CASE REPORT

# A unique case of indolent microscopic polyangiitis in an elderly gentleman: a case report and brief review

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**ABSTRACT**

Antineutrophil cytoplasmic autoantibody associated vasculitides has 3 different types: Granulomatosis with polyangiitis, eosinophilic granulomatosis and polyangiitis and microscopic polyangiitis. These vasculitides manifest differently based on which area of small and medium size vessels in our bodies that it affects. In this case report, we discuss a unique case of microscopic polyangiitis diagnosed in a 75-year-old male who was relatively asymptomatic i.e. indolent, apart from nodules present in the lung with the use of the diagnostic criteria outlined by 2022 American College of Rheumatology and European Alliance of Associations for Rheumatology. In addition, we reviewed briefly about vasculitis, its epidemiology and the workup of microscopic polyangiitis.

**KEYWORDS:** Vasculitis; Antineutrophil cytoplasmic autoantibody; ANCA associated vasculitis; Microscopic polyangiitis; Indolent vasculitis; Granulomatosis with polyangiitis; Eosinophilic granulomatosis and polyangiitis; Renal biopsy

## INTRODUCTION

Microscopic Polyangiitis (MPA) is an Antineutrophil cytoplasmic autoantibody (ANCA) associated vasculitides (AAV) that is present along in a group with two other vasculitides, Granulomatosis with Polyangiitis (GPA) and Eosinophilic granulomatosis and polyangiitis (EGPA) [1,2]. All of which affects small to medium size vessels, namely capillaries, arterioles, venules, small arteries, and veins. These vasculitides cause inflammation of these blood vessels compromising vital organs and tissues distally leading to renal, cutaneous, pulmonary, and neurological manifestations which typically causes presentations akin to that of severe organ damage and/or life-threatening disease, and uncommonly of a minor presentation.

The hallmark definition of MPA according to the 2012 Chapel Hill Consensus Conference (CHCC) is a form of necrotizing vasculitis affecting predominantly small vessels, with little to no immune deposits involvement and an absence of granulomatous inflammation [3].

This case report discusses a unique case of a patient who was referred to the respiratory clinic after incidental findings of multiple nodules in the lung on a Computed Tomography (CT) scan and raised atypical ANCA. The CARE guidelines were utilized for the reporting of this case [4].

## CASE REPORT

A 75-year-old male initially presented to the Emergency Department after experiencing a 3-day history of small teaspoon size hemoptysis accompanied with tiny amounts of phlegm. Around the same time, he was experiencing other symptoms such as a hoarse voice, a sore throat and dysphagia. He has a background history of hypertension, hypothyroidism, gastro-esophageal reflux disease with Barrett's esophagus. His surgical history in chronological order includes a right neck dissection with adjuvant chemoradiotherapy for a carcinoma of unknown origin, right-sided hemicolectomy for a stage I colon cancer, endoscopic retrograde cholangiopancreatography for a biliary stricture and an aortic valve replacement for symptomatic aortic stenosis. He was admitted under the care of Ear, Nose and Throat (ENT) team, who ordered a head, neck and chest CT scan and completed a video laryngoscopy and a biopsy of a previously known vocal cord lesion, to exclude malignancy and an ENT cause of hemoptysis. The biopsy returned as a benign lesion. The CT scan reported multiple nodular lesions within the left lung in a centrilobular distribution, right infrahilar soft tissue thickening, scattered ground glass opacities, calcified pleural plaques and a few mediastinal lymph nodes with mild calcification. An outpatient respiratory referral was recommended by the radiologist and carried out by the ENT team. He was discharged after; no other management was carried out during his admission.

Following discharge, he was reviewed in the respiratory clinic. He reported no hemoptysis at that time but did have persistent hoarse voice and mild dyspnea most notably on exertion. He reported no constitutional symptoms. He has a 25-pack year smoking history, with approximately 5 years of asbestos exposure during his career as a boiler maker. Because of his dyspnea a full lung function test was carried out which showed a normal spirometry, with normal helium

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diffusion and were replicable results. An echocardiogram was also carried out which was unremarkable, most importantly the right ventricular size and right ventricular systolic pressure (RVSP) was normal. A second high resolution CT (HRCT) scan was done two months after the previous one which showed an improvement in size and number of the left sided nodules previously found. A resolution of the scattered ground glass opacities with persistence of the infrahilar thickening. Due to the improvement but not resolution of the nodules and the ground glass opacities, it was suggestive that the underlying pathology could have been of an infective origin although his clinical history and presentation was not one of an infective presentation. However, given the current improvement based on

