Case Report

Journal Homepage: http://crcp.tums.ac.ir

Complicated Progress of Granulomatosis with Polyangiitis - A Case Presentation and Review of Literature

Matineh Sadat Tabatabaei [1], **Mostafa Mortazi** [2]

1. School of Nursing and Midwifery, Tehran University of Medical Sciences, Tehran, Iran
2. Faculty of Medicine, Alborz University of Medical Sciences, Alborz, Iran

Use your device to scan and read the article online

Citation Tabatabaei M S, Mortazi M. Complicated Progress of Granulomatosis with Polyangiitis - A Case Presentation and Review of Literature. Case Reports in Clinical Practice. 2023; 8(6): 270-274.

Running Title Journey of Granulomatosis With Polyangiitis

Article info:
Received: October 30, 2023
Revised: November 22, 2023
Accepted: December 29, 2023

Keywords:
Granulomatosis with polyangiitis; ANCA associated Vasculitis; Polyangiitis; Rituximab; Cyclophosphamide

ABSTRACT

Granulomatosis with polyangiitis, previously known as Wegener's, is a necrotizing vascular disease that affects small blood vessels and may cause damage to the respiratory tract and kidneys. In this article, we report on a 50-year-old male with a complicated disease process who experienced rare bladder and renal complications and several adverse drug reactions. Despite using drug alternatives, the side effects remained mostly the same. Therefore, by studying different cases and articles, we establish the relation between these findings and the specifications of granulomatosis with polyangiitis. This case underscores the complexity of managing this condition and the need for personalized treatment strategies.

Introduction

Granulomatosis with polyangiitis, or GPA (Wegener's), is a rare systemic disease characterized by necrotizing granulomatous inflammation of the skin, ears, eyes, respiratory tract, and focal necrotizing glomerulonephritis. It is an immune-based process in which antibodies develop against cytoplasmic components in the neutrophil, leading to the release of proteases, which further induce inflammation and local tissue necrosis [1]. The main reported symptoms are glomerulonephritis, sinusitis, ear pain, otitis, hemoptysis, pulmonary infiltrates, eye pain, vision loss, cough, fever, and headaches. In diagnosing Wegener's, laboratory tests can assist by identifying elevated serum immunoglobulins (IgA and IgE), creatinine clearance, and specific parameters such as ANCA and CMV antigen [2].

The two principal aims in the treatment of GPA are to limit the extent and severity of permanent organ damage by controlling the disease promptly, and to minimize the short- and long-term morbidity that often results from therapy [3]. For about 50 years, the gold standard for GPA treatment has been the combination of prednisone and cyclophosphamide

*** Corresponding Author:**
Matineh Sadat Tabatabaei
Address: *School of Nursing and Midwifery, Tehran University of Medical Sciences, Tehran, Iran*
E-mail: *matinehtabatabaei00@gmail.com*

(Cyc) [4]. It is now mainly treated with corticosteroids, cyclophosphamide, methotrexate, azathioprine, leflunomide, and immunosuppressive drugs like Endoxan [3, 5]. In this article, we are going to discuss the mentioned patient's disease progress, test results, and graphs.

Case presentation

We present a case of a 50-year-old male who visited Shariati Hospital in Tehran, Iran, with abdominal RUQ pain and left inguinal hernia. He was hospitalized with necrotizing pancreatitis and was diagnosed with Granulomatosis with Polyangiitis in the winter of 2021. He had been referred to an otolaryngologist due to frequent severe headaches and ear pain. After being referred to a rheumatologist and undergoing blood tests (with detected CMV and ANCA-C 180) and graphics, he was diagnosed with GPA.

