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Graves' Disease as the Initial Manifestation of Wegener's Granulomatosis: A Case Report

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ABSTRACT

Wegener's granulomatosis is a necrotizing granulomatous vasculitis with the prevalence of 3 in 100000. Pulmonary involvement is the most common form of disease manifestation detected in 95% of cases but onset of disease with other symptoms such as proptosis and hyperthyroidism is very rare.

Our patient was a 29-year-old man who had been presented to the hospital with goiter, palpitation, fatigue, and proptosis in 1997. He underwent subtotal thyroidectomy and was treated with methimazole.

After six years of treatment, he admitted to the hospital for the second time with arthritis, arthralgia, fever, hematuria and nodular pulmonary lesions. Open lung biopsy confirmed the diagnosis of wegener's granulomatosis. ***(Tanaffos 2006; 5(4):75-78)***

Key words: *Graves' Disease, Wegener's Granulomatosis, Vasculitis*

INTRODUCTION

Vasculitis is a clinicopathological course resulting from inflammation and trauma of vessel walls. This inflammation can cause ischemia and tissue necrosis by interrupting the blood circulation. The main problem in diagnosing such diseases is the non-specific findings.

Nonetheless, presence of specific clinical disorders alone or along with other disorders suggests the diagnosis of vasculitis. Palpable purpura, pulmonary infiltration, microscopic hematuria, chronic inflammatory sinusitis, multiplex mononeuritis, idiopathic ischemic events, and glomerulonephritis associated with systemic disease should suggest the diagnosis of vasculitis (1).

Wegener's granulomatosis is a necrotizing granulomatous vasculitis with the prevalence of 3 in 100,000. The disease was first described in 1931 by a medical student in Germany named Heinz Klinger. Afterwards, in 1936 Dr. Wegener a young German pathologist gave a detailed explanation regarding three patients suffering from this disease (2).

Although it is an uncommon disease, if not diagnosed and treated in-time my cause renal failure and severe pulmonary complications including diffuse pulmonary hemorrhage. Therefore, timely diagnosis and treatment is important in preventing

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related morbidity and mortality. Pulmonary involvement is the most common form of the disease manifested in 95% of cases but onset of the disease with rare symptoms such as proptosis (in 2% of the cases) and hyperthyroidism (in 1% of the cases) has been reported as well.

CASE REPORT

Our patient was a 29-year old man from Yazd province, Iran. He was non-smoker. The symptoms including goiter, palpitation, fatigue, minimal weight loss, and proptosis started in 1997. The patient underwent a 6-month therapy with methimazole (MMI) and eventually underwent a subtotal thyroidectomy recommended by a surgeon. Apparently, he did not have any complications following the operation except for some mild ophthalmic complications due to the continuation of proptosis.

In 2003, the patient again developed sputum containing streaks of blood which was treated symptomatically and improved spontaneously. In October 2004, the patient referred to the hospital complaining of the arthralgia of major joinsts of the upper and lower extremities and intermittent fever. He also mentioned bouts of dark urine (probably gross hematuria)

Eventually, the patient developed signs of arthritis of both wrists. He was hospitalized in Shaheed Sadoughy Hospital (Yazd) for evaluation and precise examination by a rheumatologist. During the hospitalization period, hematuria occurred twice. Also, fever of 38ºC and ESR of 80 were recorded several times. Considering the suspicious lesions at the base of both lungs detected on chest x-ray, pulmonary CT-scan was obtained, in which nodular infiltration without mediastinal lymphadenopathy was seen (Figure 1).

The patient's history and the clinical and paraclinical findings were highly suggestive of vasculitis, considering the fact that other causes were ruled out in differential diagnosis. Therefore, C-ANCA and P-ANCA were requested for the patient (C-ANCA titre was reported to be over 100). At this time, open lung biopsy was performed as well.

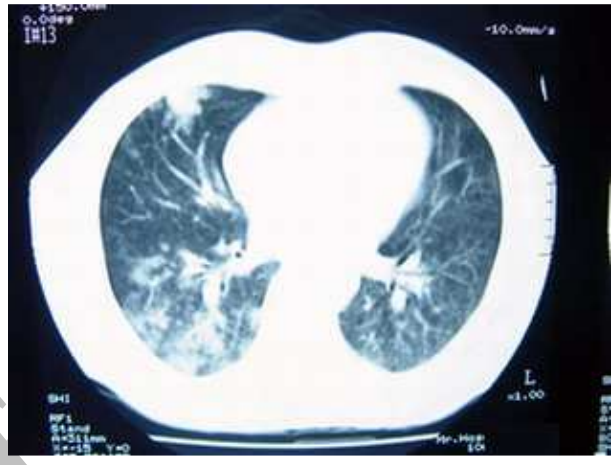

Figure 1. Pulmonary CT-scan of patient.

