Case Presentation

Fever, Shortness of Breath, with Multiple Pulmonary Nodules

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A 55 year-old man presented to the outpatient clinic complaining of fever, drenching night sweat, loss of appetite, and significant loss of body weight for 3 months. His condition is associated with a progressive exercise intolerance and shortness of breath. There is no cough, no joint or skin involvement.

His past medical illness is significant for a history of conductive deafness due to chronic bilateral otitis media with many acute exacerbations for which he was treated with courses of antibiotics. He is not smoker, has no history of exposure to animals or contact to patient with TB. He works as a health worker exposed to pesticide.

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Clinical examination is unremarkable apart from high temperature (38°C), and scattered inspiratory course crackles. Routine biochemical tests are normal, complete blood count is remarkable only for neutrophelia, and eosinophilia. ESR was 110.

Chest X ray and HRCT of the chest have shown in (**Figure 1**) and (**Figure 2**) respectiively. General urine examination reveals significant proteinuria with Red Blood Cells and granular casts. Twenty-four hour urine for protein is 1000 mg.

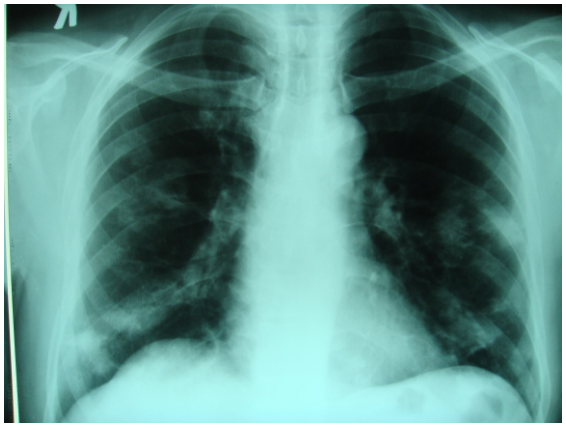

Figure 1: PA veiw chest X ray shows diffuse bilateral multiple nodules of variable sizes mainly in lower zones with relative sparing of the upper zones before treatment

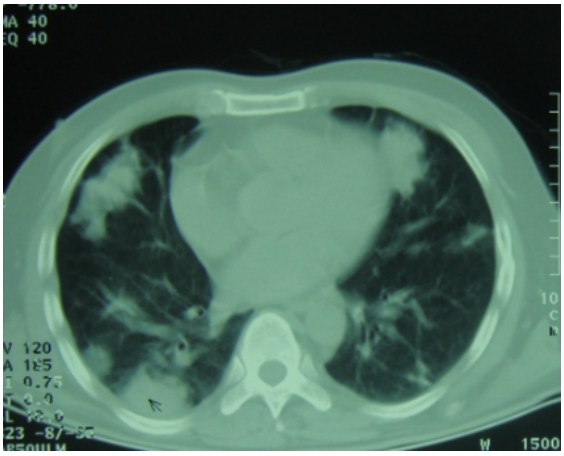

Figure 2: HRCT scan of the chest at the level of lower lobes before treatmnet showing bilateral multiple sizes paranchymal nodules some of them are pleurally based.

ANA is weakly positive; C3 and C4 are mildly increased, c-ANCA is positive. All other immune markers for connective tissue disorders are negative.

Bronchoscopy shows no remarkable pathology, sputum and bronchoalveolar lavage (BAL) for cytology and AFB are negative. Open lung biopsy shows multiple epithelial cell granulomas with central necrosis and multiple multinucleated Langerhan's giant cells surrounded by other chronic

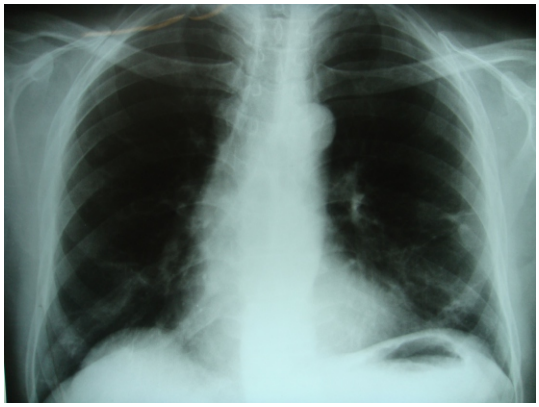

Figure 3: PA veiw chest X ray 2 months after treatment showing remarkable decrease in numbers and sizes of the nodules

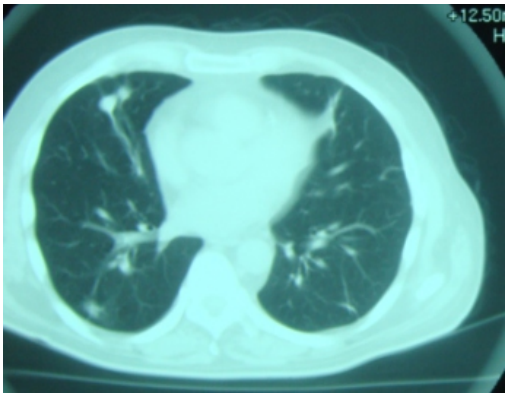

Figure 4: HRCT Scan of the chest has taken 2 months after treatment showing remarkable decrease in numbers and sizes of the nodules

inflammatory cells and minimal fibrosis. There is necrotizing vasculitis in the wall of the vessels.

