

Intestinal perforation in Wegener's granulomatosis: a case report

Wegener granülo-matozunda intestinal perforasyon: Olgu Sunumu

Tamer AKÇA, Tahsin ÇOLAK, Mehmet ÇAĞLIKÜLEKÇİ, Koray ÖCAL, Suha AYDIN

Wegener's granulomatosis is a disease characterized by a necrotizing vasculitis and granulomatous inflammation. The localized form involves the upper and/or lower respiratory tracts while in the common generalized form there is a widespread necrotizing vasculitis and renal involvement. Although gastrointestinal involvement which has been detected at necropsy in 24% of the cases is an uncommon finding, it might cause severe complications. We report a patient with clinical Wegener's granulomatosis who subsequently developed gastrointestinal perforation.

Gastrointestinal perforation was treated with surgical resection and the patient survived under the treatment of cyclophosphamide and prednisolone with no further gastrointestinal complications.

The present case indicates that the gastrointestinal complications might be considered in natural history of Wegener's granulomatosis.

Key words: complication, immunosuppressive therapy, intestinal involvement, perforation and Wegener's granulomatosis.

Wegener granülo-matozu nekrotizan vaskülit ve granülo-matöz inflamasyonla karakterize bir hastalıktır. Lokalize formu alt ve/veya üst solunum yollarını tutmakta, yaygın formu ise yaygın nekrotizan vaskülit ve böbrek tutulumu mevcuttur. Olguların % 24'ünde saptanan gastrointestinal tutulum olağandışı bir bulgu olmasına rağmen ciddi komplikasyonlara yol açabilmektedir. Daha sonra gastrointestinal perforasyon gelişen bir klinik Wegener granülo-matozu hastasını sunmaktayız.

Gastrointestinal perforasyon cerrahi rezeksiyonla tedavi edilmiş, hasta başka herhangi bir gastrointestinal komplikasyon olmaksızın siklofosfamid ve prednisolon tedavisi altında yaşamını sürdürmüştür.

Bu olgu Wegener granülo-matozunun doğal seyrinde gastrointestinal komplikasyonların da göz önüne alınabileceğini göstermektedir.

Anahtar sözcükler: komplikasyon, immüno-supresif tedavi, intestinal tutulum, perforasyon ve Wegener granülo-matoz.

INTRODUCTION

Wegener's granulomatosis is a rare systemic necrotizing vasculitis of unknown etiology with distinct clinical and histological features. Classically, the localized forms of Wegener's granulomatosis involve the upper and/or lower respiratory

tracts and kidneys. It might rarely involve any part of the body as well as gastrointestinal tract^[1-4]. Gastrointestinal signs and symptoms are uncommon. Intestinal involvement may be severe and numerous cases of perforation and bleeding of gastrointestinal tract have been reported.^[5-7] but only a few cases had the histological evidence of vasculitis

Mersin Üniversitesi Tıp Fakültesi, Genel Cerrahi
Anabilim Dalı, Mersin

Mersin University, Faculty of Medicine, Department
of General Surgery, Mersin, Turkey

İLETİŞİM (Correspondence): Dr. Tamer Akça. Mersin Üniversitesi Tıp Fakültesi Hastanesi, Cerrahi ABD, Zeytinlibahçe C. 33079
Mersin, Türkiye. tel: +90 324 3374300; Faks: +90 324 3374305 e-posta: takca@mersin.edu.tr

at the site of perforation [8-10]. We report a patient with clinical Wegener's granulomatosis who subsequently developed gastrointestinal perforation.

CASE REPORT

A 56 year-old male patient who received immunosuppressive drugs for Wegener's granulomatosis was admitted with severe abdominal pain, nausea, vomiting, abdominal distension and obstipation. As his medical history revealed, four months before admission dyspnoea, severe polyarthralgia and three months before admission systemic bullous lesions had developed. Examination at the Department of Diseases of Chest revealed that there were systemic necrotizing, ulcerous lesions, and yellowish plaques at the tongue, hyperkeratotic lesions at the lower lip and ulcerous, necrotizing, hemorrhagic, bullous lesions at the extremities (Figure 1). Chest x-rays and computerized tomography of the chest showed nodular lesions in the left mid zone with right upper and basal zones of the lungs. Biopsies of lower lip and skin lesions showed systemic vasculitis typical of Wegener's granulomatosis and the treatment was planned with cyclophosphamide and prednisolone.