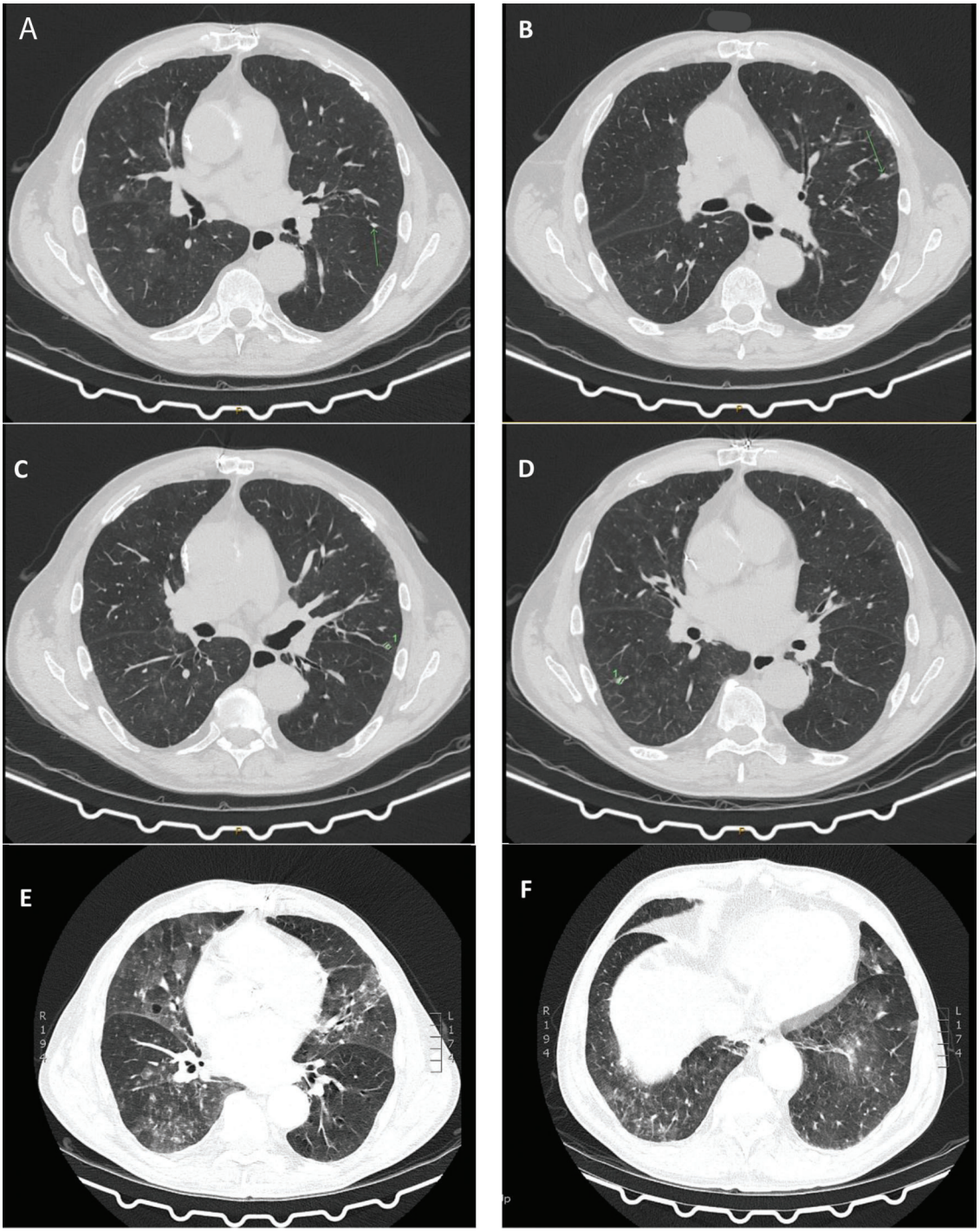


**Fig. 1.** Third CT scan findings showing 4 different nodules along with interstitial lung changes A) Arrow showing nodule adjacent to left oblique fissure. B) Arrow showing left upper lobe nodule. C) Box for border showing a different left upper lobe nodule. D) Box for border showing right upper lobe nodule. E) Bilateral basal mosaic attenuation with interlobular septal thickening. F) Bilateral basal mosaic attenuation with subpleural changes.

CT findings and the patient feeling largely asymptomatic, no further investigations or management was done except a follow up appointment and a third CT scan.

