

## CASE REPORT

# Anemia Combined Significantly Increased High-Sensitivity C Reactive Protein and Lung Lesions Lead to the Diagnosis of Granulomatosis with Polyangiitis Proven by Lung Biopsy and Anti-neutrophil Cytoplasmic Antibody Test

Yan L. Ge<sup>1</sup>, Cong H. Liu<sup>2</sup>, Meng H. Wang<sup>3</sup>, Jia B. Zhang<sup>1</sup>, Hao Chen<sup>4</sup>, Xiao Y. Zhu<sup>1</sup>, Zhen Z. Li<sup>1</sup>, Hong L. Li<sup>1</sup>, Zi Y. Cui<sup>1</sup>, Li Q. Li<sup>1</sup>, Ai S. Fu<sup>1</sup>, Hong Y. Wang<sup>1</sup>

<sup>1</sup> Department of Respiratory Medicine, North China University of Science and Technology Affiliated Hospital, Tangshan, Hebei, China

<sup>2</sup> Department of Endocrinology Medicine, North China University of Science and Technology Affiliated Hospital, Tangshan, Hebei, China

<sup>3</sup> Department of Hospital Information Management, North China University of Science and Technology Affiliated Hospital, Tangshan, Hebei, China

<sup>4</sup> Department of Cardiovascular Medicine, North China University of Science and Technology Affiliated Hospital, Tangshan, Hebei, China

## SUMMARY

**Background:** To report an atypical case misdiagnosed as lung abscess over the past 2 months, but persistent anemia combined with significantly increased hs-CRP and lung lesions indicated systemic lesion, which led to the diagnosis of granulomatosis with polyangiitis proven by lung biopsy and anti-neutrophil cytoplasmic antibody test (ANCA).

**Methods:** The complete blood count, hs-CRP, and anti-neutrophil cytoplasmic antibody (ANCA) test were performed. The pathology consultation for the lung biopsy was arranged.

**Results:** Hemoglobin was 8.5 g/L, hs-CRP was > 200 mg/L, c-ANCA directed against anti-proteinase 3 (PR3) was positive, pathology consultation reported granulomatous inflammation.

**Conclusions:** When patients have multiple organ dysfunction combined with anemia and significantly increased hs-CRP, physicians should pay attention to systemic vasculitis.

(Clin. Lab. 2019;65:xx-xx. DOI: 10.7754/Clin.Lab.2018.180733)

---

### Correspondence:

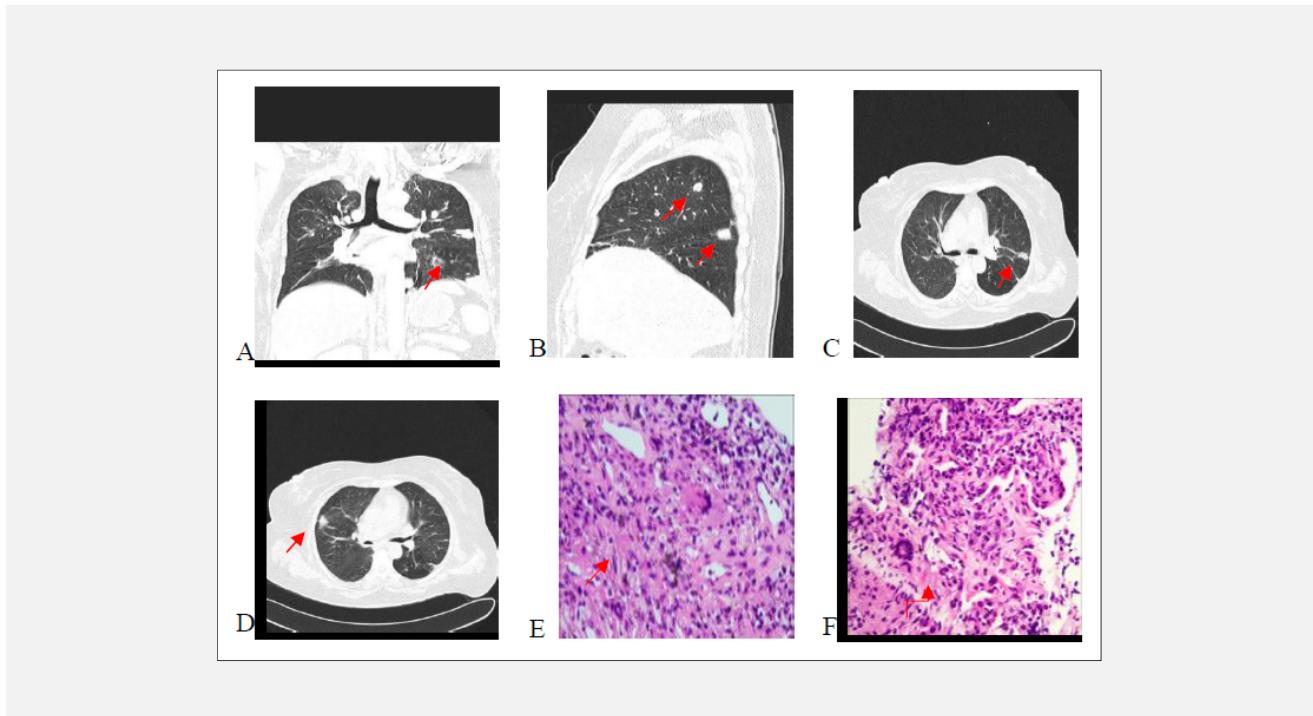
Fu Ai-Shuang  
Department of Respiratory Medicine  
North China University of Science and  
Technology Affiliated Hospital  
Jianshe Road 73  
063000 Tangshan  
Hebei  
China  
Email: maxfas@163.com