However, severe generalized abdominal pain developed at 70. treatment day. The physical examinations revealed abdominal distension, tenderness and involuntary guarding. Bowel sounds were absent on abdominal auscultation. Digital rectal examination was painful. His axillary temperature was 38.5°C. Plain abdomen and chest radiograms showed free air under the diaphragm. Laboratory investigations including a complete blood count and all biochemical parameters were within normal limits, except white blood cells (WBC) count was 15,400 cells/ μ L. Investigations confirmed the presence of an acute-phase response with raised erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Autoantibody screen was positive for antineutrophil cytoplasmic antibodies (c-ANCA). Elevation in carcinoembryonic antigen and cancer antigen (CA) 125 and CA 15-3 were found but alpha-fetoprotein, CA 19-9 and human chorionic gonadotropin levels were within normal ranges.

At laparotomy, approximately two liters of infected fluid were aspirated with inflammation,



Figure 1: Ulcerous, necrotising, hemorrhagic, bullous lesions at the extremities of our patient with Wegener's granulomatosis

necrosis and demarcation line at the last forty centimeters of the terminal ileum. There was a simple 10X10 mm perforated lesion at the antimesenteric side of the terminal ileum. Other abdominal organs were normal. Partial small bowel resection and ileocolostomy were performed. Cyclophosphamide and prednisolone treatment were stopped for first postoperative 90 days, thereafter the patient survived on the same treatment regimen.

An incisional hernia developed within seven months after surgical intervention and herniorrhaphy with mesh was performed. No gastrointestinal complication developed within fifteen months of the follow-up.

Histological examination of the surgical material revealed vascular congestion, mucosal ulceration, and massive mixed inflammatory cell infiltration of serosa with eosinophilic and lymphocytic infiltration of lamina propria. In the perforation area, mucosal ulcer, fistula tract and massive congestion, serosal purulent inflammation and fibrosis were showed. As a result, transmural infarct was reported.

DISCUSSION

Fauci et al. suggested that in order to establish the diagnosis of Wegener's granulomatosis there should be clinical evidence of disease in two or three principal sites (upper airway, lung and kid-

neys) with histological confirmation in at least one and preferably two sites. Thus, our case had diagnostic criteria (clinical findings upper airway and lungs and histological vasculitis at the lip biopsies) and was started immunosuppressive therapy. Before the institution of effective immunosuppressive therapy with cyclophosphamide alone or in combination with corticosteroids, the prognosis for of the patients with Wegener's granulomatosis was extremely grave ^[11]. Koldingness et al. reported that treatment with cyclophosphamide and corticosteroids led to a 10 year survival rate of %75 in Wegener's granulomatosis without preventing severe organ damage ^[12]. The mean survival of the untreated patients was five months with 82% of the patients dying within one and more than 90% of them within two years ^[5]. Today, experiences gained so far showed that cyclophosphamide alone or in combination with corticosteroids were the cytotoxic drug of choice in Wegener's granulomatosis ^[5]. The treatment protocol of our case was planned according the previous experiences reporting favourable clinical responses and significant long-term remissions.

However, gastrointestinal perforation developed five months after the diagnosis and 70 days after the initiation of the immunosuppressive treatment. Storesund et al. reported that the initial bowel manifestations occur within the first two years of the disease ^[9]. In our case, the main problem is to determine whether necrosis and perforation at the terminal ileum secondary to Wegener's granulomatosis or immunosuppressive treatment was the etiological factor. Because the use of cytotoxic agent in non-neoplastic disease is still a matter of concern with regard to short- and long-term side effects, it is important to evaluate both the efficacy and possible toxic side effects seen over a prolonged period of the therapeutic regimen. Mueller et al. reported an intestinal ulceration as a rare complication of immunosuppressive drugs inpatients after heart transplantation ^[13] Beaver et al. also reported an intestinal perforation after lung transplantation ^[14]. Contrastly C, Fauci et al. stated that various complications occurred in patients with Wegener's granulomatosis related to cyclophosphamide/prednisolone combination in 21 years, however, none of this complications originated from gastrointestinal tract ^[5]. Fauci and Takwoingi et al. sug-

gested that gastrointestinal complications might occur due to immunosuppressive regimens. ^[5, 15].

Although a few cases of gastrointestinal perforation secondary to Wegener's granulomatosis have been reported ^[6,7] histopathological evidence of vasculitis is rarely found ^[9,10]. In the same way Skafie et al. published a case report where small bowel ischemia and perforation were the sole presenting features of Wegener's granulomatosis in a patient taking no medication before presentation^[8]. Garmley reported a case of symptomatic colitis as the initial presentation of Wegener's granulomatosis ^[16] Duclos et al. accounted a specific gastric lesion in Wegener's granulomatosis not due to immunosuppressive therapy ^[17].

