CASE REPORT

A rare case of granulomatosis with polyangiitis with involvement of the gastrointestinal system

Helin Şahintürk, M.D.,[1] Emre Kandemir, M.D.,[1] Fatma İrem Yeşiler, M.D.,[1] İrem Şerifoğlu, M.D.,[2] Günay Şahin Dalgıç, M.D.,[3] Çiğdem Erol, M.D.,[4] Cihat Burak Sayin, M.D.,[5] Tugan Tezcaner, M.D.,[6] Elif Çiloğlu, M.D.,[7] Ender Gedik, M.D.,[1] Pınar Zeyneloğlu, M.D.,[1] Zeynep Kayhan, M.D.[1]

[1]Department of Anesthesiology and Critical Care, Başkent University Faculty of Medicine, Ankara-*Türkiye*
[2]Department of Pulmonary Diseases, Başkent University Faculty of Medicine, Ankara-*Türkiye*
[3]Department of Internal Medicine, Division of Rheumatology, Başkent University Faculty of Medicine, Ankara-*Türkiye*
[4]Department of Infectious Disease and Clinical Microbiology, Başkent University Faculty of Medicine, Ankara-*Türkiye*
[5]Department of Internal Medicine, Division of Nephrology, Başkent University Faculty of Medicine, Ankara-*Türkiye*
[6]Department of General Surgery, Başkent University Faculty of Medicine, Ankara-*Türkiye*
[7]Department of Medical Pathology, Başkent University Faculty of Medicine, Ankara-*Türkiye*

ABSTRACT

We report a rare case of a 37-year-old man with granulomatosis with polyangiitis (GPA) with gastrointestinal system (GIS) involvement who needed 526 units of blood and blood product transfusions and was followed up in the intensive care unit (ICU). GIS involvement due to GPA is a rare condition that increases morbidity and mortality of patients. Patients may require ultramassive blood product transfusions. Thus, patients with GPA can be admitted to ICUs because of massive hemorrhage due to multisystem involvement, and survival is achievable with meticulous care through a multidisciplinary approach.

Keywords: Gastrointestinal system; granulomatous polyangiitis; intensive care unit; massive transfusion.

INTRODUCTION

Granulomatosis with polyangiitis (GPA) is an autoimmune vasculitis-including small and medium vessels-associated with anti-neutrophil antibody (ANCA), which mostly affects the respiratory system and kidneys. Its microscopy typically shows necrotizing and granulomatous inflammation.[1] Gastrointestinal system (GIS) involvement is seen in 10–24% of the cases. However, the majority of patients do not show any symptoms while they are alive. Many organs may be affected by GPA such as the ears, nose, throat (70–100%), lungs (50–90%), kidneys (10–50%), skin (10–50%), eyes (14–60%), and finally GIS (0–26%).[2] GIS involvement may be asymptomatic or accompanied by massive hemorrhage and perforations.[3]

We presented a rare case of a 37-year-old man with GPA with GIS involvement who needed 526 units of blood and blood product transfusions and was followed up in the intensive care unit (ICU).

CASE REPORT

A 37-year-old male patient was referred to our hospital with complaints of rashes on his legs, widespread aphthae in his mouth and weight loss, cavitary lesions in the bilateral upper lung zone, proteinuria, and occult blood in the stool. Department of chest diseases accepted the patient as a referral from a rural medical center.

Cite this article as: Şahintürk H, Kandemir E, Yeşiler Fİ, Şerifoğlu İ, Şahin Dalgıç G, Erol Ç, et al. A rare case of granulomatosis with polyangiitis with involvement of the gastrointestinal system. Ulus Travma Acil Cerrahi Derg 2023;29:435-439.

