Wegener Granulomatosis - Rare Case Presentation

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Abstract

Wegener granulomatosis is often misdiagnosed as pneumonia and most common cause for bilateral lung infiltrates' are bacterial, viral, pneumocystis jiroveci infection. We describe a 35 year old female with 15 days history of nasal obstruction, breathlessness and fever. Investigations in this patient revealed chronic necrotizing vasculitic and granulomatous lesion in nasal biopsy, vasculitic pauciimmune glomerulonephritis in renal biopsy, serology test was positive for C-ANCA, nodular with cystic lesion in CT-thorax. All these findings confirmed the diagnosis of Wegener granulomatosis.

Introduction

Wegener’s granulomatosis is a distinct clinicopathologic entity characterized by granulomatous vasculitis of the upper and lower respiratory tracts together with glomerulonephritis. In addition, variable degrees of disseminated vasculitis involving both small arteries and veins may occur.

Wegener’s granulomatosis is an uncommon disease with an estimated prevalence of 3 per 100,000. It is extremely rare in blacks compared with whites; the male-to-female ratio is 1:1. The disease can be seen at any age; ~15% of patients are <19 years of age, but only rarely does the disease occur before adolescence; the mean age of onset is ~40 years.

Clinical features suggest involvement of upper and lower respiratory tract, skin, renal system, ocular system, central nervous system, cardiac system needs to be differentiated from an indolent parenchymal infection (Pneumocystis jiroveci pneumonia in a patient with AIDS, mycobacterial or fungal pneumonia), eosinophilic pneumonia, cryptogenic organizing pneumonia, pulmonary edema, pulmonary embolism, lung carcinoma, radiation and hypersensitivity pneumonitis.

Case Report

A 35 years female was admitted with chief complaints of 15 days of nasal discharge, cough with expectoration, breathlessness, fever and haemoptysis. There was no history of haematuria, loose stools, convulsions, vomiting, skin rashes, chest pain. The patient was treated initially empirically for the sinusitis with antibiotics and biopsy of nasal mass was done before coming to our hospital with no response. General physical examination reveal pallor, vital parameter were normal, respiratory rate is 22per/min. Examination of respiratory system revealed mass in the right nasal cavity, bilateral diffuse course crepts. Other system examination was normal.

Investigations

Complete haemogram; showed hemoglobin -7.6gm% with normocytic normochromic anaemia with neutrophilia in peripheral blood film, urine routine showed albumin [3+], red blood cells [15-20], pus cells [8-10], epithelial cells [2-4] per high power field, 24 hour urine protein [1.5 gm] blood urea [76mg/dl], creatinine (3.5 mg/dl), serological test was positive for C-ANCA, negative for P-ANCA, and ANTI-GBM antibodies, sputum smear was negative for Acid fast bacilli, KOH mount for fungal elements was negative, sputum culture showed coagulase negative staphylococcus and sensitive for AMOXY-CLAV, chest x-ray showed perihilar non homogenous opacity with air bronchogram with nodular shadows in left upper zone and right lower zone [Figures 1, 2]. CT-SCAN of paranasal sinuses [Figure 3] showed mass in right maxillary sinuses and nasal cavity, CT-SCAN of thorax showed [Figures 4, 5] bilateral pneumonic consolidation with nodular and cystic components, nasal biopsy showed chronic necrotizing vasculitic and granulomatous lesion, kidney biopsy showed [Figure 6] showed vasculitis with glomerular crescent and pauciimmune glomerulonephriti, 2D-ECHO was normal. All these findings confirmed the diagnosis of Wegener’s granulomatosis.

Patient was started on intravenous methyl prednisolone pulse therapy her symptoms improved dramatically and we switch over to oral prednisone 1mg/kg and cyclophosphamide 2mg/kg and discharged the patient. She consulted after 4 months with symptoms of mononeuritis multiplex (Figure 7) and convulsions suggestive of small vessel vasculitis due to drug noncompliance. Patient was started on intravenous methyl prednisolone pulse therapy and antiepileptic drugs her symptoms improved and discharged with residual deficits. Follow up was done with neutrophil count [>1500/L]. Patients did not come for follow up and she was again admitted with fever, breathlessness and neutropenia and died secondary to septicemia due to cyclophosphamide toxicity.

