WEGENER'S GRANULOMATOSIS IN A PATIENT WITH RHEUMATOID ARTHRITIS

Z. Ahmadi-nejad, A. Gransar, H. Jabbari, M. Taj

Department of Infections Disease, School of Medicine Tehran University of Medical Sciences, Tehran, Iran

Abstract - Wegener's Granulomatosis is a necrotizing granulomatous vasculitis involving small and medium sized vessels. The syndrome is classically defined as having Involvement of kidney, lungs and upper respiratory tract (i.e. sinuses). Wegener's Granulomatosis may be present in other autoimmune or inflammatory diseases, particularly systemic lupus erythematosis (SLE), but most frequently has been associated with polyarteritis and glumerulonephritis.

We present a case of wegener's Granulomatosis (WG) in a middle age lady with Rheumatoid Arthritis (RA); and discuss the implication of these two conditions co-existing in one patient.

As far as we are aware, through medline and internet research, this is probably the fourth case with such an association of WG and RA and the first one in Iran. Presentation of new uncontrollable sign and symptoms, in a previously well controlled RA patient, might suggest a new overlapping syndrome like Wegener's Granulomatosis besides to flare up of previous disease as a differential diagnosis.

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INTRODUCTION

Wegener's granulomatosis (WG) is a small to medium vessel vasculitis with extravascular manifestations (1,2).

Although any anatomic area can be affected by Wegener's Granulomatosis, the three most common sites of involvement are the Sinuses and upper airway, the lung; and the kidneys (1).

Sinusitis present at initial presentation in about one half to two thirds of patients with WG and is seen in 85 percent of cases during the entire course of the disease, but pulmonary manifestations occur in 45 percent of cases at presentation and in 87 percent during the course of the disease (1,3).

The most common radiologic findings are pulmonary infiltrate (67%) and nodules (58%). Pulmonary nodules in WG are usually multiple and bilateral and often cavitate (50%). Less common pulmonary manifestations of WG include pleural effusion, diffuse Pulmonary hemorrhage, and mediastinal or hilar lymph node enlargement or mass (3).

Morphologically, the upper respiratory tract lesions range from mucosal granuloma to ulceration and in the lungs, from dispersed focal necrotizing granuloma to nodules that may undergo cavitation (2).

Microscopically, the granulomas reveal a geographic pattern of necrosis rimmed by lymphocytes, plasma cells, macrophages, and variable numbers of giant cells. In association with such lesions there is a necrotizing or granulomatous vasculitis of small and some times larger arteries and veins, certainly creating a more than superficial resemblance to a tubercle. Thus the major pathologic differential diagnosis is mycobacterial or fungal infection. Lesions may ultimately undergo progressive fibrosis and organization (2).

A definitive diagnosis requires adequate tissue Biopsy of either lung or kidney. Tests for cytoplasmic Anti-neutrophil cytoplasmic Antibody (c-ANCA) are positive in 90% of patients with renal involvement and 70% of patients without renal disease at presentation (1,4). Patients are treated with a combination of Cyclophosphamide (both P.O and I.V), Metothrexate and prednisolone (1,2,3,5).

The mortality of untreated WG approaches 100%. Eighty percent of the patients die within 1 year (2).

WG may be present in other autoimmune or inflammatory diseases, particularly systemic lupus erythematosis (SLE), but most frequently has been associated with polyarteritis and glumerulonephritis (4).

We describe a patient who presented at the age of 35 with rheumatoid arthritis (RA) and two years later developed features of Wegener's granulomatosis.

Case report

A 37 year old housewife, married and hailing from Tehran was referred to this centre with the chief complaint of chronic cough of 2.5-3 months duration. She was a known case of migraine headache lasting 10 years and RA lasting 2 years.

Patient's RA was diagnosed 2 years back with complaints of Joints pain (especially the hip and knees), morning stiffness, positive rheumatic factor (RF) and radiologic evidences of Juxta-articular osteoporosis.

