DIGITAL ULCERATION IN A PATIENT WITH INTERSTITIAL LUNG DISEASE: AN UNUSUAL CASE OF MICROSCOPIC POLYANGIITIS

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ABSTRACT

OBJECTIVES

Microscopic polyangiitis (MPA) is part of the associated vasculitis family of the neutrophil cytoplasmic antibody (ANCA). MPA can be distinguished by its positivity for antibodies against myeloperoxidase (MPO-ANCA). The condition can involve any organ of the body, particularly the lungs, kidneys, and skin. This case highlights an atypical case of MPA in which a patient had interstitial lung disease (ILD) and later developed a vasculitic skin lesion without renal involvement. A 65-year-old female already diagnosed with ILD was evaluated for digital ulcers associated with bilateral pins and needle sensation in both upper and lower limbs. Examination revealed lesions on the index and middle finger of the left hand. The MPO-ANCA antibody test was positive, and a diagnosis of MPA was made based on a skin lesion biopsy. There was subsequent initiation of combination therapy consisting of azathioprine, hydroxychloroquine, prednisolone, and nifedipine. The patient was instructed for close follow-up. This case report highlights the importance of considering an underlying vasculitis in patients with ILD and emphasizes the significance of a thorough diagnostic evaluation and multidisciplinary management. This case also highlights that patients with interstitial lung diseases should be evaluated for secondary causes, and early treatment of the exact causes can prevent the late sequelae of the disease, such as skin manifestations in this patient.

KEYWORDS: *Microscopic Polyangiitis, Antineutrophil Cytoplasmic Antibodies, p-ANCA, ILD*

INTRODUCTION

ANCA-associated vasculitides (AAVs) represent a subset of vascular pathologies primarily affecting small blood vessels. Microscopic polyangiitis (MPA) is characterized by antineutrophil cytoplasmic antibodies (ANCAs) with anti-myeloperoxidase (MPO) specificity.[1] The estimated prevalence of this syndrome ranges from 3 to 10 cases per million population.[2] There is an increased incidence rate correlated with advanced age. This correlation suggests a potential link between age-related factors and the development of MPA.[3] MPA often presents musculoskeletal and cutaneous features. The kidneys and lungs are the two most affected organs in MPA. Renal involvement often manifests as rapidly progressive glomerulonephritis, characterized by hematuria, proteinuria, and declining kidney function. Some patients may experience slowly progressing kidney injury leading to end-stage renal disease without extrarenal manifestations. Pulmonary involvement has been observed in 25-55% of patients.[4,5] High-resolution computed tomographic (HRCT) scans often reveal characteristic findings, such as ground-glass opacities and reticular shadows.[6] Patients with MPA often present with erythematous macules as the first cutaneous manifestation. A biopsy of the lesions reveals small vessels with neutrophilic infiltration indicative of leukocytoclastic vasculitis.[7] Given its potential for multi-system involvement, a multidisciplinary approach is necessary for accurate diagnosis and tailored management of MPA. Interstitial lung disease (ILD) is now known to be a significant, albeit uncommon, clinical symptom of MPA. The prevalence of ILD in patients with MPA ranges from 27% - 45%, more commonly seen in men 65 years of age.[8] This case report aims to highlight the temporal presentation of MPA in a patient already diagnosed with ILD. The patient showed no renal symptoms but pulmonary and cutaneous manifestations.

CASE PRESENTATION:

A 65-year-old female patient diagnosed with ILD with a history of frequent hospitalization for exertional dyspnea was evaluated for the sudden onset of digital ulcerations of the left hand. The condition was associated with a sensation of bilateral pins and needles in both upper and lower limbs. The patient's ILD was diagnosed six months back when she was first evaluated for dry cough and exertional dyspnea. Pulmonary function tests at that time showed a restrictive pattern, and HRCT showed bilateral ground

glass opacities. (Figure 1)

