19].

Conclusion

The simultaneous presence of the two diseases is not just a co-incidence. Common genetic and immune mechanisms might explain this rare condition for which further studies and researches are needed.

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