Address for correspondence: Fatma İrem Yeşiler, M.D.
Başkent Üniversitesi Tıp Fakültesi, Anesteziyoloji ve Reanimasyon ABD, Yoğun Bakım Bilim Dalı, Ankara, Türkiye
Tel: +90 312 - 203 68 68 E-mail: fatmairem84@hotmail.com

Ulus Travma Acil Cerrahi Derg 2023;29(3):435-439 DOI: 10.14744/tjtes.2022.78567 Submitted: 19.10.2021 Revised: 14.03.2022 Accepted: 02.04.2022

The patient had no medical-family history. The blood group of the patient was A Rh positive. In the first laboratory tests in our hospital, low hemoglobin (Hgb) (8.3 mg/dL), high C-reactive protein (199.1 mg/L), high procalcitonin (1.2 µg/L), and prolonged international normalized ratio (INR) (2.13) were detected. The sedimentation was normal (15 mm/h). Hematuria (580 units/site) and proteinuria (70 mg/dL) were detected. A biopsy was performed on the rash lesions on his legs. Immunoglobulin profile, cytoplasmic ANCA (c-ANCA), perinuclear anti-neutrophil cytoplasmic antibody, anti-nuclear antibody, anti-mitochondrial antibody, smooth muscle antibody, and liver kidney microsomal antibody tests were performed on a blood sample. Empirical antibiotherapy was administered due to fever of 39°C and a cavitary lesion on thorax computed tomography (CT) (Fig. 1). There were not significant pathologies in the abdominal ultrasonography and echocardiography.

On the 3rd day of hospital admission, as abdominal pain and vomiting complaints developed and the patient was urgently operated for perfusion disorder in the distal ileum and suspicious signs of perforation on abdominal CT (Fig. 1). Segmental small bowel resection was performed with the presence of necrotic areas due to mesenteric vein occlusion. Following an ileostomy, the patient was extubated and taken to the ICU postoperatively in a conscious state. His acute physiology and chronic health assessment score was 18 at ICU admission. During the intraoperative period, four units of packed red blood cells (PRBCs) and three units of fresh frozen plasma (FFP) were replaced, and his Hgb levels were monitored closely. On the 1st post-operative day, the patient's bowel pathology was reported as acute leukocytoclastic vasculitis characterized with fibrinoid necrosis, and the previous skin biopsies also supported this diagnosis (Fig. 2). Methylprednisolone (5 mg/kg/day) was initiated intravenously and c-ANCA positivity was also detected.

The patient experienced rapid Hgb depletion and ileostomy-related bleeding on the 3rd post-operative day, and the

