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Severe Active ANCA-Associated Vasculitis (GPA/MPA): Defining Disease

Announcer:
You're listening to ReachMD. This medical industry feature, titled "Severe Active ANCA-Associated Vasculitis (GPA/MPA): Defining Disease," is sponsored by Amgen. Here's your host, Dr Zach Wallace.

Dr Wallace:
This is ReachMD, and I'm Zach Wallace. Today, we are talking about antineutrophil cytoplasmic antibody-, or ANCA-, associated vasculitis. Specifically, we'll look at granulomatosis with polyangiitis, or GPA, and microscopic polyangiitis, or MPA. We'll discuss a validated definition of severe active GPA and MPA, and how it may be applicable in clinical practice, and then review some patient case examples.

Joining me are Drs Anisha Dua and Frank Cortazar. Dr Dua is the Director of the Northwestern Vasculitis Center and a Professor of Medicine in the Division of Rheumatology at Northwestern University Feinberg School of Medicine in Chicago.

Dr Dua, welcome to the program.

Dr Dua:
Thanks for having me.

Dr Wallace:
Also with us is Dr Cortazar, who's the Director of the New York Nephrology Vasculitis and Glomerular Center in Albany, New York. Dr Cortazar, it's great to have you with us as well.

Dr Cortazar:
Thanks, it's great to be here.

Dr Wallace:
To begin, we know that treatment decisions in patients with GPA and MPA are often influenced by disease severity.[1] However, there is no consensus definition of severe active GPA or MPA.[2]

So to start us off, Dr Dua, why is it important to have a consistent framework for defining severe active GPA and MPA?

Dr Dua:
No two patients really look the same.[3] Some patients may already present with life- or organ-threatening disease, such as rapidly progressive glomerulonephritis or diffuse alveolar hemorrhage. Others have active disease that may appear less dramatic at presentation but still are at near-term risk of progression to life- or organ threatening disease.[1] That's why having a consistent framework matters. It gives clinicians a shared way to think about disease severity[2] and identify patients who may require urgent evaluation, closer monitoring, and other treatment options[4]—while still leaving room for clinical judgement.

Dr Wallace:
Turning to you now, Dr Cortazar, from a nephrology perspective, what are some of the consequences when clinicians don't have a common framework for assessing severity?

Dr Cortazar:
These patients often see multiple specialists—a nephrologist, rheumatologist, pulmonologist, otolaryngologist—so having a shared lexicon is important.[4] When everyone is approaching disease severity from a common framework, it's easier to recognize patients who

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may have severe active GPA or MPA, coordinate care across the multidisciplinary team, and make more aligned treatment decisions.[4]

Dr Wallace:
With all that in mind, let's zero in on a validated definition of severe active GPA/MPA. Specifically, the definition describes severe active GPA or MPA as evidence of active disease—whether that disease is new, relapsing, persistent, or worsening—that results in life- or organ-threatening disease, or places the patient at near-term risk of progression to life- or organ-threatening disease. It also describes some of the possible manifestations of severe active GPA or MPA, but makes clear that the list included is not exhaustive.[5]

Dr Dua, what stands out to you when you hear this definition?

Dr Dua:
Two things stand out. First, the definition recognizes that disease activity can occur at multiple points along the disease journey. Not just at initial diagnosis, but as a relapse, or when the disease is worsening or not adequately responding to treatment.[5] Second, it reminds us that severity isn't just about what's happening today. It's also about where the disease may be headed.[5]

Dr Wallace:
And from your perspective, Dr Cortazar, how does this framework compare with the way clinicians currently assess disease severity in practice?

Dr Cortazar:
I don't think this changes how experienced clinicians think about disease severity in ANCA-associated vasculitis. What it does is provide a common language for describing the factors we already consider in a framework that does not require complex scoring systems or extensive specialized testing.[5]

Dr Wallace:
Dr. Dua, can you walk us through how it was shown that the definition aligned with the way experts assess severe active GPA and MPA in clinical practice?

Dr Dua:
Sure. Experts who care for patients with GPA and MPA, including rheumatologists, nephrologists, and pulmonologists, reviewed a series of patient-inspired cases using their own clinical judgment and then reassessed those same cases using the definition we just discussed.[6] Across the 74 cases reviewed, 62 received the same severity classification through clinical judgement and application of the definition, suggesting that, in general, the definition reflected how experienced clinicians already think about the disease. [6]

Dr Wallace:
So, while the definition generally aligned with expert opinion, there were cases where the clinicians classified severity differently from the definition.[6]

Dr. Cortazar, what do you take away from that?