A mixed treatment regimen including Endoxan, Methotrexate, and Prednisolone was initiated in the spring of 2021. After taking three vials of Endoxan (which can be rarely found in Iran), complications such as dizziness, foot edema, pneumonia, and leg cramps were observed (a score of 6 on the Naranjo scale was measured, which is considered as a possible ADR). Consequently, Endoxan was replaced with Rituximab and was used until late spring 2023. After three doses of Rituximab, side effects like productive cough, night sweats, swelling and redness on the belly, sore throat, and tongue wound occurred (a score of 7 on the Naranjo scale was measured, which is considered as a possible ADR). The tongue wound was treated with Voriconazole after 2.5 weeks. The patient also experienced other GPA signs such as scapula pain, anemia, blurred vision, and hearing difficulties. Due to abdominal and pelvic ultrasound, the protrusion of the renal pyramid was observed, suggesting a diagnosis of Granulomatosis with Polyangiitis (Figure 1). A mild bladder infection was associated with increased wall thickness and irregular mucus (Figure 2).

Additionally, proteinuria was measured by a urine test, with a result of 0.2 g/24h. After the last intake of Rituximab (the 5th injection, late spring 2023), the patient experienced intense muscle pain. During the hospitalization period, the patient's creatinine levels were measured daily (Figure 3).

The patient reported that while taking Rituximab, his belly abruptly enlarged, resulting in some striae on the RLQ of his abdomen (Figure 4).

Discussion

The patient presented in this paper was diagnosed with Granulomatosis with Polyangiitis, exhibiting rare renal symptoms and adverse drug reactions (ADR). There are disparities in comparison to other case reports, which will be mentioned below:

1.Serum creatinine level: High serum creatinine levels are common among cases of GPA. A recent case report of GPA featured a rare vasculitis patient who had a serum creatinine level of 4.7 mg/dL [6]. Another patient, who was referred to the hospital due to migratory joint pain, fatigue, and cough with bloody sputum, had a serum creatinine level of 247 µmol/L (2.7 mg/dl) [7,8]. However, as shown in Figure 3, the creatinine level in this scenario was mostly within the normal range.

2.ADR after cyclophosphamide (Endoxan) infusion: Our presented patient's Naranjo scale score after using Endoxan was measured at 7. One of the unusual side effects of cyclophosphamide in this patient

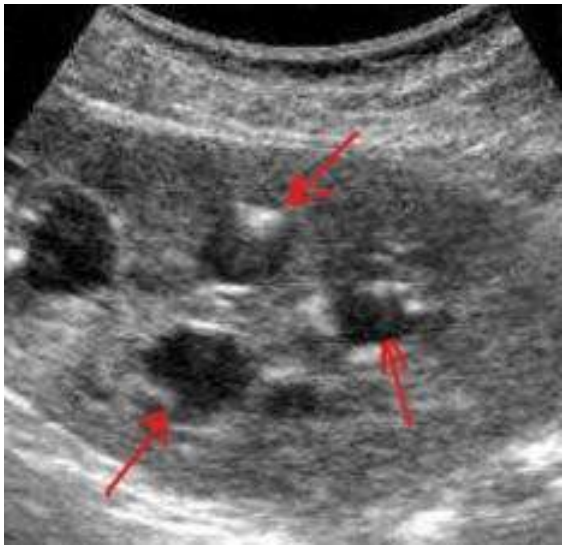

Fig. 1. (Renal pyramid protrusion)

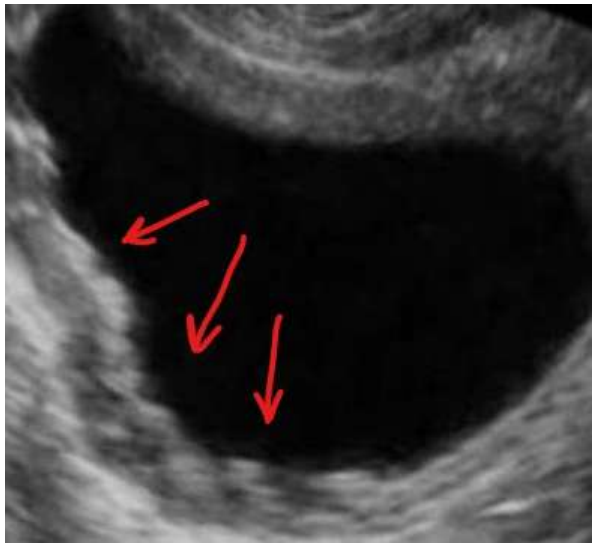

Fig. 2. (Mild bladder infection)