His third CT scan that was ordered for 8 months after the second showed multiple new bilateral centrilobular nodules, with some bilateral basal mosaic attenuation (Figure 1). The previous noted left sided nodules were still present. He reported no new symptoms, some phlegm, and a persistent dyspnea. There was still no hemoptysis and no constitutional symptoms. At this point, the main categories for differentials were between infective and inflammatory/autoimmune.

For each of these visits to the respiratory clinic, he examines well with no acute respiratory distress, no signs of cutaneous vasculitis lesions, no signs of systemic lupus erythematosus, no signs of scleroderma or systemic sclerosis, no stigmata of rheumatoid arthritis and no signs of mixed connective tissue diseases. His heart sounds were dual with no murmur with a loud P2 sound. There was no splitting of his second heart sound. There were no signs of cor pulmonale. His chest yielded mild bibasilar fine crackles, with otherwise normal air entry.

A sputum microscopy, culture, and sensitivity (MCS) were sent which showed growth of Staphylococcus aureus, Escherichia coli and Klebsiella pneumoniae. Further investigations revealed a normal full blood count, raised erythrocyte sedimentation rate (ESR) of 17, normal angiotensin converting enzyme (ACE) at 115, low rheumatoid factor (RF) of less than 20, high levels of atypical ANCA at 1:640 titer, negative titer for cytoplasmic-ANCA (c-ANCA) and perinuclear-ANCA (p-ANCA), presence of high Myeloperoxidase-ANCA (MPO-ANCA) at >740, and a normal level of leukocyte proteinase 3 (PR3-ANCA) at 2. A down trending average eGFR over a year from an initial 68mL/min/1.73m2 to 38mL/min/1.73m2. A random urine protein level was high at 130 (<100). His urine albumin-to-creatinine ratio (ACR) was high at 1.6 (<1) and the protein-to-creatinine ratio (PCR) was high at 21 (<15). A repeat full lung function test also showed similar results to that of the first.

A discussion between a few physicians agreed that a kidney biopsy was more suitable and less risky as opposed to a CT guided lung biopsy of his nodules due to the location and size. His kidney biopsy involved examination of multiple slides consisting of glomeruli, vessels, tubules and interstitium. Total of 43 glomeruli were attained, 10% of which were globally sclerosed and most of these were clustered within a discrete cortical scar. The non-sclerosed glomeruli otherwise showed a normal appearance. No glomerular hypercellularity, tuft necrosis, crescent formation or areas of segmental sclerosis were seen. The arterial vessels showed variable fibrointimal thickening, focal arteriolar hyalinosis and some vessels showed severe narrowing. No inflammation of vessels and no features of thrombotic microangiopathy were seen. Cortical tubular atrophy and interstitial fibrosis was present in approximately 20% of the cortex, other areas showed focal atrophy and fibrosis.

With the diagnostic criteria outlined by 2022 American College of Rheumatology (ACR)/European Alliance of Associations for Rheumatology (EULAR) classification criteria for MPA, his largely asymptomatic clinical presentation, workup findings, sub-nephrotic urinalysis, and histopathological evidence, he was given the diagnosis of MPA [5]. This is further elaborated on in the next section.

He was commenced on a remission-maintenance therapy for MPA due to the absence of pathological symptoms suggestive of active disease, which included oral methotrexate 2.5mg/week, with an increase of 5mg per week to be kept in view. In addition, oral prednisone was also commenced at a dosage of 10mg per day. He was followed up closely at a monthly frequency going forward for review of clinical status and repeat measures of ANCA, ESR, CRP and folic acid levels.

## DISCUSSION

This reported case of MPA, is one of an AAV that is not largely symptomatic but rather likely one within an indolent phase. He possessed mildly increased inflammatory marker, ESR, while his MPO-ANCA levels remained significantly high with a high atypical ANCA titer. This lack of correspondence between inflammatory markers and MPO-ANCA levels have been observed in the past when seen in patients with indolent MPA [6]. The features of the renal biopsy although not showing any active glomerulonephritis, has shown glomerulosclerosis, tubular atrophy, interstitial fibrosis, and tubular atrophy which are more commonly in line with MPA with positive MPO-ANCA. Furthermore, kidney injury secondary to glomerulonephritis in MPA typically show features in line with chronic injury when diagnosed as opposed to active glomerulonephritis [7-9]. This would be in keeping of his down trending eGFR suggesting chronic kidney damage and giving rise to his sub-nephrotic range of proteinuria. When using the 2022 ACR/EULAR criteria (Table 1), this patient meets the criteria of a high positive MPO-ANCA and early fibrotic interstitial changes in his last 2 CT scans showing mosaic attenuation,

