An Insidious Disaster Composed of Sinusitis, Myocarditis, Lung Mass And Rapidly Progressive Glomerulonephritis: Wegener Granulomatosis

Sinüzit, Miyokardit, Akciğerde Kitle ve Hızla İlerleyen Glomerülonefrit: Wegener Granülomatozu

ABSTRACT

Wegener's Granulomatosis is a multisystemic granulomatous inflammation of small vessels that typically effects the kidney, skin, joints and lower and upper airway tracts. Because of the multisystemic involvement, the signs and symptoms of disease may arise in heterogeneous fashion. Under the appearance of a nonspecific sytemic complaints, the suspicion of clinician may be a final clue for diagnosis. Here we present a patient with Wegener's granolomatosis sufferring from generalized malaise, fever, heart failure, lung mass and acute renal failure. Multidisciplinary and close colloborative management is important to establish early diagnosis. We belive that plasmapheresis at initial acute onset of vasculitis syndromes especially in severe extrarenal involvements may be a life-saving management.

KEY WORDS: Wegener's granulomatosis, Myocarditis, Iung mass, Acute renal failure

ÖZ

Wegener granulomatozu klasik olarak alt ve üst hava yolları, böbrekler, deri ve eklemleri etkileyen nekrotizan granülomatoz yangılı vaskülitik sendromdur. Bir çok organ etkilenebileceğinden tutulan organa bağlı heterojen klinik bulgu verme özelliği vardir. Özgün olmayan sistemik klinik bulgular eşliğinde bazen, sadece klinisyenin şüphesi ile tanı konulabilir. Burada, genel durum bozukluğu, ateş, klinik kalp yetmezliği ve akciğerde kitle tanısı ile izlenen ve takipte akut böbrek yetmezliği gelişen Wegener Granulomatozlu bir hasta sunulmuştur. Multidisipliner yaklaşım tanı ve tedavide önemlidir. Akut vaskülit sendromların özellikle şiddetli böbrek dışı tutuluşlarında sitotoksik tedavi ve/veya plazma değişimi hayat kurtarıcı olabilir.

ANAHTAR SÖZCÜKLER: Wegener granulomatozu, Myokardit, Akciğerde kitle, Akut böbrek yetmezliği

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INTRODUCTION

Wegener's Granulomatosis (WG), is a multisystemic granulomatous inflammation of small vessels typically effects kidney and lower and upper airway tracts. Because of the multisystemic involvements signs and symptoms of disease may arise in a heterogenous fashion (1-4). It also important to point out that systemic involvelments of myocard, lungs and also kidney can be fatal under non specific scenes. This paper presents a patient with severe systemic WG involves upper and lower respiratory tracts, heart and kidney.

Case:

A 42-year-old man was admitted to Infectious Disease Department due to fever, rhinorrhoea and nosebleed. Sinusitis was diagnosed and antibiotic treatment was started. One week later patient was readmitted with malaise, fever, weight loss dysuria. Complete blood count showed increased liver function tests [SGOT:125 U/L (<35), SGPT: 77 U/L (<45), ALP: 259 U/L (40-129), GGT: 315 U/L (<55)], with hypoalbuminemia [Albumin : 2.8 mg/d L (3.5-5.2)] and increased serum CRP levels [(CRP: 26.5 mg/d L (<0.5)] with elevated