Storesund et al. have indicated histological evidence of vasculitis is lacking in half the intestinal specimens resected for perforation ^[9]. Therefore immunosuppressive regimen might play a role in the reduction of classical histological features. Although our case had received immunosuppressive drug therapy, after surgery the patient survived on the treatment with cyclophosphamide and prednisolone without any gastrointestinal symptoms.

Our case is still alive in remission and without any complication due to Wegener's granulomatosis or immunosuppressive therapy at fifteen months of the follow-up period. It has been shown that Wegener's granulomatosis might involve gastrointestinal system and immunosuppressive treatment might exacerbate already existing areas of ulcerations.

We concluded that surgeons have to be aware of the gastrointestinal complications associated with Wegener's granulomatosis disease or immunosuppressive therapy which show themselves as severe clinical manifestations.

REFERENCES

1. Langford CA, Hoffman GS. Rare diseases 3:Wegener's Granulomatosis. *Thorax* 1999; 54: 629-637
2. Hoffman GS, Kerr GS, Leavitt RY, Hallahan CW, Lebovics RS, Travis WD et al. Wegener's Granulomatosis: an analysis of 158 patients *Ann Intern Med* 1992; 116: 488-498
3. Fallows GA, Hamilton SE, Taylor DS, Reddy SB. Esophageal involvement in Wegener's Granulomatosis: a case report and review of the literature. *Can J Gastroenterol* 2000; 14: 449-451
4. Lie JT. Wegener's Granulomatosis: histological documentation of common and uncommon

- manifestations in 216 patients. *Vasa* 1997; 26: 261-270
5. Fauci AS, Haynes BF, Katz P, Wolff SM. Wegener's granulomatosis: prospective clinical and therapeutic experience with 85 patients for 21 years. *Ann Intern Med.* 1983; 98: 76-85.
6. Haworth SJ, Pusey CD. Severe intestinal involvement in Wegener's granulomatosis. *Gut* 1984; 25: 1296-300.
7. Coward RA, Gibbons CP, Brown CB, Raftery AT, Parsons MA, Shortland JR. Gastrointestinal haemorrhage complicating Wegener's granulomatosis. *Br Med J.* 1985; 291: 865-66.
8. Skaife P, Lee S, Ramadwar M, Maitra D, Edwardson KE. Intestinal perforation as a presentation of Wegener's granulomatosis. *Hosp Med.* 2000; 61: 286-87.
9. Storesund B, Gran JT, Koldingsnes W. Severe intestinal involvement in Wegener's granulomatosis: report of two cases and review of the literature. *Br J Rheumatol.* 1998; 37: 387-90.
10. Tokuda M, Kurata N, Daikuhara H, Akisawa M, Onishi I, Asano T et al. Small intestinal perforation in Wegener's granulomatosis. *J Rheumatol.* 1989; 16: 547-49.
11. Regan MJ, Hellmann DB, Stone JH. Treatment of Wegener's granulomatosis. *Rheum Dis Clin North Am.* 2001; 27: 865-886
12. Koldingness W, Nossent H. Predictors of survival and organ damage in Wegener's granulomatosis. *Rheumatology* 2002; 41: 572-581
13. Mueller XM, Tevaearai HT, Stumpe F, Hurni M, Ruchat P, Fischer AP. et al. Gastrointestinal disease following heart transplantation. *World J Surg* 1999; 23: 650-655
14. Beaver TM, Fullerton DA, Zamora MR, Badesch DB, Weill D, Brown JM et al. Colon perforation after lung transplantation. *Ann Thorac Surg* 1996; 62: 839-843.
15. Takwoingi YM, Dempster JH. Wegener's Granulomatosis: an analysis of 33 patients seen over a 10 year period. *Clin Otolaryngol* 2003; 28: 187-194
16. Wilson RH, Kerr PP, McLoughlin J, Gormley M. Symptomatic colitis as the initial presentation of Wegener's Granulomatosis. *B J Clin Pract* 1993; 47: 315-318
17. Duclos B, Baumann R, Sondag D, Jouin H, Weill-Bousson M, Weill JP . Specific gastric localization of Wegener's disease. *Gastroenterol Clin Biol* 1987; 11: 154-157