Clinical Feature

Clinical feature reveal involvement of upper airways [95%of patients], Pulmonary involvement [85–90% of patients], Renal disease [77% of patients], Eye involvement [52% of patients], Skin lesions [46% of patients] upper airways and Pulmonary manifestations include nasal obstruction, purulent discharge, sinusitis, chronic ulceration-even, in some cases, necrosis of nasal cartilage and bone and bilateral pneumonitis. Cough, haemoptysis and pleurisy are usually accompanied by constitutional symptoms of malaise, weakness and fever. Nervous system manifestations (23% of patients) include mononeuritis multiplex, polyneuropathy, myopathy, seizures, stroke, hemorrhage, dural venous thrombosis, pachymeningitis, cerebritis, and myelopathy Orbital pseudotumors cause exophthalmos and ophthalmoplegia. Involvement of the optic nerve, seventh and eighth cranial nerves, chiasm, and pituitary gland can occur. Pituitary involvement causes diabetes insipidus.
Eye manifestations are found eventually in some 60% of patients, including corneal/scleral ulceration, granulomatous keratitis or uveitis, conjunctivitis, proptosis, orbital pseudotumour, dry eyes, retinal vein occlusion and retinal artery thrombosis. Skin lesions (46% of patients) appear as papules, vesicles, palpable purpura, ulcers, or subcutaneous nodules.

Laboratory findings include elevated ESR, mild anemia and leukocytosis, 90% of patients with active Wegener’s granulomatosis have a positive antiproteinase-3 ANCA.

Diagnosis

The diagnosis of Wegener’s granulomatosis is made by the demonstration of necrotizing granulomatous vasculitis on tissue biopsy. Pulmonary tissue offers the highest diagnostic yield, revealing granulomatous vasculitis. Biopsy of upper airway tissue usually reveals granulomatous inflammation with necrosis but may not show vasculitis. Renal biopsy can confirm the presence of pauci-immune glomerulonephritis, positive antiproteinase-3 ANCA. Granulomatous masses up to several centimetres in diameter may be apparent on the chest radiograph. These are fairly well defined and often cavitate; they may resolve spontaneously, while new masses appear. Cavitating lesions may have thick or thin walls, depending on how much of the necrotic material is expectorated. Multiple cavities can closely mimic tuberculosis. Other frequent radiographic signs are small pleural effusions and paranasal sinus opacification.

However, if all the typical features are not present at once, it needs to be differentiated from the other vasculitides, Goodpasture’s syndrome, relapsing polychondritis, tumors of the upper airway or lung, and infectious diseases such as histoplasmosis, mucocutaneous leishmaniasis and rhinoscleroma as well as noninfectious granulomatous diseases. midline granuloma, Cocaine-induced tissue injury, lymphomatoid granulomatosis and upper airway neoplasms.

Treatment

Cyclophosphamide given in doses of 2 mg/kg per day for 1 year following the induction of complete remission and gradually tapered and discontinued thereafter. Prednisone, 1 mg/kg per day initially (for the first month of therapy) as a daily regimen, with gradual conversion to an alternate-day schedule followed by tapering and discontinuation after –6 months.

Using the above regimen, the prognosis of this disease is excellent; marked improvement is seen in >90% of patients, 50% of remissions are later associated with one or more relapses. Reinduction of remission is almost always achieved; Certain types of morbidity are related to toxic side effects of treatment. Cyclophosphamide-related toxicities are more frequent and severe. Cystitis to varying degrees occurs in at least 30% of patients, bladder cancer in 6%, myelodysplasia in 2%, and there is a high risk of permanent infertility in both men and women. Methotrexate or azathioprine should be used for remission maintenance to avoid Cyclophosphamide-related toxicities. In patients who are unable to receive methotrexate or azathioprine or who have relapsed through such treatment, emerging data suggest that mycophenolate mofetil, 1000 mg twice a day, may also sustain remission following cyclophosphamide induction in selected patients. Methotrexate Induction as an alternative for initial therapy for Nonsevere Disease. Trimethoprim-Sulfamethoxazole decrease relapses in upper airway disease, Subglottic tracheal stenosis and endobronchial stenosis are examples of disease manifestations that do not typically respond to systemic immunosuppressive treatment.

Discussion

Wegener’s granulomatosis is an uncommon disease with an estimated prevalence of 3 per 100,000. The classic histopathologic finding in Wegener granulomatosis is a focal segmental necrotizing and crescentic glomerulo nephritis “Intracapillary thrombosis” with deposition of eosinophilic “fibrinoid” material is common in early lesions together with endothelial cell swelling. The vasculitis in Wegener granulomatosis may affect small and medium sized renal arteries, veins, and capillaries. The vasculitis, which is focal in nature, has been reported in 5% to 10% of biopsies of Wegener patients. Most reports describe only focal low intensity immunofluorescence staining, a pattern referred to as “pauciimmune Often, upper-airway biopsies

![Fig. 1: During admission X-RAY Showing nodular infiltrates in left upper, mid zone and non homogenous infiltrates in right mid zone and lower zone.](image1)

![Fig. 2: After 2 weeks X-RAY Showing resolution of nodular infiltrates in left upper, mid zone and non homogenous infiltrates in right mid zone and lower zone.](image2)
are non diagnostic because the inflammatory infiltrate obscures the vasculitis, so that multiple upper-airway biopsies or lower respiratory biopsies are required before histologic diagnosis is ultimately made.2

The immunopathogenesis of this disease are aberrant cell-mediated immune response.1

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Abbreviations


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