Received: 12.08.2009
Accepted: 23.11.2009

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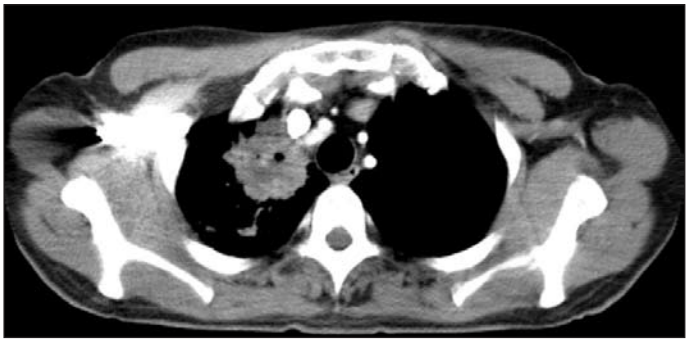
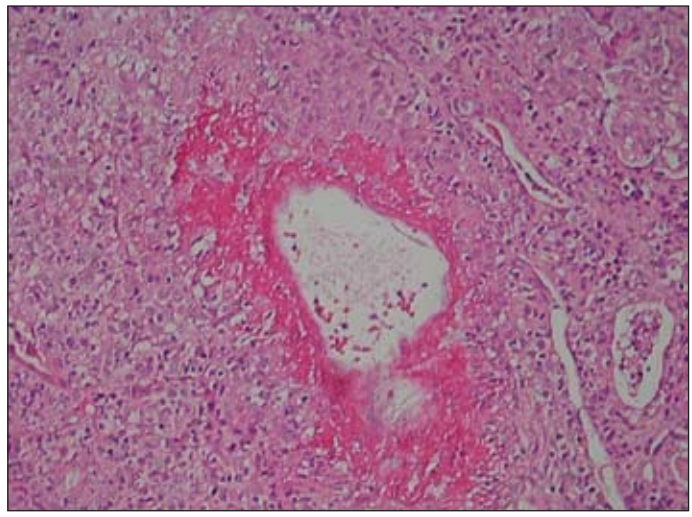
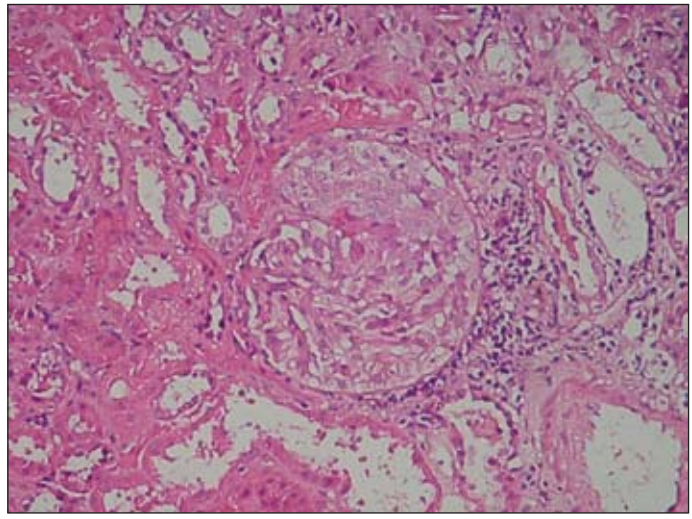
ESR 91 mm/h and marked leukocytosis [(Leucocyte count: 27.6X103 /mm3 (4.5-11)]. Serum urea and creatinine levels were normal. Urine analysis showed leukocytouria and hematuria. After sampling of urine for bacteriological culture antibiotic treatment was started emprically. A few days later patient had suffered from chest pain, palpitation and dyspnea. Physical examination also revealed pericardial rubs. Electrocardiography revealed sinus tachycardia Echocardiography showed pericarditis and globally hypokinesia with left ventriculer ejection fraction (LVEF) 25%. The patient was transferred to the Cardiology Department because of a suspicion of myocarditis. Endocardial biopsy showed intense inflammation including polymorphonuclear leukocytes (PMNL), lymphocytes and plasma cells, myocyte hypertrophy and arteriolar fibrointimal thickening. Serial blood and urine cultures showed no definitive organism. Rutine chest X-Ray film showed right apical consolidation and chest computerized tomography (CT) revealed solid mass mimicking lung cancer (Figure 1). Transthoracic fine neddle lung parenchyme biopsy with bronchoscopy revealed intense polymorphonuclear leukocyte infiltration, epitelioid histiocytes with one multinuclear giant cell at specimen. Subsequently urine output decreased and kidney function test increased (Urine output: 250-300 cc/day, serum creatinine: 7.2 mg/dL, serum urea: 183 mg/dL). Kidney ultrasound examination showed normal kidney size with gradually increased thickness of renal parenchyme without postrenal obstruction highly suspicious for intrinsic acute renal failure. Urinalysis has still been showed hematuria. Serum complement levels were normal. Hemodialysis (HD) treatment was started due to high levels of urea and creatinine with hyperkalemia. Kidney biopsy was performed under urgent conditions and small vessel vasculitis was diagnosed (Figure 2A,B,C). Paranasal computerized tomography showed destructed medial wall of right maxillary bone (Figure 4). Pathological findings of right nasal cavity demonstrated mucosal inflammation, submucosally located multinucleated giant cells, epithelloid histiocytes, lymphocytes, plasma cells and PMNL (Figure 4). İmmunologic markers also supported cANCA positivity (1/80). Plasmapheresis plus intravenous pulse prednisolone plus intravenous cyclophosphamide therapy was started. Two weeks later HD therapy stopped and the patient discharged with induction therapy and a follow-up lung CT revealed significant regression in the previous solid mass (Figure 5).