**Table 1**. Diagnostic criteria for microscopic polyangiitis, adapted from 2022 American College of Rheumatology/European Alliance of Associations for Rheumatology Classification Criteria for Microscopic Polyangiitis [5].

| 2022 American College of Rheumatology/European Alliance of Associations for Rheumatology Classification Criteria for Microscopic Polyangiitis. Arthritis & Rheumatology | |
|---|---|
| **Key Considerations when applying criteria:**<br>• *Alternative vasculitis mimicking diseases needs to first be excluded*<br>• *To be used to classify a patient as having microscopic polyangiitis when a diagnosis of small-or medium-vessel vasculitis has been made*<br>*When done to sum up the total score of applicable items, a summative score of ⩾5 is needed for classification of Microscopic Polyangiitis* | |
| **Clinical Criteria** | |
| Nasal involvement: bloody discharge, ulcers, crusting, congestion, blockage, or septal defect/perforation | −3 |
| **Laboratory, Imaging and Biopsy Criteria** | |
| Positive test for perinuclear antineutrophil cytoplastic antibodies (pANCA) or antimyeloperoxidase (anti-MPO) antibodies ANCA positive | +6 |
| Fibrosis or interstitial lung disease on chest imaging | +3 |
| Pauci-immune glomerulonephritis on biopsy | +3 |
| Positive test for cytoplasmic antineutrophil cytoplasmic antibodies (cANCA) or antiproteinase 3 (anti-PR3) antibodies | −1 |
| Blood eosinophil count ⩾ 1 x $10^9$/liter | −4 |

**Table 2.** Characteristics of different types of vasculitis [12].

| | Age | Affected vessels | Pathology |
|---|---|---|---|
| GPA | More common with increasing age | Small vessels | Necrotizing granulomatous inflammation |
| MPA | More common with increasing age | Small vessels | Necrotizing vasculitis with few or no immune deposits and no granulomata |
| EGPA | More common with increasing age | Small to medium vessels | Eosinophil-rich and necrotizing granulomatous inflammation |

**Table 3.** ANCA specificity and frequency of different types of vasculitis [13,14].

| | ANCA specificity | Frequency |
|---|---|---|
| GPA | PR3-ANCA | 75% |
| MPA | PR3-ANCA | 20-30% |
| | MPO-ANCA | 60% |
| | Atypical ANCA | 5-10% |
| EGPA | PR3/cANCA | 5% |
| | MPO | 40% |

**Table 4.** Incidence of microscopic polyangiitis around the world, adapted from Watts et al. [12].

| Region | Approximate incidence per 100,000 persons aged >50 years old |
|---|---|
| North America | 18 |
| South America | 18 |
| Canada | 8 |
| Peru | 8 |
| Argentina | 12 |
| Australia | 7 |
| Norway | 10 |
| Sweden | 10 |
| Germany | 13 |
| United Kingdom | 13 |
| Lithuania | 3 |
| Spain | 5 |
| Greece | 10 |
| Turkey | 3 |
| Japan | 20 |
| Kuwait | 19 |

subpleural and interstitial thickening – giving him a total of 9 points. Hence, a combination of these alongside the clinical history, progression and investigations culminated with the final diagnosis of MPA.

Vasculitides is an umbrella term used to describe a group of 3 conditions typified by their ability to cause vessel inflammation with or without necrosis [2,10]. Each of their disease characteristics, typical age of presentation and underlying pathology are listed in Table 2. Specificity of these ANCA auto antibodies can be classified into two major types. These are; ANCA–MPO (ANCA - Myeloperoxidase) and ANCA-PR3 (ANCA - Leukocyte proteinase 3) [1]. As shown in Table 3, if the disease is genetically driven by a specific phenotype, it influences the ANCA specificity. Therefore, in a vasculitis screen, ANCA PR3 and MPO are both assessed. It not only aids in the diagnosis of vasculitis but carries prognostic purpose in that studies have shown that ANCA-PR3 positive patients have a lower survival rate compared to others [5,11]. The most common AAV phenotypes are GPA and MPA [1,2,10].

MPA has an incidence of about 0.5-24.0 cases per million person-years [12]. The prevalence of MPA varies greatly depending on geographical location, however a multinational review article suggests that it is within 9.0 to 94.0 cases per million people [14]. MPA occurs typically in patients from ages 55 to 75, with no sexual preference [3,5]. Table 4 shows the rough distribution of MPA and the approximate incidences since the 2000s.

