Granulomatosis with Polyangiitis Presenting as Postoperative Gastrointestinal Stromal Tumors: A Case Report

Ye Rui-hai1*, Yang Li1*, Yang Jun-choa1, Mao Yu-ping2, Zhang Chun-ri2, Xu Jun1, Zhu Yuan-hong1 and Wang Zhen1*

1Department of Respiratory Medicine, Zhejiang Hospital of Traditional Chinese Medicine, 54 Post Road, Hang zhou, China
2Department of Pathology, Zhejiang Hospital of Traditional Chinese Medicine, 54 Post Road, Hang zhou, China

Corresponding author: Wang Zhen, Department of Respiratory Medicine, Zhejiang Hospital of Traditional Chinese Medicine, 54 Post Road, Hang zhou, China, E-mail: yehoo2003@163.com

Received date: March 29, 2016; Accepted date: May 12, 2016; Published date: May 19, 2016

Copyright: © 2016 Zhen W, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution and reproduction in any medium, provided the original author and source are credited.

Abstract

Introduction: Granulomatosis with polyangiitis (GPA) is a systemic vasculitis syndrome, previously known as Wegener's granulomatosis, characterized by necrotizing granulomatous inflammation of the respiratory tracts, systemic necrotizing vasculitis, and necrotizing glomerulonephritis. This disorder represents a significant diagnostic dilemma due its diverse presentations, although presentation in the form of postoperative gastrointestinal stromal tumors is uncommon. Here, we report one of the first identified cases of GPA presenting as postoperative gastrointestinal stromal tumors (GISTs).

Case presentation: A 78-year-old Chinese man presented to our Respiratory Department in Zhejiang Hospital of Traditional Chinese Medicine with a history of progressively worsening fever and pulmonary nodules. He had history of postoperative gastrointestinal stromal tumors. Because of failed treatment with antibiotics, he had been diagnosed with a fungal infection of the lung, which was empirically treated with voriconazole for approximately two months. However, the condition did not improve until the patient was successfully treated with moderate-dose steroids. His clinical course was fever, pulmonary nodules and nasosinusitis, which are associated with granulomatosis with polyangiitis.

Conclusion: The recognition of a multi-system disease is critical for diagnosing GPA. Postoperative GISTs may be associated with manifestations of the disease, in which case, immediate and aggressive treatment with steroids can be life-saving.

Keywords: Granulomatosis with polyangiitis; Wegener's granulomatosis; Gastrointestinal stromal tumors; Anti-neutrophil cytoplasmic antibody

Abbreviations

GISTs: Gastrointestinal Stromal Tumors; GPA: Granulomatosis with Polyangiitis; ANCA: Anti-neutrophil Cytoplasmic Antibody; c-ANCA: Cytoplasmic Anti-neutrophil Cytoplasmic Antibody; CRP: C-reactive protein; PR3-ANCA: Proteinase 3 anti-neutrophil Cytoplasmic Antibody; Contrast Enhanced Computed Tomography (CECT)

Introduction

Heinz Klinger was first to describe the disease process of Wegener's granulomatosis (WG) in 1932 [1]. Subsequently, Frederick Wegener published two papers in 1936 [2] and 1939 [3], describing post-mortem studies of two patients who died of disseminated vasculitis. The identification of systemic vasculitides is one of the most difficult diagnostic challenges in clinical medicine. The diagnosis of vasculitis granulomatosis with polyangiitis (GPA), previously known as Wegener's granulomatosis, is particularly difficult due to its diverse presentation as a triad of airway necrotizing granulomas, systemic vasculitis and focal necrotizing glomerulonephritis. This serious systemic illness can be mistaken for an isolated complaint. The diagnosis of GPA is based on clinical findings and positive serology for anti-neutrophil cytoplasmic antibodies against proteinase 3 (c-ANCA-PR3). Mazur et al. first introduced the term "gastrointestinal stromal tumor" in 1983[4], although the ability to distinguish gastrointestinal stromal tumors (GISTs) reliably from other histopathological subtypes of mesenchymal tumors was reported by Hirota et al. [5]. GISTs are the most common mesenchymal tumors of the gastrointestinal tract, with most occurring in the stomach. GISTs may present with clinical symptoms (e.g., gastrointestinal bleeding) or may be found incidentally during surgery, endoscopy, or imaging. At the initial stage, GISTs commonly appear as well-defined, round, solid masses.