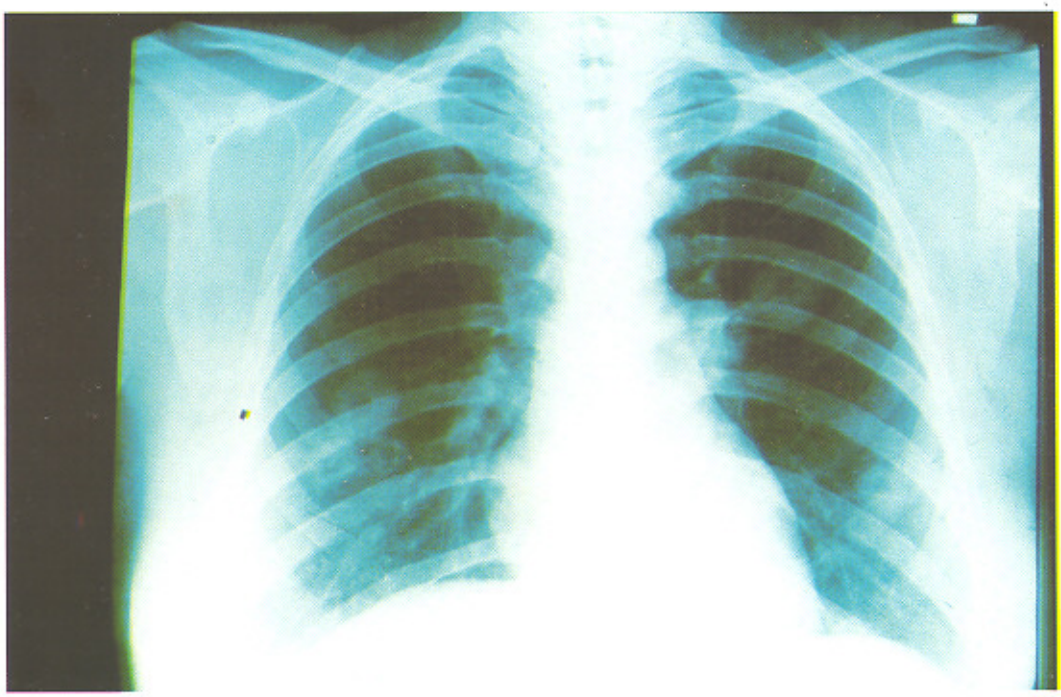

Fig. 1. Bilateral multinodular infiltration

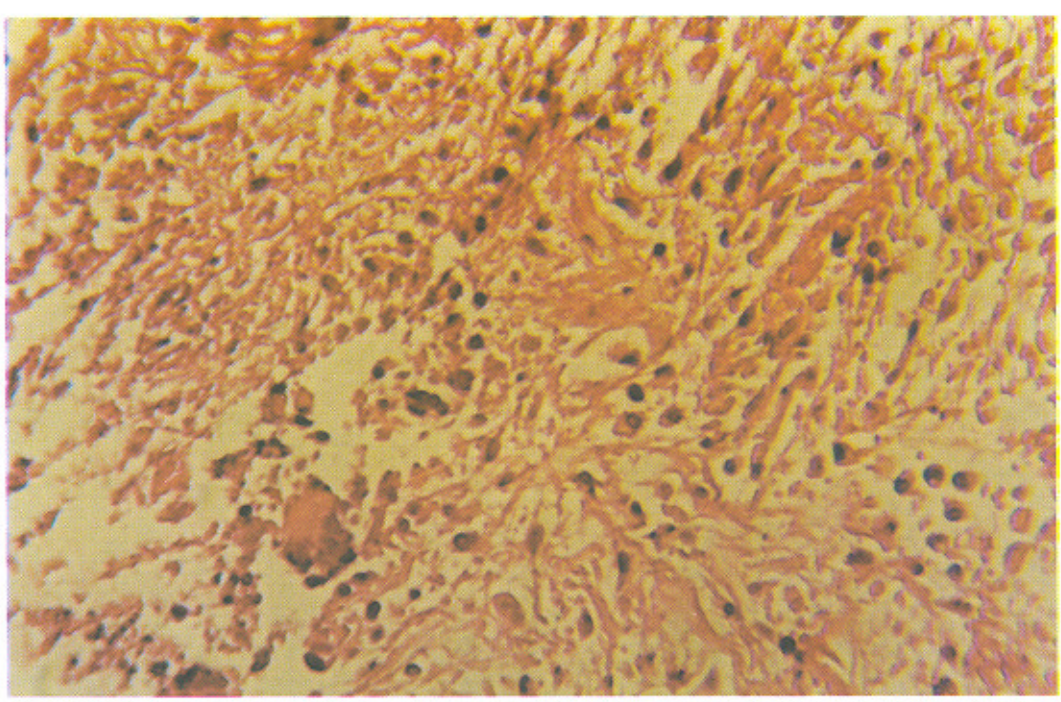

Fig. 2. Necrotizing granulomatous inflammation × 400

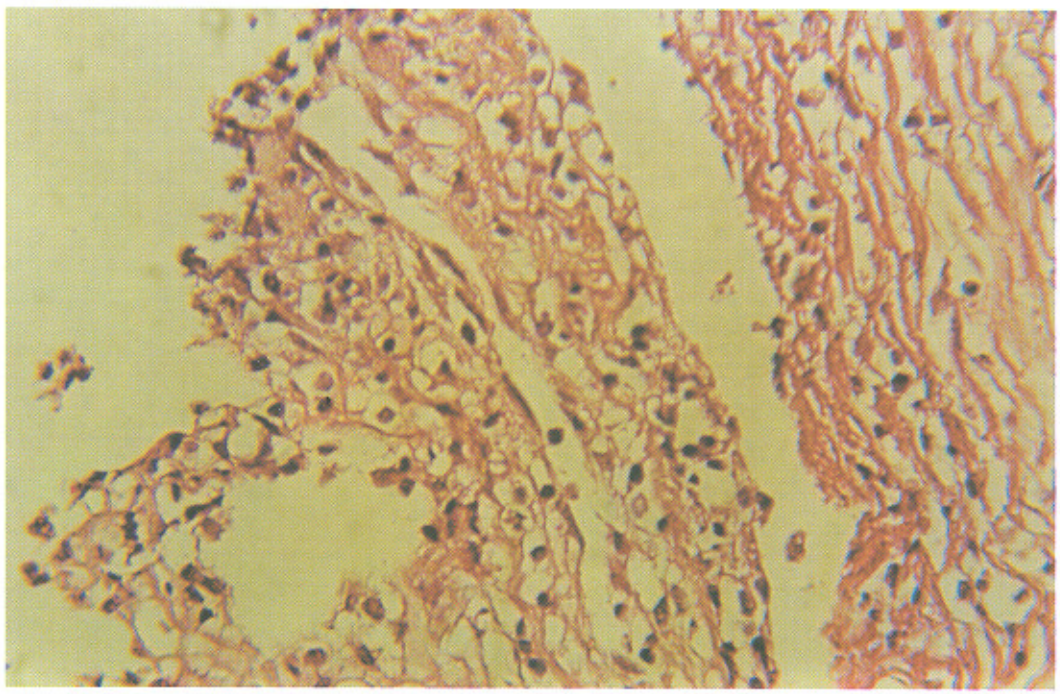

Fig. 3. Vascular channels infiltrated with inflammatory cells (vasculitis) × 400

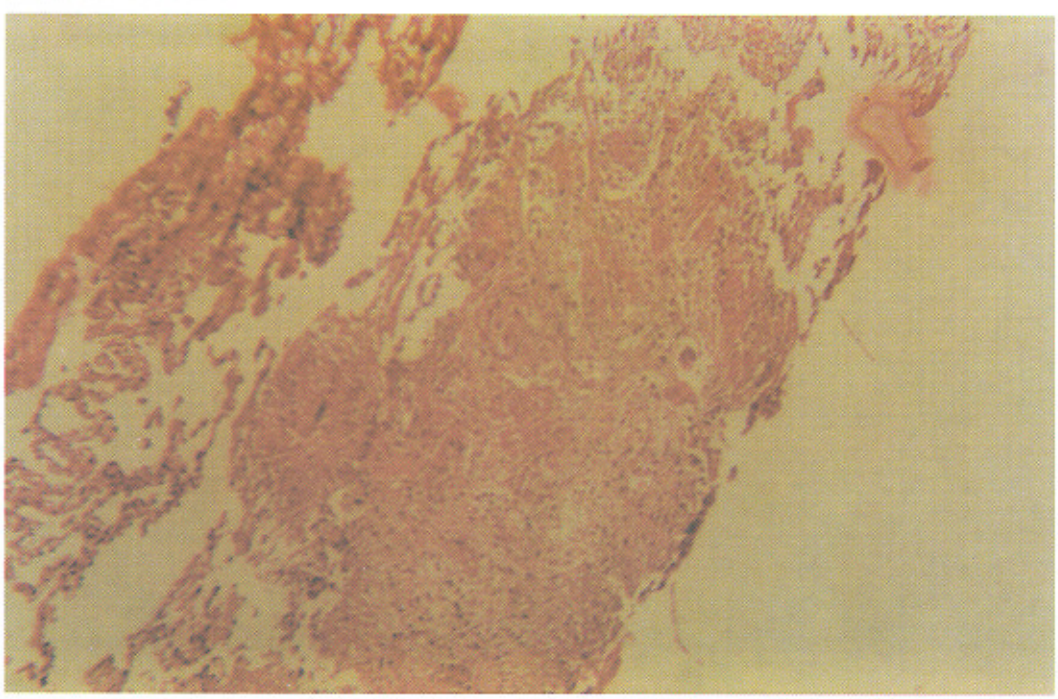

Fig. 4. Necrotizing granulomatous inflammation × 30

Her present complaints started 5 months before her admission, when after filling a decayed tooth by dentist, a nasal stuffiness, right ear pain and decreased hearing was noticed. She was referred to an otolaryngologist, her prednisolone dose was increased to 15mg/d, but no improvement ensued. Three months prior to admission, the patient developed a productive cough (with whitish thin purulent sputum) with occasional blood streaks in sputum, associated with low grade fever, night sweating and weight loss. Chest x-ray revealed bilateral multiple pulmonary nodules (Fig. 1) for which she was referred to the infectious diseases unit.