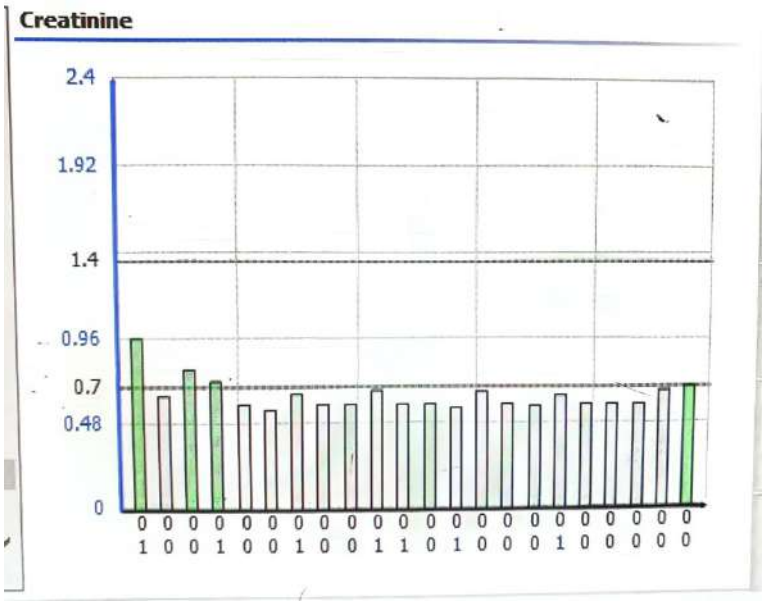

Fig. 3. (Creatinine serum level test results from October 8th to November 1st)

was pneumonia, which has also been reported in the treatment of systemic lupus erythematosus and prophylaxis [9,10]. Due to ultrasound results, mild cystitis was recognized, which was the result of cyclophosphamide. Studies over the years have proven that although cyclophosphamide has been in use for the management of autoimmune-mediated diseases, it can induce nephrotoxicity and cystitis [11].

3.Renal Calcinosis: Although we couldn't find recently conducted studies, renal calcinosis is a condition resulting from the deposition of calcium salts in the kidneys. It can be caused by various factors such as dehydration, kidney diseases, certain drugs, etc. Although the exact relationship between renal calcinosis and GPA is not fully understood, GPA can cause damage to the kidneys, which may lead to calcinosis [12].

4.Protrusion of the renal pyramids: The protrusion of the renal pyramids is a sign of deficient renal function that can be observed on imaging studies (Figure 1). GPA primarily affects the respiratory tract and kidneys, but its clinical presentation can vary widely. Therefore, renal pyramid protrusion is not typically considered a specific sign of Granulomatosis with Polyangiitis [13]. However, there are some reported cases who experienced renal masses as early signs of GPA [14,15]. As we mentioned, this patient (while having a normal-sized kidney), had renal pyramid