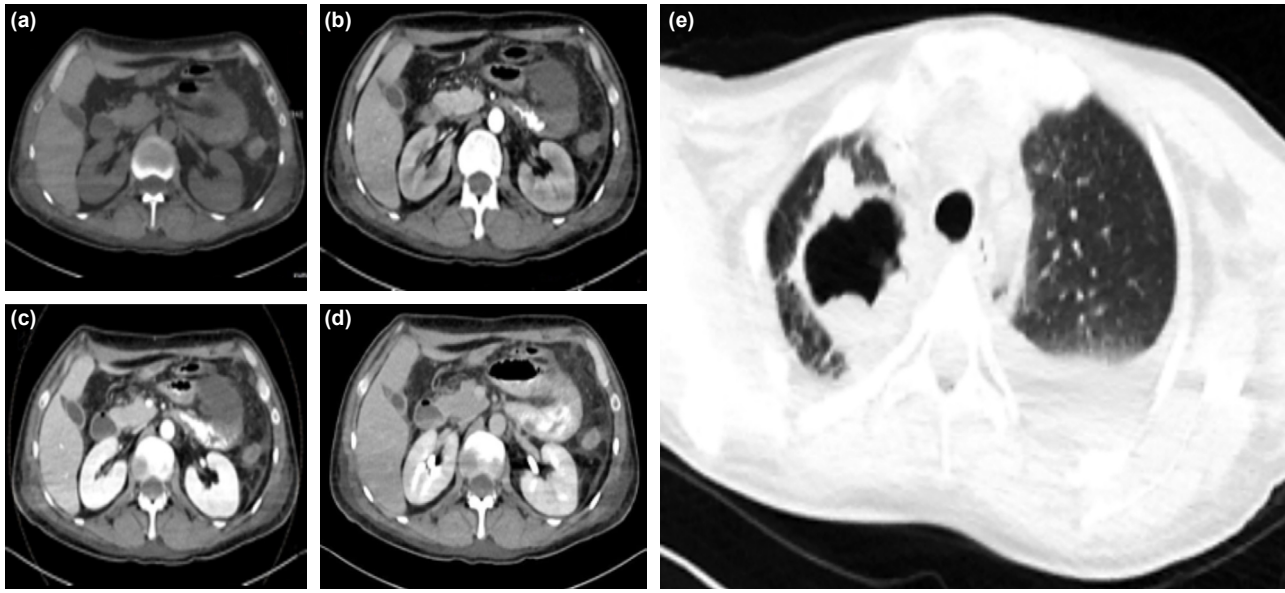

Figure 1. (a) Abdomen CT: Pre-contrast phase, **(b)** Abdomen CT: Arterial phase, **(c)** Abdomen CT: Portal phase, **(d)** Abdomen CT: Late phase, In the pre-contrast phase, the contrast agent is not visible in the intestinal lumen. In the other phases duodenum 3–4. Appears to begin to escape into the intestinal lumen, consistent with active bleeding from the continental level, **(e)** Thorax computer tomography (CT): Cavitary lesion in the lung.

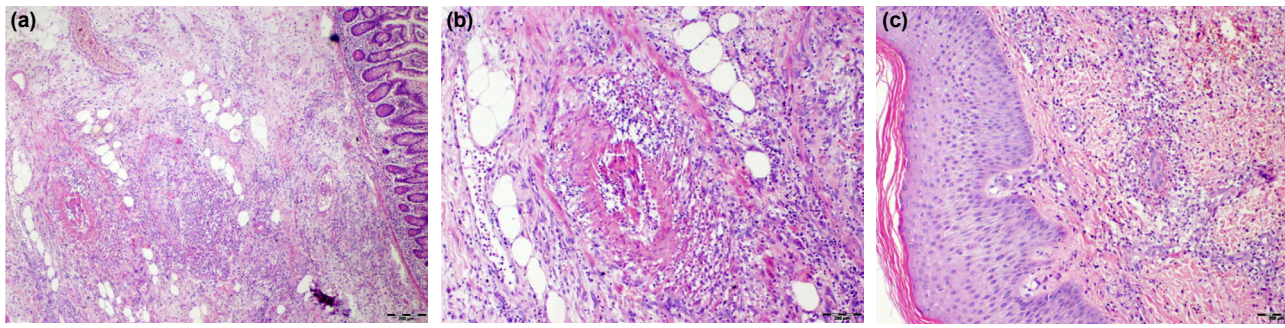

Figure 2. (a and b) In bowel resection spesimen, necrotising leukocytoclastic vasculitis with fibrinoid necrosis and fibrin thrombi noted in submucosal vessels. In addition, ischemic secondary changes in overlying mucosa were detected. (H&E, ×40, ×100), **(c)** In skin biopsy, inflammatory infiltrate which made up neutrophil and lymphocytes with fibrinoid necrosis was observed in wall of dermal vessels. These feature was in keeping with acute small (leukocytoclastic) vasculitis. (H&E, ×40).

abdomen CT showed bleeding from the jejunal wall into the intestinal lumen. No active bleeding was detected in the mesenteric angiography. Another surgery was planned as the patient's bleeding continued, and the laparotomy revealed minimal perforation in the jejunum that was repaired. Intraoperative endoscopy revealed diffuse ulcer bleeding foci in all GIS mucosa starting from the esophagus to ileostomy tract. The patient was readmitted to the ICU postoperatively. Blood product transfusions were performed if needed by hemogram and coagulation monitoring. Viscoelastic tests such as thromboelastogram and ROTEM could not be monitored because they were not available in our hospital. Norepinephrine infusion was used between 0.01 and 0.5 mcg/kg/min. The methylprednisolone therapy dose increased from 5 mg/kg/day to 15 mg/kg/day. Tranexamic acid and Vitamin K were administered. Proton pump inhibitor infusion was initiated intravenously. He was intubated for 5 days in the ICU. High flow oxygen therapy was used for 3 days after extubation. Because of the ongoing bleeding, parenteral nutrition was provided. There was no need for renal replacement therapy.

