Granulomatosis with polyangiitis: An example of diagnostic (confirmation) bias

University of Colorado Anschutz Medical Campus

Margaret M. Nguyen and Marina Mutter, M.D., M.S.

Abstract

58-year-old woman with a history of bilateral mastoiditis presented with worsening malaise, headache, and mastoid tenderness concerning for either vasculitis or an infection. Given her history, elevated inflammatory markers, and nuclear medicine bone scan concerning for osteomyelitis, she was started on empiric antibiotic therapy and underwent an extensive infectious workup. After the workup failed to reveal an infectious etiology and her condition worsened despite treatment, the team reconsidered vasculitis. An elevated c-ANCA titer, PR3 >30, a urinalysis without RBC casts, and a computerized tomography without pulmonary nodules confirmed the diagnosis of granulomatosis with polyangiitis with limited involvement.

This case highlighted the impact of diagnostic (confirmation) bias in clinical decision-making as the clinical history and imaging findings led to an extensive infectious workup despite negative microbiology.

Keywords: Granulomatosis with polyangiitis, Case report, Confirmation Bias

Background

Granulomatosis with polyangiitis (GPA) is a rare auto-immune small-vessel vasculitis that classically presents with upper and lower respiratory tract symptoms and renal involvement.[1]

CLINICAL CRITERIA	
Nasal involvement: bloody discharge, ulcers, crusting, congestion, blockage, or septal defect / perforation	+3
Cartilaginous involvement (inflammation of ear or nose cartilage, hoarse voice or stridor, endobronchial involvement, or saddle nose deformity)	+2
Conductive or sensorineural hearing loss	+1
LABORATORY, IMAGING, AND BIOPSY CRITERIA	
Positive test for cytoplasmic antineutrophil cytoplasmic antibodies (cANCA) or antiproteinase 3 (anti-PR3) antibodies	+5
Pulmonary nodules, mass, or cavitation on chest imaging	+2
Granuloma, extravascular granulomatous inflammation, or giant cells on biopsy	+2
Inflammation, consolidation, or effusion of the nasal/paranasal sinuses, or mastoiditis on imaging	+1
Pauci-immune glomerulonephritis on biopsy	+1
Positive test for perinuclear antineutrophil cytoplasmic antibodies (pANCA) or antimyeloperoxidase (anti-MPO) antibodies	-1
Blood eosinophil count ≥ 1 x10^9/liter	-4

Sum the scores for 10 items, if present. A score of ≥ 5 is needed for classification of GRANULOMATOSIS WITH POLYANGIITIS.

Figure 1. 2022 American College of Rheumatology/European Alliance of Associations for Rheumatology classification criteria for GPA.

However, as a relatively uncommon condition with a large variability in clinical presentations, GPA can be challenging to diagnose. Diagnosing GPA requires a high index of suspicion, especially when the presentation deviates from expected. Having a broad differential and ruling out other pathology is also critical for diagnosis. Clinicians should suspect GPA when the patient's condition worsens despite conventional treatment.[3]

This case highlighted the impact of diagnostic (confirmation) bias in clinical decision-making as the clinical history and imaging findings led to an extensive infectious workup despite negative microbiology.

Case Presentation

03/20/20	• 58-year old Spanish-speaking woman with several months of smoldering ear symptoms suspected to be an infection but refractory to several rounds of antibiotics and steroids..
06/11/20	• Admitted for bilateral mastoiditis and facial nerve paralysis. Underwent bilateral mastoidectomies with facial nerve decompression, tympanostomy, and treatment with antibiotics despite extensive negative infectious workup.
08/25/20	• Persistent boring mastoid pain and significant hearing loss causes concern for osteomyelitis. Started on antibiotics and a nuclear medicine bone scan was ordered.
08/30/20	• Presented to the ED with malaise, headaches, mastoid tenderness, and neck pain.
09/01/20	• NM bone scan was concerning for osteomyelitis of the left temporal bone. Diagnostic differential included infection vs. vasculitis (GPA/GCA).
09/03/20	• Chest x-ray without pulmonary nodules and urinalysis without RBC casts decreased concern for GPA. Primary concern for osteomyelitis given the clinical history, elevated inflammatory markers, bone scan, CXR and UA findings. The patient was started on empiric antibiotic therapy and underwent an extensive infectious workup.
09/04/20	• MRI brain demonstrates nonspecific fluid and enhancement in mastoidectomy beds representing either granulation vs. infection.
09/08/20	• Despite treatment with antibiotics, progressing condition and extensive negative infectious work-up prompts renewed concern for GPA.
09/07/20	• CT scan of the patient's chest showed no evidence of pulmonary nodules.
09/09/20	• Treatment with high-dose IV steroids and Rituximab infusions with good effect.
09/14/20	• Patient received her first Rituximab infusion. The diagnosis of AAV-GPA with limited involvement was made with a c-ANCA of 1:12560 , PR3 >30., UA without RBC casts, and CT without pulmonary nodules.
08/10/21	• Tolerating therapy well with no signs of active disease.