Diagnosis: *Wegner's Granulomatosis.*

Patient is started on prednisolone 30 mg daily with cyclophosphamide 1.5 mg /kg. Two months followup reveals complete disappearance of fever and proteinuria. Chest X ray and HRCT after treatment have shown in figure 3 and 4 respectively.

WEGNER'S GRANULOMATOSIS (WG)

What is Wegner's Granulomatosis?

Wegener's granulomatosis (WG) is a necrotizing granulomatous vasculitis which has a clinical predilection for the upper airways, lungs, and kidneys.[1]

Is it common to have WG in respiratory medicine?

WG is the commonest vasculitides affecting the lungs.[2] Although WG can affect any age and both gender, but it predominantly involves middle age, and male patients. Its prevalence in the USA is about 3/100,000[3], accordingly we expected to see about 900 cases of WG in Iraq. More than 90 % of the cases involves upper and lower respiratory tract during the course of the disease.[4]

What are the systems involves?

Here percentages represent involvement of these organs during the course of the disease.[4]

Upper airways (92 %): nose destruction, sinusitis, otitis media with deafness, and subglottic stenosis.[5]

Lower airways (85 %): Ranges from mild to life threatening, may be unilateral or bilateral.

Kidneys (80 %): Glomerulonephritis is the most serious manifestation

Joints (76 %).

Eyes (52%).

Skin (46%).

Nerves (20%).

What are the radiological patterns of lung involvement in WG?

Infiltrative (63 %), infiltrative with cavity (up to 10 %), nodules (31%), and nodules with cavity (10%).[6]

What are important clinical points to be kept in mind regarding renal involvement in WG?

We should keep in mind two important things:

First: it can progress rapidly to complete renal failure in the absence of symptoms.[7]

Second: on presentation about 20 % showed renal involvement, but 80% of the patients will show such involvement at some points during the course of their disease, so continual follow up for signs and symptoms of glomerulonephritis is essential.[8]

What are the American College of Rheumatology criteria for diagnose Wegner's granulomatosis?

1)Nasal or oral inflammation: Development of painful or painless oral ulcers or purulent or bloody nasal discharge.

2) Abnormal chest radiograph: Chest radiograph showing the presence of nodules, fixed infiltrates, or cavities.

3) Urinary sediment: Microhematuria (>5 red blood cells per high power field) or red cell casts in urine sediment.

4) Granulomatous inflammation on biopsy: Histologic changes showing granulomatous inflammation within the wall of an artery or in the perivascular or extravascular area (artery or arteriole).

Diagnosis of WG needs the presence of at least 2 out of the above criteria, yields a sensitivity of 88.2% and a specificity of 92.0%.[9]

What is another way of diagnosis?

The diagnosis of WG is usually made by the histological demonstration of vasculitis, granulomatous inflammation, and necrosis in clinically compatible setting.[10]

What is the role of c-ANCA in the diagnosis of WG?

c-ANCA has a high sensitivity for diagnosis of WG. It is positive in more than 90 % patients with untreated active WG. The rate of positivity declines substantially when the disease is in remission, but the test is not sufficiently sensitive to serve as a guide to therapy.[11]

Is it possible for c-ANCA to replace Biopsy in the diagnosis of WG?

Although a positive c-ANCA may be useful in the suggesting the possibility of WG, it should not normally be used in place of a biopsy sample to make the diagnosis, because Positive c-ANCA has also been reported to occur in other diseases that are part of the differential diagnosis of WG.[12]

How can we treat a patient with WG?

The current cytotoxic drug of choice is cyclophosphamide in a dosage of 1-2 mg /kg/day, either alone or in combination with low doses of corticosteroid for at least a year after a decline in disease activity.[13]

Azathioprine can be a less toxic alternative to cyclophosphamide for long term maintenance therapy.[14]

What is the prognosis of a patient with WG?

Without treatment WG had a poor prognosis; the average survival was about 5 months.[10]

With treatment, 75-90% of patients treated with the above regimen experience a complete remission.[13] However, relapses can occur in some patients after discontinuation of therapy which necessitates the use of maintenance therapy.[14]

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Questions and answers about this case on CME pages