During his stay in the ICU, a multidisciplinary approach was provided with the Departments of Rheumatology, Gastroenterology, Hematology, General Surgery, Infectious Diseases, and Chest Diseases. Therapeutic plasma exchange (TPE) was performed as massive bleeding from the ileostomy continued despite increased steroid dosage. Cyclophosphamide IV (500 mg) and a second immunosuppressive agent, rituximab (1 g), were added. Ultramassive blood and blood product transfusions were performed as needed. On the 20th day of his admission, he had the largest transfusion requirement and a total hemorrhagic drainage of approximately 14,000 mL from the ileostomy. Within 24 h, 22 units of erythrocyte suspension PRBCs, 16 units of FFP, 4 units of platelet suspension, and 10 units of cryoprecipitate transfusion were replaced. During his entire stay, a total of 526 units of blood and blood product transfusions, including 177 units of PRBCs, 171 units of FFP, 30 units of pooled platelet suspension, 10 units of apheresis platelet suspension, and 138 units of cryoprecipitate were transfused in the ICU. Hemogram and coagulation values were presented in Table 1. Cryoprecipitate and fibrinogen concentrates were administered due to hypofibrinogenemia (<100 mg/dL). Coagulation factors II-VII-XI-X complexes and recombinant coagulation factor VIIa injections were applied intermittently. Tranexamic acid and Vitamin K administration were also continued. We administered tranexamic acid IV, topically, and through the nasogastric tube in endoscopy. The patient was followed-up in a single room with negative pressure isolation in the ICU, and one-to-one nursing care was provided to him due to immunosuppressive treatment. *Escherichia coli* was detected in deep tracheal aspirate, and vancomycin-resistant *Enterococcus* was detected in his urine culture. Antibiotics were administered accordingly. Stool from ileostomy was normal and Hgb decline was slowed. In addition, 500 mg of cyclophosphamide was re-administered IV on the 37th day of admission. After the bleeding was under control, the patient was transferred to the rheumatology ward on the 39th day of his ICU stay.

Our patient's ileostomy was closed during the 18th month of follow-up, and his treatment continues on an outpatient basis in the 2nd year following his discharge from the hospital.

DISCUSSION

GPA is an autoimmune vasculitis-including small and medium vessels-associated with ANCA, which mostly affects the respiratory system and kidneys. Its microscopy typically shows necrotizing and granulomatous inflammation.[1] GIS involvement is seen in 10–24% of the cases. However, the majority of patients do not show any symptoms while they are alive. Comarmond and Cacoub. listed organs that are affected by GPA such as the ears, nose, throat (70–100%), lungs (50–90%), kidneys (10–50%), skin (10–50%), eyes (14–60%), and finally GIS (0–26%).[2] GIS involvement may be asymptomatic or accompanied by massive hemorrhage and perforations.[3] Although our patient had multisystem involvement, including the lungs, skin, oral mucosa, kidneys, and GIS, the most important feature was that it affected the entire GIS tract.

Table 1. Laboratory parameters of admission and follow-up in the intensive care unit

Day	On ICU admission	On 20th ICU day	On ICU discharge	Min. level	Max. level
Hgb (g/dl)	8.3	7.8	10.2	6.4	11.8
Hct (%)	24.5	21.7	28.3	20	35.2
Platelet (10^3/µl)	381	45	295	10	512
Fibrinogen (mg/dl)	397	150	440	50	527
PT (sec.)	23.7	13.4	12	10.3	23.7
INR (%)	2.13	1.11	1.05	0.9	2.13
APTT (sec)	24.1	21.1	18.9	18.5	30.1
Ca^{+2} (mg/dl)	6.8	7.7	8.9	6.6	8.9

Hgb: Hemoglobin; Hct: Hematocrit; PT: Prothrombin time; INR: International normalized ratio; APTT: Activated partial thromboplastin time; Ca^{+2}: Calcium; ICU: Intensive care unit; Min: Minimum; Max: Maximum.