Şekil 1: *Chest CT (Mediastinal window). A contrast-enhanced axial CT scan at the level of brachiocephalic truncus. Right apicoposterior solid mass just near the superior vena cava and brachiocephalic truncus with irregular shape.*



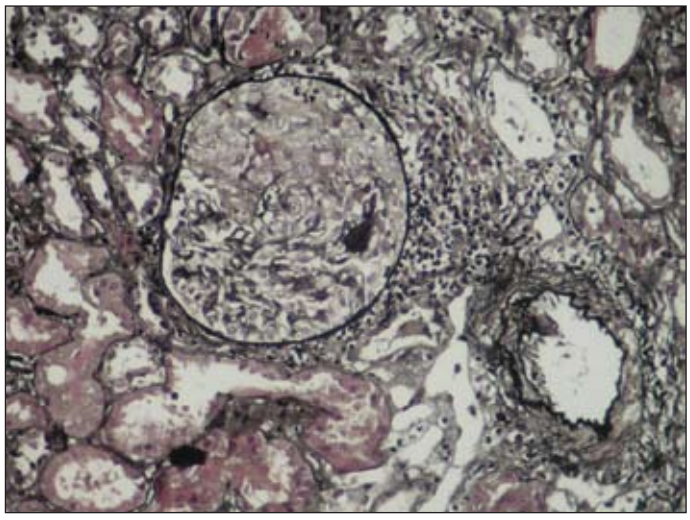
Şekil 2A: *Arterial fibrinoid necrosis. Transmural fibrinoid necrosis of one renal arteriol with intense inflammatory cell infiltration of tubulointerstitial area. (Hematoxylen-eosin. Original magnification X20).*



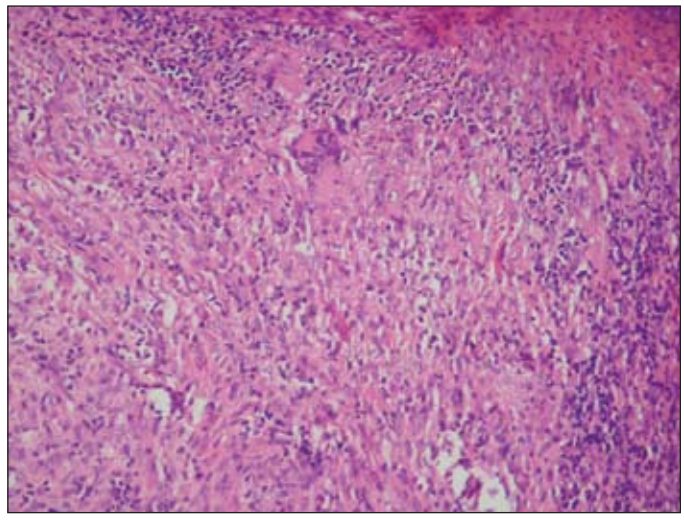
Şekil 2B: *Crescentic glomerulonephritis Cellular crescent formation at upper half of renal glomeruli with inflammatory cell infiltration. (Hematoxylen-eosin. Original magnification X20).*

DISCUSSION

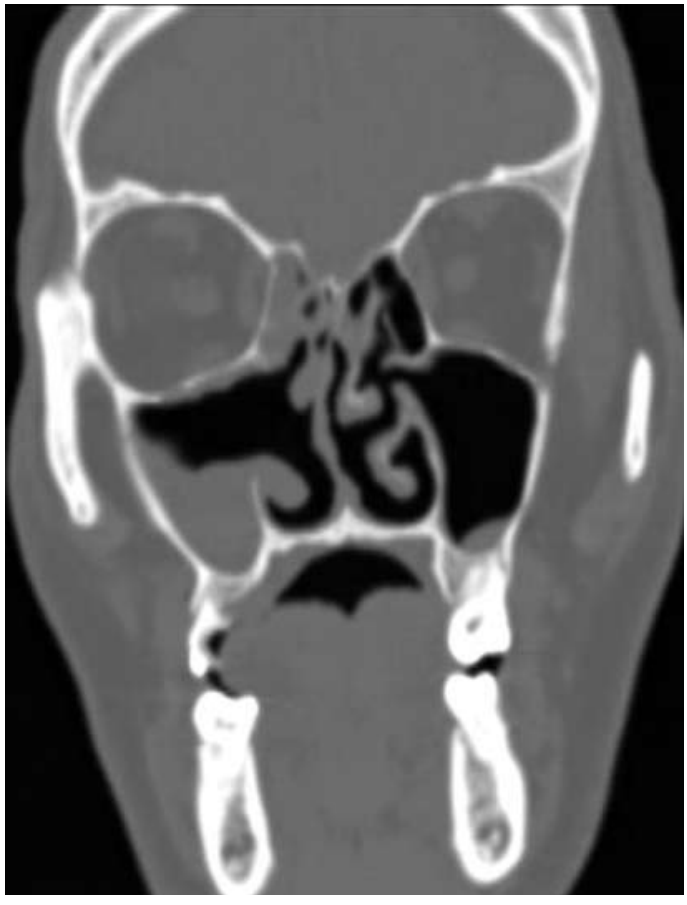
WG affects especially the respiratory system and the kidney. Because of the multisytemic disease, manifestations may be heterogenous (1-5). This is the first we have ever seen such an agressive Wegener granulomatosis with severe myocarditis,