Dr Cortazar:
I think that's ok. This definition isn't meant to be a replacement for clinical judgment. It's a tool to support it. Physicians still need to consider the full clinical picture when assessing an individual patient.

Dr Wallace:
For those just tuning in, you're listening to ReachMD. I'm Dr Zach Wallace, and today I'm speaking with Drs Anisha Dua and Frank Cortazar about anti-neutrophil cytoplasmic antibody-, or ANCA-, associated vasculitis. Specifically, we're discussing granulomatosis with polyangiitis or GPA and microscopic polyangiitis or MPA, including a validated definition of severe active disease.

Dr Wallace:
With that in mind, let's apply the proposed definition to a couple of patient scenarios that clinicians may encounter in practice. Our first patient is based on a 2024 case report by Hu et al, published in AJO International, of a 45-year-old man with PR3-ANCA-positive GPA. At diagnosis, he presented with chronic sinus disease, scleritis, episodic blood-tinged sputum, microscopic hematuria, and inflammatory joint symptoms.[7] Over time, some manifestations improved with treatment, but he continued to experience recurrent ocular inflammation, including both scleritis and panuveitis.[7] Despite escalation of therapy, disease activity repeatedly returned during glucocorticoid tapering, and he was unable to maintain disease control when prednisone was reduced below approximately 20 milligrams daily.[7]

Given those case details, Dr Dua, what features immediately stand out to you?

Dr Dua:

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Well, the first thing that I notice is this disease isn't staying under control as glucocorticoids are tapered. The second thing is the recurrent ocular inflammation.[7] Recurrent scleritis and panuveitis are signs of active disease that are organ-threatening.[7]

Dr Wallace:
Now, let's apply the definition directly to this case, and I'd love to hear each of your thoughts on this. Starting with you, Dr Dua, when you look at the proposed definition, would this patient meet criteria for severe active GPA?

Dr Dua:
Yes, I believe the patient would meet the definition of severe active GPA. The patient has evidence of active disease with ongoing ocular involvement, including scleritis, which is one of the representative manifestations included within the definition.[5]

Dr Wallace:
And, Dr Cortazar, if we focus on the patient's glucocorticoid dependence for a moment, how does that influence your assessment of disease severity?

Dr Cortazar:
Glucocorticoids remain an important part of induction therapy, but high doses are not intended to be a long-term strategy. When disease repeatedly returns during tapering, it raises concern that the patient may still have severe active disease.[7] While glucocorticoid dependence isn't specifically included in the definition, it provides important clinical context that helps inform my assessment of disease severity.[5]

Dr Wallace:
Thank you both for sharing your thoughts on that. And now I'd like to contrast that scenario with another case.

This patient scenario is based on a patient-inspired case from the validation study. This is a 45-year-old woman with newly diagnosed PR3-ANCA-positive GPA who presents with several weeks of sinus congestion, inflammatory joint symptoms, a petechial rash involving the lower extremities, and progressive hoarseness.[5] Evaluation by otolaryngology demonstrates subglottic inflammation and subglottic stenosis with 20 percent narrowing.[5] Her kidney function is normal, and there's no evidence of proteinuria or hematuria.[5]

Dr Cortazar, what stands out to you when you first hear this case?

Dr Cortazar:
As the patient's kidney function is normal, what immediately catches my attention is the airway disease. Even though the subglottic stenosis is relatively mild at this point, the presence of airway disease immediately raises concern about the potential for significant airway compromise if inflammation continues. Putting this in the context of the definition, one of its strengths is that it encourages clinicians to think about whether current active disease places the patient at near-term risk of progression to life-threatening disease.[5]

Dr Wallace:
And from your perspective, Dr Dua, would this patient meet the proposed definition of severe active GPA?

Dr Dua:
Yes, in addition to agreeing with Dr. Cortazar that the potential for airway compromise is of concern, subglottic stenosis is specifically mentioned in manifestations that could represent severe active GPA.[5]

Dr Wallace:
Thank you so much for all of your insights. I think these two cases really highlight the value of the definition across different clinical scenarios. It provides a structured way to think about severe active ANCA-associated vasculitis, GPA and MPA, while reinforcing that clinical judgment remains central.

Dr Dua and Dr Cortazar, it was great speaking with you both today.

Dr Dua:
Thanks for having me!

Dr Cortazar:
It was great to be here.

Dr Wallace:
For ReachMD, I'm Dr Wallace.

Announcer:
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