Case Presentation

A 78-year-old Chinese man presented to our Respiratory Department with a history of progressively worsening fever and pulmonary nodules. The patient had history of postoperative GISTs. Over the previous 6 months, gastric tumors without obvious symptoms had been found during physical examinations in our hospital, where he...
had undergone laparoscopic gastric resection. Exploratory surgery did not reveal any evidence of tumor metastasis. The tumor (approximately 4×3 cm) was located in the anterior wall of the stomach and was identified pathologically as GIST (Figure 1).

The patient did not receive chemotherapy for a number of reasons. On admission, laboratory tests demonstrated a normal white blood cell (WBC) count (9.2×10^9/L), normal renal function (creatinine 82 μmol/L), and a high C-reactive protein (CRP) (108.80 mg/L). He was mildly hypoxic (pO2 69 mmHg without oxygen administration) and his procalcitonin (PCT) was raised (0.1, normal <0.05). Chest computed tomography (CT) imaging performed on admission demonstrated multiple nodules, which were considered metastatic lesions, as well as bilateral pleural effusions (Figure 2).

Blood urea nitrogen and creatinine were normal. Furthermore, urine analysis revealed elevation of β2-microglobulin (2347.5 μg/L, normal <300) and significant proteinuria (432.5 mg/dL, normal <150). His antinuclear antibody panel (ANA) and rheumatoid factor (RF) titers were negative. Over approximately one month after surgery, the patient experienced recurrent fever, presumed to be caused by pneumonia; however, treatment with a wide range of antibiotics such as penicillin, cephalosporin, enzyme alkene hydrocarbon and quinolones was ineffective. He was diagnosed with a fungal lung infection, which was treated empirically with voriconazole for approximately two months. However, during the following two months, the patient was readmitted because of fever (38.3–38.6), fatigue, nasal congestion and headache. A chest CT scan (Figure 2) revealed a few bilateral pulmonary infiltrates with multiple parenchymal nodules appearing localized in the peripheral lobes. At this point, the patient tested positive for proteinase 3 (PR3)-specific cytoplasmic anti-neutrophil cytoplasmic antibodies (c-ANCA), suggesting a diagnosis of GPA. Paranasal sinus radiography revealed significant nasosinusitis and granuloma changes including multi-nuclear giant cells and epithelial cells typical of vasculitis granulomatosis were revealed in a biopsy (Figure 3).

Following the diagnosis of GPA, our patient was treated immediately with methylprednisolone (1 mg/kg per day). The dose of steroids was tapered after two weeks and the patient is in currently in remission. Furthermore, chest CT imaging after six months demonstrated clear diminution of multiple nodules (Figure 4).

Discussion

Until the latter part of the 20th Century, GPA was still universally fatal, usually within weeks to months. Current diagnostic and treatment methods have reduced this mortality rate to less than 5% [6]. Early recognition of this rapidly progressive disease is critical to minimize harm and reduce the risk of mortality; however, diagnosis of GPA remains a clinical challenge. Detailed history and physical examination are crucial to a comprehensive understanding of presenting symptoms. It is important to consider a diagnosis of vasculitides for patients presenting with constitutional symptoms or inflammation with antibiotic failure. GPA is a systemic vasculitis of the small arterioles, capillaries, and venules. A biopsy from affected tissue (kidney, nose, lung, etc.) may not be required to confirm the diagnosis even in cases presenting with the classic triad of upper airway, pulmonary, and renal disease and positive PR3-specific c-ANCA serology. However, in many cases such as the one presented here, the clinical findings are not completely typical and a biopsy is indicated to establish the diagnosis. Revision of the paranasal sinus biopsy showed a picture virtually diagnostic of GPA, which had not been recognized six months earlier. In the first large study on WG involving 85 patients, followed-up over 21 years, Fausi et al. [7] reported that 22% of patients had nasal symptoms at presentation and 64% during follow-up [8]. The vast majority of GPA patients, including the present case, have PR3-specific c-ANCA antibodies. However, it is important to note that the sensitivity of ANCA tests varies depending on disease progression. In a setting with clear clinical signs and symptoms, PR3-ANCA is most the
most sensitive marker of GPA using this test, showing a sensitivity exceeding 90% [9].