Pagnoux et al.[4] presented the symptoms of abdominal pain (97%), nausea-vomiting (34%), diarrhea (27%), hematochezia or melena (16%), and hematemesis (6%) in 62 patients with vasculitis with GI involvement. Even though endoscopic examination revealed gastroduodenal–esophageal–colorectal ulcers in 30 patients, only three of them were histopathologically diagnosed with vasculitis in biopsies taken from GIS lesions. GIS ulcers were reported in six patients with GPA: One of them had esophageal ulcers, two had gastroduodenal, and two had colorectal ulcers. In a similar manner with this study, our patient's first sign of GIS involvement was abdominal pain. The intestinal biopsies taken during surgery for mesenteric vein occlusion were reported as vasculitis histopathologically. As the ulcers were observed throughout the entire GIS tract instead of a specific region in the endoscopy, we were facing a rare type of GIS involvement. In line with the fact that c-ANCA positivity in patients diagnosed with GPA reaches a rate of 90%, the c-ANCA positivity of our patient also supported our diagnosis. GIS lesions of GPA can be seen in many different forms including submucosal edemas, ulcers, hemorrhages, mesenteric ischemia, ileuses, and perforations. The multiplicity and level of these lesions are important factors that determine the course of the disease. Cases of GPA with massive hemorrhages and perforations have been reported despite the low number of cases.[3] However, there has only been one case that reported a GIS tract wholly affected from the esophagus to the rectum.[5] The course of treatment we followed included steroids, cyclophosphamide, and rituximab, as reported previously.[2,3] In accordance with the knowledge that TPE treatment reduces the risk of end-stage renal failure, TPE was administered to our patient twice. What distinguishes our patient with GPA from other reported cases was that the entire GIS tract was involved from the esophagus to the rectum, and our patient had a total of 526 units of blood and blood product transfusions in 39 ICU days because of massive hemorrhages. Ultramassive transfusion is defined as ≥20 units of PRBCs in 24 h.[6] The risk of lung injury associated with ultramassive transfusions, especially transfusion-related acute lung injury, transfusion-associated circulatory overload viral-bacterial infection transmission, intra-abdominal hypertension, compartment syndrome, and electrolyte imbalanced have been considered. Our patient was followed-up in a single room with negative pressure isolation to decrease the risk of infection. Electrolyte monitoring was performed daily and replaced if needed. We were able to discharge our patient from the hospital without any morbidities.

We believe that there are several important aspects of this case. Despite its low incidence rate at 10–24%, GIS involvement due to GPA is a condition that greatly increases morbidity and mortality, and the clinician should be alert in cases of GIS involvement. The lesions may widely range from edemas to perforations, and despite massive hemorrhage, there may not be a chance of surgery or embolization as in our case. Rituximab should be added to the treatment regimen in cases that are resistant to cyclophosphamide. Complications can be avoided with close follow-up and by being careful in cases that require ultramassive blood product transfusions.

Conclusion

Patients with GPA can be admitted to the ICU with ultramassive hemorrhage due to multisystem involvement, and survival can be achieved with meticulous care through a multidisciplinary approach.

Informed Consent: Written informed consent was obtained from the patient for the publication of the case report and the accompanying images.

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: P.Z., E.G., Z.K., H.Ş.; Design: H.Ş., Ç.E., C.B.S.; Supervision: P.Z., E.G., Z.K., H.Ş.; Materials: E.Ç., Ç.E., C.B.S., İ.Ş.; Data: E.K., F.İ.Y., H.Ş., İ.Ş., Ç.E., G.Ş.D., T.T., E.Ç.; Analysis: H.Ş., İ.Ş., G.Ş.D., Ç.E., C.B.S., T.T.; Literature search: E.K., F.İ.Y., İ.Ş., G.Ş., T.T., E.Ç.; Writing: H.Ş., E.K., F.İ.Y.; Critical revision: P.Z., E.G., Z.K.

