

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

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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 to 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 multisystem 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. The symptoms of GISTs can vary from vague abdominal pain to severe acute bleeding that is life-threatening. Due to the non-specific presentation of the disease, the initial diagnosis of GIST may be delayed. Here, we report an unusual case of GPA, in which the patient presented with postoperative GISTs. We also explore the diffuse diagnosis and discuss the treatment of this patient during the hospitalization.

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).

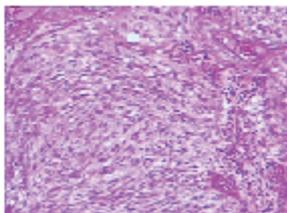


Figure 1: Tumor of stomach biopsy shows round epithelioid appearance, clear cytoplasm and cell membrane clear boundaries (HE staining, 100×).

The patient did not receive chemotherapy for a number of reasons. On admission, laboratory tests demonstrated a normal white blood cell (WBC) count ($9.2 \times 10^9/L$), normal renal function (creatinine 82 $\mu\text{mol/L}$), and a high C-reactive protein (CRP) (108.80 mg/L). He was mildly hypoxic (pO_2 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).



Figure 2: Initial non-contrast chest computed tomography scan showing some bilateral pulmonary infiltration with multiple parenchymal nodules apparently localized in the peripheral lobes.

Blood urea nitrogen and creatinine were normal. Furthermore, urine analysis revealed elevation of β_2 -microglobulin (2347.5 $\mu\text{g/L}$, 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 appearance 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).

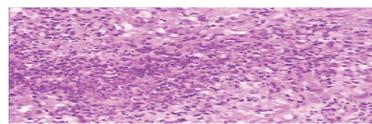


Figure 3: Nasal sinus mucosa biopsy revealing the typical granuloma changes including multi-nuclear giant cells and epithelial cells (hematoxylin and eosin staining, 100×).

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).



Figure 4: Subsequent chest computed tomography scan after six months demonstrating clear diminution of multiple nodules.

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 significant 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, Fauci 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 PR 3-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 difficulty 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

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