The pathologic report confirmed the diagnosis of necrotizing vasculitis typical of Wegener's granulomatosis. The patient with the diagnosis of Wegener's disease received immunosuppressive drugs according to the "American College of Rheumatology Guidelines" (prednisolone 1mg/kg plus endoxan 1000 mg). He was discharged from the hospital in good condition and refers for the continuation of treatment and follow up.

DISCUSSION

Wegener's granulomatous vasculitis has a prevalence of 3 in 100,000, but due to the high rate of related morbidity and mortality, it should be diagnosed and treated early (1).

The American College of Rheumatology developed the criteria for the classification of Wegener's granulomatosis by comparing 85 patients who had this disease with 722 control patients with other forms of vasculitis.

For the traditional format classification, 4 criteria

were considered as follows:

1) Abnormal urinary sediments (red cell casts or greater than 5 red blood cells per high power field).
2) Abnormal findings on chest radiography (nodules, cavities or infiltration).
3) Oral ulcers or nasal discharge
4) Granulomatous inflammation on biopsy.

The presence of 2 or more of these 4 criteria is associated with a sensitivity of 88.2% and a specificity of 92%. It is important to distinguish patients with Wegener's granulomatosis from patients with other forms of vasculitis because WG requires cyclophosphamide therapy, whereas many other forms of vasculitis can be treated with corticosteroids alone (3).

In 158 WG patients evaluated by the USA National Institute of Health, involvement of the upper respiratory system (in 95% of cases) was the most common manifestation (1).

Thyroid diseases are of the clinical manifestations of Wegener's granulomatosis. Proptosis and hyperthyroidism are seen in 2% and 1% of cases respectively. For this reason, common pathogenic factors have been suggested (1). Graves' disease and Hashimoto's thyroiditis may occur prior to the onset of WG classic clinical symptoms. Also, it is reported that these patients usually suffered from a more severe form of disease (4, 5, 6).

Our patient had signs and symptoms of hyperthyroidism, goiter and proptosis for a relatively long time which is extremely rare form of onset of this disease.

In several studies, a correlation between Wegener's granulomatous vasculitis and use of anti-thyroid drugs for hyperthyroid patients has been reported. In some of these studies including the one performed by the division of rheumatology, New York University in 1998, the use of propylthiouracil (PTU) in some patients with Graves' disease has been associated with some complications mainly anti-neutrophilic cytoplasmic antibody (ANCA)-mediated granulomatous vasculitis (7).

In a study in Taiwan in 2004, the prevalence of P-ANCA (perinuclear- ANCA) positivity in Taiwanese patients with Graves' disease treated with propylthiouracil (PTU) and methimazole (MMI) was investigated. Eighty-nine patients with Graves' disease who were currently being treated with PTU (n=47) or MMI (n=42) were included in the study. And 20.2% of patients with Graves' disease receiving PTU and MMI were seropositive for ANCA. The frequency of P-ANCA-positive status in the PTU treatment group was significantly higher than in the MMI treatment group (8).

Several studies have reached a consensus that anti- thyroid drugs used during the treatment of hyperthyroidism could induce ANCA-associated vasculitis (9, 10, 11, 12, 13). Ocular and orbital involvement occurs in 28-58% of patients with Wegener's granulomatosis.

More often, the anterior segments of the eye are involved; whereas, inflammation of the posterior segments is quite uncommon (14,15). These involvements could be the initial manifestation of Wegener's granulomatosis (16). The main forms of involvement are scleritis, uveitis, inflammatory enlargement of lacrimal glands, central retinal artery occlusions, proptosis, and orbital lesions. But sometimes granulomatous lesions mimic the characteristics of subretinal tumors which can be mistaken with neoplasms (17, 18, 19). Bilateral blindness resulting from retinal phlebitis, vitreous hemorrhage and neovascular glaucoma have been reported as well (16).

In our patient, an interval of several years between the treatment with methimazole and onset of typic clinical findings of WG especially the systemic granulomatous form gives the idea that the disease might have been induced by the use of methimazole.

Considering the fact that the proptosis did not resolve after completion of the treatment of Graves' disease and also the patient's favourable response to steroid therapy during his recent hospitalization, the risk of Wegener's ophthalmopathy is suggested. But since this finding is also present in primary Graves' ophthalmopathy, we can not distinguish these two from each other.

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