### KEY WORDS

granulomatosis with polyangiitis, anti-neutrophil cytoplasmic antibody, anemia, hs-CRP

### CASE PRESENTATION

In the present study, we report a case of a 56-year-old female who presented with a history of fever and cough with a little white sputum for 2 months. She also complained of dyspnea on exertion, but without ulcers, hemoptysis, hearing loss, nasosinusitis or hoarseness of voice, and no pain in small and large joints. Past medical records revealed that she was treated for pneumonia and lung abscess with antibiotics nearly a month in another hospital; she had no symptomatic benefit. So, she received ultrasound-guided lung biopsy. The lung biop-



**Figure 1. Patient imaging and histological results.**

The chest contrast-enhanced CT scan showed multiple subpleural nodules, some with cavity (Figure 1A - 1D). Histopathology showed multiple granulomatous vasculitis of small arteries and veins of the lung (Figure 1E, 1F).

sy pathology showed nonspecific inflammatory reaction (she did not provide the lung biopsy pathology slices at first visit). She was referred to our hospital to receive advanced treatment. The patient was admitted in our department. The physical examination was normal. Complete blood count showed hemoglobin of 8.5 g/L, white blood cell count and platelet count were normal. Serum creatinine and urine routine tests were normal. Serum high-sensitivity C reactive protein (CRP) was  $> 200$  mg/L (a value of  $< 8$  mg/L was used as the biological reference for hs-CRP); erythrocyte sedimentation rate (ESR) was elevated (23 mm/1st hour). Chest CT scan showed multiple subpleural nodules, some with cavity (Figure A-D). We suggested the patient receive a lung biopsy again, which she rejected. We considered the whole history and treatment of the patient. She had lung and hematological system lesions and combined with anemia and significantly increased hs-CRP. We should pay attention to systematic vasculitis. So, we arranged an ANCA test to exclude connective tissue disease causing chronic fever; c-ANCA directed against PR3 was positive. So, we arranged a pathology consultation for the lung biopsy. The pathology consultation result in our hospital was granulomatous inflammation (Figure 1E, 1F). Then the definite diagnosis was granulomatosis with polyangiitis. She was started on intravenous pulse methylprednisolone (500 mg qd  $\times$  5 days), then with maintenance treatment with oral prednisolone

(40 mg qd). She had significant improvement in clinical symptoms after the treatment. Chest CT scan was done in another hospital after a month of treatment which showed partial resolution of nodules, so we could not get the chest CT scan images. The patient was still in follow-up.

## DISCUSSION

Granulomatosis with polyangiitis, formerly called Wegener's granulomatosis, is an ANCA-associated systemic necrotizing vasculitis. Lung, renal, skin and paranasal sinus involvement are common manifestations [1-4]. Its severity is variable, ranging from asymptomatic lesions to dramatic life-threatening clinical presentations such as acute renal failure and diffuse alveolar hemorrhage [4,5]. In typical granulomatosis with polyangiitis, there are usually multiple organs lesions [5-7]. The EULAR/PRINTO/PRES for GPA include histopathology (Granulomatous inflammation within the wall of an artery or in the perivascular or extravascular area), upper airway involvement, laryngo-tracheo-bronchial involvement, pulmonary involvement, renal involvement, and ANCA test [8]. In our case, the patient lacked typical clinical manifestations and the lung biopsy pathology showed nonspecific inflammatory reaction the first time making diagnosis challenging, especially in discriminating in-

fectious or non-infectious lesion. Though the patient was treated with antibiotics nearly a month, the manifestations still existed, because the most common causes for sub-acute and chronic fever are tumors, tuberculosis, and connective tissue disease. So, an ANCA test was performed to exclude ANCA-associated systemic necrotizing vasculitis. c-ANCA directed against PR3 antibodies are associated with granulomatosis with polyangiitis [9-11]. Then the diagnosis was definite. We arranged the pathology consultation for the lung biopsy in our hospital and the pathology reported multiple granulomatous inflammations, which is in accordance with granulomatosis with polyangiitis [12]. At the same time, we reviewed the chest CT scan manifestations of granulomatosis with polyangiitis. The lung lesions in granulomatosis with polyangiitis on radiologic findings have been described as interstitial involvement, nodular lesions, fixed infiltrates, and pleural disease. Among those lesions, multiple nodules are more significant [13, 14]. For this patient, in the beginning, the physician could not oconnect the multiple nodules with granulomatosis with polyangiitis which reflected the lack of fully understanding the disease.