There was no history of other autoimmune diseases in the patient and her family. She has been taking the following drugs for management of "RA" the past 2 years:

Metotrexate: 7.5mg per week
Prednisolone: 5mg, P.O, daily
Chloroquine: 250mg (salt), P.O, daily
Amitriptyline: 25mg, P.O, Qhs

Physical examination done at the time of admission revealed a temperature of 36.7° c, a blood pressure of 110/70 mmHg, a pulse rate of 120 beats/min, and a respiratory rate of 20/min. Her lungs were clear bilaterally. Rest of examination was unremarkable except for mild right upper quadrant tenderness.

The values obtained during initial laboratory examination were as follows: WBC count, 8900 cells/mm^3 with 72% granulocytes; hemoglobin, 8.8 g/dl; Hematocrit, 28.7%; Retic count, 1.6% and platelet count, 490000 cells/mm^3.

The Erytrocyte sedimentation rate was elevated at 120 mm/h, and C Reactive protein reported positive.

Work up for her anemia revealed a serum Iron titer, 10 mg/dl (Normal range: 40-140) and total iron binding capacity, 206 μg/dl (Normal range: 250-460).

Liver and Tyroid function tests revealed normal values.

Urine analysis was normal and cultures of urine and blood were negative.

Sputum and Gastric lavage smear for acid fast bacilli were negative. Rheumatoid factor (latex) was positive, ANA, LE cell and anti double strand DNA were negative. Tuberculine test was 5 mm.

Regarding history, physical examination and Laboratory data, following differential diagnosis were considered: Nocardiosis, Actinomycosis, Tuberculosis, Wegener's Granulomatosis, Rheumatoid lung nodule and fungal diseases such as cryptococcusis, Aspergillosis.

Pathologic report of CT-guided lung biopsy from one of the peripheral nodules was compatible with "Tuberculosis", so, trial anti T.B. drugs was started while working up the patient for other differential diagnosis.

Lack of proper response to anti T.B. drugs, receiving positive C-ANCA titer (1/160) with subsequent raising titer associated with radiologist's report of pansinusitis in imagings, resulted in considering WG at the top of the list of differential diagnosis.

Meanwhile patient developed renal involvement as depicted by hematuria, pyuria and granular and hyaline casts on repeated urine analyses.