Contrast enhanced computed tomography (CECT) is considered to be the imaging modality of choice for GIST diagnosis, while its surgical removal is the primary treatment of choice [10]. In this case, the tumor was located in the anterior wall of the stomach and was approximately 4×3 cm in size. In terms of the pathology (Figure 1), the tumor was round epithelioid appearance, with clear cytoplasm and a well-defined cell membrane. Immuno histochemical evaluation showed that the tissue was CD117-positive. No evidence to support tumor metastasis was found in exploratory surgery. Furthermore, CECT of the abdomen and the head MRI were negative, indicating a relatively low probability of metastasis. Because of the failure of antibiotic treatment, the patient had been diagnosed with a fungal lung infection, which was treated empirically with voriconazole for approximately two months. However, to avoid the risk of tumor recurrence associated with immunosuppressive agents, cyclophosphamide was not added to the treatment regimen. Under treatment with tapering doses of steroids, the patient is in currently in remission, with visible diminution of multiple nodules in chest CT imaging.

Because of its difficultly associated with diagnosis, we have described the details of this case of GPA presenting as postoperative GISTs, which is one of the first of its kind to be reported. They may be an isolated incident or contact. Despite these unfortunate sequelae, consideration of GPA allows early diagnosis and appropriate treatment, which significantly reduces the morbidity/mortality of this condition.

Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying image. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests

The authors declare that they have no competing interests.

Acknowledgement

We are grateful for the cooperation of the patient's family.

References

1. Klinger H (1931) Grenzformen der Periarteritis Nodosa. Fr Z Pathol 42: 455-480.
2. Wegener F (1936) Uber generalisierte, septische Gefäßerkrankungen. Verh Dtsch Ges Pathol 29: 202-210.
3. Wegener F (1939) Uber eine eigenartige rhinogene Granulomatose mit besonderer Beteiligung des Arteriensystems und der Nieren. Beitr Path Anat 102: 36-38.
4. Mazur MT, Clark HB (1983) Gastric stromal tumors. Reappraisal of histogenesis. Am J Surg Pathol 7: 507–519.
5. Hirota S, Isozaki K, Moriyama Y, Hashimoto K, Nishida T, et al (1998) Gain-of-function mutations of c-kit in human gastrointestinal stromal tumors, Science 279: 577–580.
6. Hoffman GS, Langford CA, Specks U (2012) Granulomatosis with polyangiitis (Wegener’s). In Inflammatory Diseases of Blood Vessels (2nd ed.) Edited by Hoffman GS, Weyand CM, Langford CA, Goronzy JJ Chichester, West Sussex: Wiley-Blackwell 238-251.
7. Fauci AS, Haynes BF, Katz P, Wolff SM (1983) Wegener’s granulomatosis: prospective clinical and therapeutic experience with 85 patients for 21 years. Ann Intern Med 98: 76–85.
8. Falk RJ, Jennette JC (1988) Anti-neutrophil cytoplasmic autoantibodies with specificity for myeloperoxidase in patients with systemic vasculitis and idiopathic necrotizing and crescentic glomerulonephritis. N Engl J Med 25: 1651-1657.
9. Rutgers A, Sanders JSE, Tervaert JWC, Kallenberg CGM (2012) Autoantibodies and vascular inflammation. In Inflammatory Diseases of Blood Vessels. Second edition edition. Edited by Hoffman GS, Weyand CM, Langford CA, Goronzy JJ. Chichester, West Sussex: Wiley-Blackwell 61–70.
10. Stamatakos M, Douzinis E, Stefanaki C, Safioleas P, Polyzou E, et al. (2009) Gastrointestinal stromal tumor. World J Surg Oncol 7: 61.