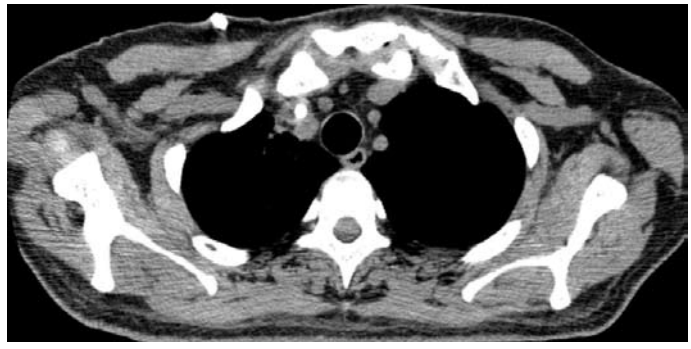
Şekil 2C: *Crescentic glomerulonephritis. Cellular crescent formation at upper half of renal glomeruli with inflammatory cell infiltration. (Methenamin silver. Original magnification X20).*



Şekil 4: *Granulomatous foci of nasal cavity Multinucleated giant cell with scattered epitelloidhistiocytes surrounded by polymorphonuclear leukocytes end lymphocytes forming granuloma at right nasal cavity. Hemotoxylen eosin. Original magnification X20).*



Şekil 3: *Paranasal CT scan revealed pansinusitis and maxillary bone medial part destruction with nasal septum deviation.*



Şekil 5: *An axial CT image of lung in mediastinal window. Almost complete resolution of solid mass at brachiocephalic level as compared to findings of figure 2.*

low ejection fraction (LVEF<30%), lung parenchymal solid mass, mimicking lung cancer and acute renal failure. Because of the varying and sometimes nonspecific presentations of WG, multidisciplinary and close colloborative management is important to establish early diagnosis. In our case, nonspecific symptoms were fever, malaise, weight loss with solitary lung mass and were highly suspicious for lung cancer especially if we take into account that our patient is also a cigarette smoker. Multiorgan involvement may be an insidious course in WG as in our case. Cardiac involvement in WG is not as uncommon, ranging from 6-44% of patients. Pericarditis, arteritis, myocarditis, valvulitis and arrhytmias, mostly atrial tachycardia, atrial fibrillation or flutter, are classical signs and symptoms (6). In our case pericarditis and myocarditis with atrial tachycardia have been detected. In fact late nephrology consultation in this patient because of hematuria had been recorded several times

from the day of admission and resulted in delayed diagnosis of WG. Upper and/or lower airway involvement can be seen in all of the patients with WG. Unless pulmonary mass, nodules or hemopthysis have been detected in airway involvement, signs and symptoms can be silent or more conflicting. In addition characteristic granulomata may be absent or difficult to detect anywhere (5). Delay in diagnosis may result in irreversible organ dysfunction even death. However up to 80% to 83% patients with WG have renal lesions (7-8). Detected hematuria with acute renal failure, especially enlarged renal parenchymal thickness mostly due to oedema, in systemic inflammatory conditions, almost always takes vasculitis into consideration. Renal lesions, resembling vasculitic histopathology, can be a final clue to make diagnosis. Aggressive immunosupressive therapy with cyclophosphamide-glucocorticoid markedly diminished mortality as survival in untreated generalized WG is otherwise extremely poor (6-12). Oral or parenteral methotrexate and glucocorticoids for induction of remission is a conflicting approach especially in patients with a serum creatinine concentration above 2.0 mg/dL (177 μmol/L) (13-16). Plasma exchange appeared to be of benefit among patients who required dialysis (17) and have severe generalized organ dysfunction (18). In our case we started agressive induction therapy including 5 days plasma exchange (fresh frozen plasma 0.4 L/ kg per day) with pulse glucocorticoid (10mg/kg per day), pulse cyclophosphamide (0.5 g/m2 of body surface area) and daily long session hemodialysis. At the seventh day, the urine output improved. Addition of plasma exchange to cyclophosphamide and glucocorticoid therapy may be a life-saving approach in such severe cases. During first month of induction therapy EF improved (LVEF= 57%, modified Simpson rule), hemodialysis was stopped and the lung parenchymal mass completely resolved. Although this is a case report, we believe that plasmapheresis at initial acute onset of vasculitis syndromes with cytotoxic therapy especially in patients with severe renal and extrarenal involvement may be life-saving. In conclusion, WG should be kept in mind in systemic inflammatory conditions with active urine sediment and abnormal chest radiograph.

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