Pathology of the pulmonary nodule biopsy again was reviewed by the same pathologist. The second review of pathology specimen was more compatible with "Wegener's Granulomatosis" rather than tuberculosis. Treatment of WG. was started by means of cyclophosphamide (50-100mg/d) and prednisolone (60mg/d) after persuading consultant rheumatologists, but during hospital course patient developed pleural effusion and tracheal stenosis associated with respiratory distress, and so, was transferred to I.C.U. but unfortunately, despite of treating with high dose intravenous pulses of methylprednisolone, developed pneumothorax under artificial ventilation and died.

Necropsy from lung and kidneys were completely compatible with vasculitis and granulomatous changes in lung necropsy specimens, resembling Wegener's granulomatosis. (Fig 2,3,4).

DISCUSSION

On original presentation, this patient fitted the accepted diagnostic criteria for Rheumatoid arthritis (arthritis in a number of peripheral joints, positive Rheumatoid factor and Radiologic evidences of juxtaarticular osteoporosis).

Two years latter she developed respiratory and renal disease typical of wegener's granulomatosis. The combination of RA and wegener's granulomatosis in one patient, based on medline and internet research, has rarely been reported.

Ohashi et al (1992), Svirskiij (1994) and Sturock and co-workers (1974) have been reported patients with rheumatoid arthritis who developed WG (one patient in each report) (6,7,8).

It is possible that there may be a subgroup of patients with systemic diseases such as RA who go on to develop a small vessel vasculitis, whether wegener's granulomatosis or a related syndrome (9). The measurement of C-ANCA can be helpful in differentiating WG from the underlying diseases.

On the other hand, both wegener's granulomatosis and Rheumatoid arthritis may terminate in a generalized necrotizing arteritis. This as well as various other similarities indicate that these two different disease entities base on an identical hyperergic reaction of the vascular wall (10). The pathological faulty diagnosis as mentioned could be due to deep pathologic

resemblance of these two entities.

Finally, we conclude that the measurement of ANCA in patients with RA and presentation of new uncontrollable signs and symptoms might be sensitive method in detecting early vasculitic disease.

REFERENCES

1. Thomas E. Anderoli charles C.J. Carpenter. Robert C. Gri GGS, Joseph. Cecil Essentials of medicine: 5 th ed; Loscalzo. 2001.

2. Ramzi S. cotran, Vinay kumar, Tucker. Collins W.B. Robbins pathologic basis of diseases: 6 th ed; Saunder's company. 1999.

3. Shaun Ruddy, Edward D, Harris Jr, Clement B. Sledge kelleys textbook of Rheumatology: 6 th ed; Saunders company, 2001.

4. Edward D. Harris Jr. Mark C. Primary care Rheumatology: st ed; Saunders company, 2000.

5. MC Cune WJ, Friedman AW. Immuno-suppressive drug therapy for Rheumatic diseases. Curr-opin-Rheumatol. 1993 May; 5(3): 282-92.

6. Ohashi H, Itoh M, Ogawa N, Sudo Y, Endo S, Okugawa T, Ito H, Mineta H, Nozue M. Wegener's Granulomatosis in a patient with a Rheumatoid arthritis. Internal Medicine, 1992 Sep; 31(9): 1128-31.

7. Svirskiij AA, Potapenkov MA, Shchipulin PP, Kharitonor VM, Zelenin VS. Wegener's Granulomatosis in a patient with Rheumatoid arthritis. Lik sprava 1994 Feb; (2): 94-4 (abstract) (Russian language).

8. Sturrock RD, Ratnesar P. Wegener's Granulomatosis occurring in a patient with pre-existing Rheumatoid arthritis. Br. J. Clin pract 1974 May; 28(5): 183-4.

9. Wedderburn LR, Kwan JT, Thompson PW, Rudge SR. Juvenile chronic Arthritis and wegener's granulomatosis. Br. J. Rheumatology 1992 Feb; 31(2): 121-3.

10 Leu HJ. Pathology of pulmonary changes in wegener's granulomatosis, Rheumatoid arthritis and polyarteritis nodosa. Zentralbl Allg pathol 1979; 123(1-2): 36-44. (abstract) (German Language).