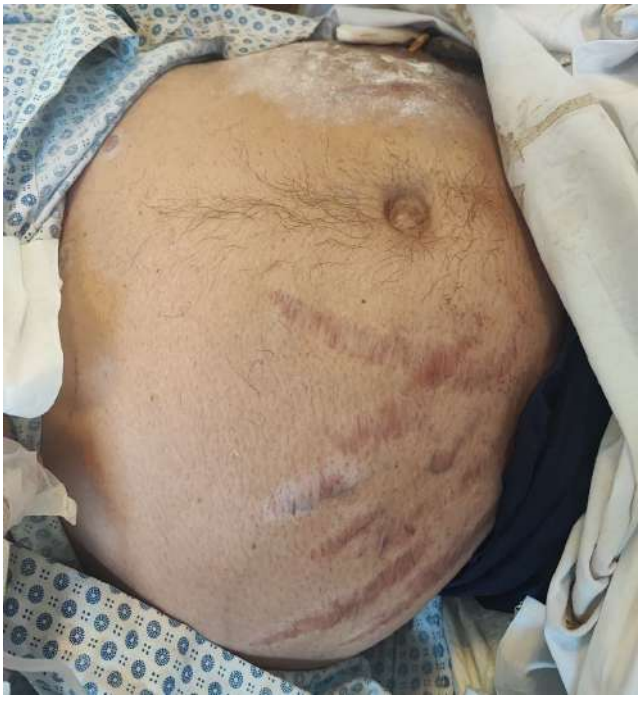

Fig. 4. (RLQ stria)

protrusion. By referring to the articles above, this is considered a rare late sign of polyangiitis.

5.ADR after Rituximab infusion: Our patient experienced muscle pain, cough, night sweats, and headache after Rituximab treatment, which are known as semi-rare side effects. By using the Naranjo scale, we measured a score of 7, which represents a possible ADR. The rare side effects mentioned above occur with the following percentages: muscle pain and spasms (17%), cough (13%), night sweats (15%), and headache (17%) [16]. Also, abdominal enlargement is claimed to be a rare side effect of rituximab, observed in 1 out of every 10,000 patients [17].

6.Rituximab and calcinosis treatment: Rituximab is a monoclonal antibody used to treat autoimmune diseases such as rheumatoid arthritis. There is some evidence that rituximab may be helpful in treating renal calcinosis. A small study of 10 patients found that rituximab was effective in reducing calcium deposits and improving kidney functions [5,18]. Thus, recovery from calcinosis is expected soon.

Conclusions

Our patient developed unexpected signs in his GPA process related to renal, bladder, skin, and serum creatinine levels. The relationship between the protrusion of the renal pyramids and the progression of Granulomatosis with Polyangiitis is strongly suggestive. The uncommon side effects of drugs and renal conditions mentioned above should be kept in mind by the primary doctors and nurses. This will allow these conditions to be tracked, cared for, and treated with appropriate drugs and care plans, aiming for impeccable and prompt management.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this article.

Funding

No funding was received to assist with the preparation of this manuscript.

Conflict of Interests

The authors have no conflict of interest to declare.

References

[1] Eisenberg PA, Collier V, Mangano A, Shergill K, Yos E. Subglottic Stenosis as a Presentation of Antineutrophil Cytoplasmic Antibody-Associated Glomerulonephritis. Cureus. 2023;15(10):e46899.

[2] Moin KA, Yeakle MM, Parrill AM, Garofalo VA, Tsiyer AR, Bishev D, et al. Ocular and orbital manifestations of granulomatosis

with polyangiitis: a systematic review of published cases. Rom J Ophthalmol. 2023;67(3):214-21. https://doi.org/10.22336/rjo.2023.38

[3] Chalkia A, Jayne D. ANCA-associated vasculitis - Treatment Standard. Nephrol Dial Transplant. 2023. https://doi.org/10.1093/ndt/gfad237

[4] Fauci AS, Wolff SM. Wegener's granulomatosis: studies in eighteen patients and a review of the literature. Medicine (Baltimore). 1973;52(6):535-61. https://doi.org/10.1097/00005792-197311000-00002

[5] Narváez J, Pirola JP, J LL, Juarez P, Nolla JM, Valenzuela A. Effectiveness and safety of rituximab for the treatment of refractory systemic sclerosis associated calcinosis: A case series and systematic review of the literature. Autoimmun Rev. 2019;18(3):262-9. https://doi.org/10.1016/j.autrev.2018.10.006