Conflict of Interest: None declared.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. Lutalo PM, D'Cruz DP. Diagnosis and classification of granulomatosis with polyangiitis (aka Wegener's granulomatosis). J Autoimmun 2014;48:94–8. [CrossRef]
2. Comarmond C, Cacoub P. Granulomatosis with polyangiitis (Wegener): Clinical aspects and treatment. Autoimmun Rev 2014;13:1121–5.
3. Deger SM, Sahin T, Vural C, Aygencel G, Kerem M, Onal B, et al. Wegener's granulomatosis with massive gastrointestinal hemorrhage due to jejunal and colonic involvement: Report of a case. Surg Today 2008;38:166–9. [CrossRef]
4. Pagnoux C, Mahr A, Cohen P, Guillevin L. Presentation and outcome of gastrointestinal involvement in systemic necrotizing vasculitides: Analysis of 62 patients with polyarteritis nodosa, microscopic polyangiitis, wegener granulomatosis, churg-strauss syndrome or rheumatoid arthritis-associated vasculitis. Medicine (Baltimore) 2005;84:115–28. [CrossRef]
5. Reddy RS, Biyyani S, Pauskar P, Fahmy NM, King JF. Extensive gastrointestinal tract and thyroid involvement with Wegeners granulomatosis. J Indian Soc Gastroenterol 2007;26:290–1.
6. Matthay ZA, Hellmann ZJ, Callcut RA, Matthay EC, Nunez-Garcia B, Duong, et al. Outcomes after ultramassive transfusion in the modern era: An Eastern association for the surgery of trauma multicenter study. J Trauma Acute Care Surg 2021;91:24–33. [CrossRef]

OLGU SUNUMU - *ÖZ*

Gastrointestinal sistem tutulumlu nadir bir granülomatöz polianjitis olgusu

Dr. Helin Şahintürk,[1] Dr. Emre Kandemir,[1] Dr. Fatma İrem Yeşiler,[1] Dr. İrem Şerifoğlu,[2] Dr. Günay Şahin Dalgıç,[3] Dr. Çiğdem Erol,[4] Dr. Cihat Burak Sayin,[5] Dr. Tugan Tezcaner,[6] Dr. Elif Çiloğlu,[7] Dr. Ender Gedik,[1] Dr. Pınar Zeyneloğlu,[1] Dr. Zeynep Kayhan[1]

[1]Başkent Üniversitesi Tıp Fakültesi, Anesteziyoloji ve Reanimasyon Anabilim Dalı, Yoğun Bakım Bilim Dalı, Ankara
[2]Başkent Üniversitesi Tıp Fakültesi, Göğüs Hastalıkları Anabilim Dalı, Ankara
[3]Başkent Üniversitesi Tıp Fakültesi,İç Hastalıkları Anabilim Dalı, Romatoloji Bölümü, Ankara
[4]Başkent Üniversitesi Tıp Fakültesi, Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Anabilim Dalı, Ankara
[5]Başkent Üniversitesi Tıp Fakültesi, İç Hastalıkları Anabilim Dalı, Nefroloji Bölümü, Ankara
[6]Başkent Üniversitesi Tıp Fakültesi, Genel Cerrahi Anabilim Dalı, Ankara
[7]Başkent Üniversitesi Tıp Fakültesi, Tıbbi Patoloji Anabilim Dalı, Ankara

Yoğun bakım ünitesinde (YBÜ) takip edilen 526 ünite kan ve kan ürünü transfüzyonu gerektiren gastrointestinal sistem (GİS) tutulumu olan 37 yaşında nadir bir granülomatöz polianjiitisli (GPA) erkek hastayı sunuyoruz. GPA'ya bağlı GİS tutulumu morbidite ve mortaliteyi artıran nadir gözlenen bir durumdur. Hastaların ultramasif kan ürünü transfüzyona ihtiyacı olabilir. Böylece multisistem tutulumuna bağlı masif hemoraji nedeniyle GPA'lı hastalar YBÜ'ye kabul edilebilir ve multidisipliner bir yaklaşımlı titiz bir bakım ile sağkalım sağlanabilir.

Anahtar sözcükler: Gastrointestinal sistem; granülomatöz polianjitis; masif transfüzyon; yoğun bakım.

Ulus Travma Acil Cerrahi Derg 2023;29(3):435-439 doi: 10.14744/tjtes.2022.78567