## CONCLUSION

For patients who have sub-acute and chronic fever combined with lung lesions, especially multiple nodules in the lungs and no symptomatic benefit after antibiotic treatment, but had anemia combined with significantly increased hs-CRP, should indicate to the physician to pay attention to systemic necrotizing vasculitis.

### Acknowledgment:

We thank the other members of the Department of Respiratory Medicine of North China University of Science and Technology Affiliated Hospital for their critical comments.

### Ethical Approval:

This study was approved by ethics committee of North China University of Science and Technology Affiliated Hospital. All procedures performed in studies were in accordance with the ethical standards. Informed consent was obtained from all individual participants included in this study.

### Support:

This work was supported by the Hebei Province Science Development Program [G201806061].

### Declaration of Interest:

No conflicts of interest.

## References:

- Russell B, Mohan S, Chahal R, Carette S, Pagnoux C. Prognostic Significance of Cavitary Lung Nodules in Granulomatosis With Polyangiitis (Wegener's): A Clinical Imaging Study of 225 Patients. *Arthritis Care Res (Hoboken)* 2018;70:1082-9 (PMID: 2892397).
- Parakh R, Parakh S, Tretiakova M. Primitive Neuroectodermal Tumor and Wegener's Granulomatosis of the Kidney: A Curious Combination of Two Rare Entities. *Case Rep Urol* 2017;2017:1750694 (PMID: 28835865).
- Keorochana N, Klanarongkan K, Satayasoontorn K, Chaiamnuay S. Necrobiotic xanthogranuloma scleritis in a case of granulomatosis with polyangiitis (Wegener's granulomatosis). *Int Med Case Rep J* 2017;10:323-8 (PMID: 29042820).
- Li J, Li C, Li J. Thoracic manifestation of Wegener's granulomatosis: Computed tomography findings and analysis of misdiagnosis. *Exp Ther Med* 2018;16:413-9 (PMID: 29896268).
- Eriksson P, Segelmark M, Hallbook O. Frequency, Diagnosis, Treatment, and Outcome of Gastrointestinal Disease in Granulomatosis with Polyangiitis and Microscopic Polyangiitis. *J Rheumatol* 2018;45:529-37 (PMID: 29419474).
- Pakalniskis MG, Berg AD, Policeni BA, et al. The Many Faces of Granulomatosis with Polyangiitis: A Review of the Head and Neck Imaging Manifestations. *AJR Am J Roentgenol* 2015;205:W619-29 (PMID: 26587951).
- van der Leeuw J, Flinsenberg TWH, Siezenga MA. Strawberry gingivitis as a manifestation of granulomatosis with polyangiitis. *Rheumatology (Oxford)* 2018;57:226 (PMID: 28977626).
- Huppertz HI. [EULAR/PreS consensus criteria 2006 for the classification of childhood vasculitides]. *Z Rheumatol* 2009;68:772-4 (PMID: 19756661).
- Olson SW, Owshalimpur D, Yuan CM, et al. Relation between asymptomatic proteinase 3 antibodies and future granulomatosis with polyangiitis. *Clin J Am Soc Nephrol* 2013;8:1312-8 (PMID: 23640980).
- Thai LH, Charles P, Resche-Rigon M, Desseaux K, Guillemin L. Are anti-proteinase-3 ANCA a useful marker of granulomatosis with polyangiitis (Wegener's) relapses? Results of a retrospective study on 126 patients. *Autoimmun Rev* 2014;13:313-8 (PMID: 24225075).
- Verstockt B, Bossuyt X, Vanderschueren S, Blockmans D. There is no benefit in routinely monitoring ANCA titres in patients with granulomatosis with polyangiitis. *Clin Exp Rheumatol* 2015;33:S-72-6 (PMID: 26016753).
- Ursea R, De Castro D, Bowen TJ, Chan CC. The role of conjunctival biopsy in the diagnosis of granulomatosis with polyangiitis. *J Ophthalmic Inflamm Infect* 2015;5:1 (PMID: 25632308).
- De Geeter F, Gykiere P. (18)F-FDG PET imaging of granulomatosis with polyangiitis -Wegener's Syndrome. *Hell J Nucl Med* 2016;19:53-6 (PMID: 26929942).
- Komarnicka J, Brzewski M, Banaszkiewicz A, Maciąg R, Krysiak R. Computed Tomography (CT) Angiography in Pre-Embolization Assessment of Location of Gastrointestinal Bleeding in Paediatric Patient with Granulomatosis with Polyangiitis (Wegener's Granulomatosis) - Case Report. *Pol J Radiol* 2017;82:589-92 (PMID: 29662590).