MPA often manifests with a combination of constitutional symptoms and system specific manifestations. Constitutional symptoms may include fever, malaise, myalgia, coryza, fatigue and unintentional weight loss [2]. Renal disease occurs in 80% to 100% of cases through one or more of the following: microscopic hematuria, foamy urine secondary to proteinuria, rising serum creatinine and falling eGFR [3]. The respiratory symptoms occur in 55% to 80% and may manifest as hemoptysis, progressive shortness of breath and/or persistent cough. Cutaneous symptoms are present in 30% to 60% of cases in forms of a purpuric rash accompanied with systemic symptoms such as fever, flu, and joint pains. Sores and ulcers that may become necrotic may also be present. Nervous system symptoms are uncommon at 30% of all cases which may present as paresthesia and/or weakness in keeping with mononeuritis multiplex or other peripheral neuropathy [1,3,15].

Physical examination often reveals non-blanching rashes or palpable purpura but may depend on which system/s are involved. Hence, skin, respiratory, cardiovascular, gastrointestinal, and neurological examination should be carried out. abdominal pain, mononeuritis multiplex manifesting as weakness, stiff and tender joints. Other findings on examination may often include fine crackles in the lungs, abdominal pain, weakness representing mononeuritis multiplex, and tender and/or swollen joints or muscle groups. Other uncommon findings may include testicular pain and decrease visual acuity.

The workup of MPA involves bloodwork which includes baseline bloods and inflammatory markers – FBC, CRP, ESR. These often demonstrate leukocytosis along with a normocytic anemia and a raised ESR [2]. Autoimmune markers for ANCA specificity should also be included – ANCA, ENA, Anti-CCP, RF and complement levels. Given its high occurrence in MPA, testing of renal function should also be done – electrolytes, urea, and creatinine (EUC), urinalysis, urine microscopy, ACR and PCR. Decreased eGFR, elevated creatinine levels, proteinuria, hematuria, red blood cell casts, and dysmorphic red blood cells may be found in these investigations [15].

Full lung function testing in MPA, although limited, could often yield a restrictive type pattern with reduced diffusion capacity of the lung – low diffusing capacity of the lung for carbon monoxide (DLCO). Interestingly, evidence is present to suggest that interstitial lung disease (ILD) changes may precede that of systemic MPA manifestations [16,17]. HRCT done often shows areas of ground glass opacities,

bronchiectasis changes, reticulation, bronchial and septal wall thickening [3,16].

The diagnosis of MPA previously involved a combination of clinical findings, laboratory tests, imaging studies and histopathological findings. Fortunately, with the introduction of the endorsed 2022 ACR/EULAR criteria which carries a specificity of 92.5% and a sensitivity of 82.4%, it added additional clinical practice caveats for the diagnosis of MPA [5]. The distinction of MPA from other forms of AAV, polyarteritis nodosa, anti-glomerular basement membrane (Anti-GBM) disease, infection, and malignancy, is crucial [1,3,10]. A score of 5 or more is required by the 2022 ACR/EULAR criteria to diagnose MPA.

The treatment of MPA is typically approached by first induction of remission followed by maintenance of remission. The pharmaceutical agents used in induction of remission are typically, cyclophosphamide along with course of oral prednisone, these agents are slowly tapered down after. The maintenance of remission phase is reached when symptom relief is reached, where cyclophosphamide is typically switched to azathioprine or methotrexate [3]. Intravenous immunoglobulin has been used in treatment of refractory symptomatic MPA [3,15].

## CONCLUSION

In conclusion, we discuss a unique case of an indolent MPA in a 75-year-old male who presented with no overt symptoms of vasculitis after an incidental finding of pulmonary nodules, apart from high levels of atypical ANCA and MPO-ANCA and findings on a renal biopsy in line with that of a chronic injury rather than that of active glomerulonephritis. A brief review of the diagnostic workup of this thus highlights the vast pathologies associated with MPA and how further research is required to aid future ease of diagnosis and treatment.

### Ethics Approval and Consent to Participate

Full and written informed consent was obtained from the next of kin of this patient. This case report was conducted and written in accordance with the Townsville Hospital and Health Service Human Research Ethics Committee (EX/2023/QTHS/101998) (Approved and endorsed on the 18th September 2023).

### Consent for Publication

The next of kin of this patient and medical personnel involved in the care of the patient has given a full and written consent in line for the publication of this case report which would include the use of clinical details, investigation findings, and various discussions which have occurred.

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### Disclosure

The authors declare that they have no conflicts of interest.

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