[6] Nasr R, Balasubramanian P, Desiderio L, Abdelattif M. A Rare Case of Nephrotic-Range Proteinuria in Antineutrophil Cytoplasmic Antibodies (ANCA)-Associated Vasculitis. Cureus. 2022;14(5):e24889. https://doi.org/10.7759/cureus.24889

[7] Aasarod K, Iversen BM, Hammerstrom J, Bostad L, Jorstad S. Clinical outcome of patients with Wegener's granulomatosis treated with plasma exchange. Blood Purification. 2002;20(2):167-73. https://doi.org/10.1159/000047004

[8] Matousovic K, Martinek V, Spatenka J, Stejskal J, Chadimova M. Malignant Wegener's Granulomatosis with Fibrosing Mediastinitis and Vena Cava Superior Syndrome. Renal Failure. 2012;34(2):244-6. https://doi.org/10.3109/0886022X.2011.647208

[9] Gupta D, Zachariah A, Roppelt H, Patel AM, Gruber BL. Prophylactic antibiotic usage for Pneumocystis jirovecii pneumonia in patients with systemic lupus erythematosus on cyclophosphamide: a survey of US rheumatologists and the review of literature. J Clin Rheumatol. 2008;14(5):267-72. https://doi.org/10.1097/RHU.0b013e31817a7e30

[10] Ishikawa Y, Tokutsu K, Nakayamada S, Kuchiba A, Fushimi K, Matsuda S, et al. Short-term effectiveness and safety of rituximab versus cyclophosphamide for life-threatening ANCA-associated vasculitis: a propensity score analysis of the real-world nationwide database. Ann Rheum Dis. 2023. https://doi.org/10.1136/ard-2023-224472

[11] Ayza MA, Zewdie KA, Yigzaw EF, Ayele SG, Tesfaye BA, Tafere GG, et al. Potential Protective Effects of Antioxidants against Cyclophosphamide-Induced Nephrotoxicity. International Journal of Nephrology. 2022;2022:5096825.https://doi.org/10.1155/2022/5096825

[12] Andrassy K, Erb A, Koderisch J, Waldherr R, Ritz E. Wegener's granulomatosis with renal involvement: patient survival and correlations between initial renal function, renal histology, therapy and renal outcome. Clin Nephrol. 1991;35(4):139-47.

[13] Tiewsoh I, Dey B, Lyngdoh M, Lynrah K, Synrem E, Mitra A. Granulomatous interstitial nephritis in granulomatosis with polyangiitis mimicking leprosy: A case report. J Family Med Prim Care. 2020;9(11):5783-6.https://doi.org/10.4103/jfmpc.jfmpc_1070_20

[14] Carazo ER, Benitez AM, Milena GL, Espigares JR, León L, Marquez B. Multiple Renal Masses as Initial Manifestation of Wegener's Granulomatosis. American Journal of Roentgenology. 2001;176(1):116-8. https://doi.org/10.2214/ajr.176.1.1760116

[15] Higashihara M, Kawamura T, Miyazaki Y, Yokoo T, Joh K. Granulomatosis with polyangiitis presenting as a solitary renal mass: a case report. BMC Nephrology. 2023;24(1):223. https://doi.org/10.1186/s12882-023-03276-1

[16] Medscape. rituximab (Rx) www.medscape.com2019 [Available from: https://reference.medscape.com/drug/rituxan-truxima-rituximab-342243.

[17] Chisari CG, Sgarlata E, Arena S, Toscano S, Luca M, Patti F. Rituximab for the treatment of multiple sclerosis: a review. J Neurol. 2022;269(1):159-83. https://doi.org/10.1007/s00415-020-10362-z

[18] Dubos M, Ly K, Martel C, Fauchais AL. Is rituximab an effective treatment of refractory calcinosis? BMJ Case Rep. 2016;2016. https://doi.org/10.1136/bcr-2015-213179