Acknowledgments

The author acknowledges Dr. Marina Mutter and the MSA team for their guidance regarding case report conceptualization and completion.

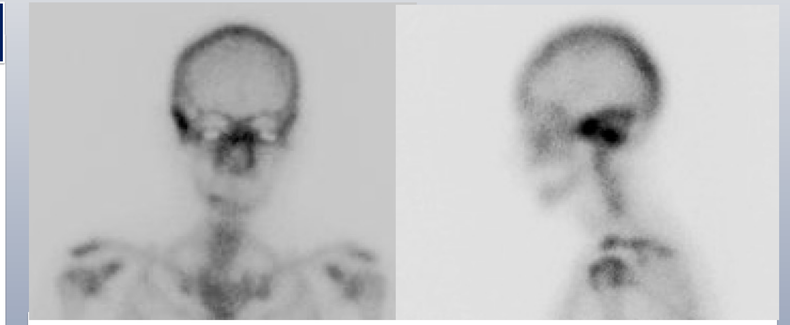

Figure 2. Nuclear medicine scan demonstrating an asymmetric increased radiotracer uptake in the left petrous portion of the temporal bone greater than the right, concerning for underlying acute OM.

Discussion

This case is noteworthy for the initial delay in diagnosis that was likely due to confirmation bias.

Diagnostic (or confirmation) bias is the tendency to give more weight to findings that support a preliminary diagnosis while failing to seek out or minimize contradictory evidence.[4]

In this case, treatment and investigations primarily focused on the management of infection due to the presumed clinical history and results of the NM bone scan. Despite the progression of the patient's condition despite empiric antibiotic workup and an extensive negative infectious workup, the treating team continued to pursue an infectious etiology as a result of diagnostic bias. It was not until the patient's condition had significantly progressed that the team broadened their differential and was able to make the diagnosis of GPA.

Several approaches could have been used to counteract bias in this case.

1. Seeking contradictory evidence and broadening the diagnostic differential.[5]
2. Utilizing metacognitive interventions or balanced testing.[6-8]

This case is useful for reflective purposes in avoid diagnostic bias as a timely diagnosis would have prevented significant patient morbidity.

Competing Interests

The authors declare no competing interests, nor any financial interests.

References

1. Jennette JC, Falk RJ, Bacon PA, Basu N, Cid MC, Ferrario F, Flores-Suarez LF, Gross WL, Guillevin L, Hagen EC, Hoffman GS, Jayne DR, Kallenberg CG, Lamprecht P, Langford CA, Luqmani RA, Mahr AD, Matteson EL, Merkel PA, Ozen S, Pusey CD, Rasmussen N, Rees AJ, Scott DG, Specks U, Stone JH, Takahashi K, Watts RA. 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. Arthritis Rheum. 2013 Jan;65(1):1-11. doi: 10.1002/art.37715. PMID: 23045170.
2. Robson, J., Grayson, P., Ponte, C., Suppiah, R., Craven, A., Judge, S., . . . Luqmani. (2023). 2022 American College of Rheumatology/European Alliance of Associations for Rheumatology Classification Criteria for Granulomatosis With Polyangiitis. Arthritis & Rheumatology., 74(3), 393-399.
3. Grygiel-Górniak B, Limphaibool N, Perkowska K, Puszczewicz M. Clinical manifestations of granulomatosis with polyangiitis: key considerations and major features. Postgrad Med. 2018 Sep;130(7):581-596. doi: 10.1080/00325481.2018.1503920. Epub 2018 Aug 2. PMID: 30071173.
4. American Psychological Association. (n.d.). *Apa Dictionary of Psychology: Confirmation Bias*. American Psychological Association. Retrieved January 20, 2022, from https://dictionary.apa.org/confirmation-bias
5. Busby LP, Courtier JL, Glastonbury CM. Bias in radiology: the how and why of misses and misinterpretations. RadioGraphics 2018;38(1): 236e47.
6. Croskerry P. Cognitive forcing strategies in clinical decisionmaking. Ann Emerg Med 2003;41(1):110e20.
7. Croskerry P. The cognitive imperative: thinking about how we think. Acad Emerg Med 2000;7(11):1223e31.
8. Elston DM. Confirmation bias in medical decision-making. J Am Acad Dermatol. 2020 Mar;82(3):572. doi: 10.1016/j.jaad.2019.06.1286. Epub 2019 Jul 3. PMID: 31279036.