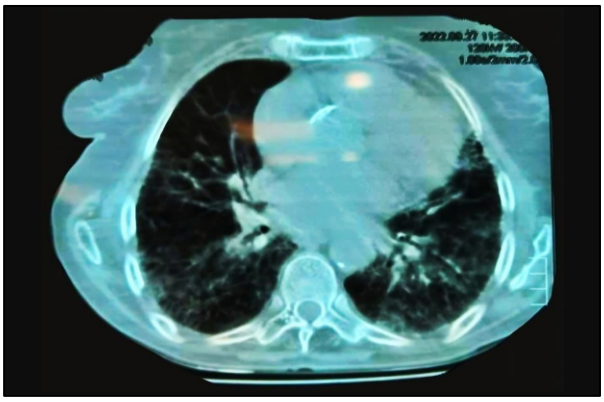

Figure 1: High-resolution computed tomographic scan showing classical bilateral ground glass opacities

Echocardiography was unremarkable, and baseline laboratory investigations were normal. The patient was prescribed oral prednisolone 30mg daily for ILD, but her condition was not improving. She was reluctant to the additional immunosuppressive therapy, which led to frequent hospitalization for respiratory distress, and she received symptomatic treatment during each hospitalization. The patient denied further workup due to financial constraints and was evaluated in the clinic for digital ulceration that developed over the last 20 days. It was associated with pins and needle sensation in both the upper and lower limbs and discoloration of the digits. No color changes were noted in response to cold. On further inquiry, she does not have joint pain, rash, heart problem, or skin tightness. The patient had a temperature of 98.4 ^{0}F, blood pressure of 130/70 mm Hg, pulse rate of 86 beats per minute, and respiratory rate of 21 breaths per minute. Clinical examination was unremarkable except for bilateral coarse crepitations on chest auscultation and ulceration of the left hand's distal phalanges of the 2nd and 3rd fingers, as shown in Figure 2.

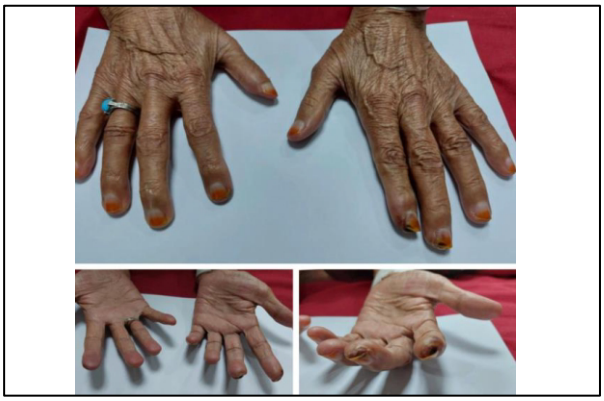

Figure 2: Shows Ulceration of the Distal Phalanges of the 3rd Fingers of the Left Hand

Initial laboratory investigations of the patient revealed an increased white blood cell count and raised erythrocyte sedimentation rate (ESR), as shown in Table.1

Table 1: Initial Laboratory Investigations

Laboratory Test	Result	Reference
Hemoglobin	12.2 g/dL	11-16
Total leukocyte count	1400 cell/uL	5000-1000
Platelet count	324,000 cells/uL	150-400 ×109
ESR	140 mm/1hour	Male: 0-15 Female: 0-20
Serum Creatinine	0.74 mg/dl	0.42-1.06
Blood Urea	45.4 mg/dl	10-50
Alkaline phosphatase	133 U/L	<150
Alanine aminotransferase	27.7 U/L	10-50
Total bilirubin	0.28 mg/dl	01-1.0
Prothrombin time	12 sec	11-15
Activated partial thromboplastin time	30 sec	25-40
INR	1.2	1.0
ANA	Negative	Negative
MPO-ANCA	100 AU	<5
PR3-ANCA	<0.1 AU	<5
Urine R/E		
Pus cells	4-6/HPF	0-5
Protein	NIL	6-7.8
RBCs	NIL	Male: 4.3-5.9 million/mm3 Female: 3.3-5.5 million/mm3

ESR: erythrocyte sedimentation rate; INR: international normalized ratio; ANA: Antinuclear Antibody; RBCs: red blood cells; cells/uL: cells per microliter; g/dL: gram per deciliter; cells/L: cells per liter; mm/h: Millimeters per hour; mg/dl: milligrams per deciliter; U/L: Units per liter; HPF: Hematopoietic-promoting factor; million/mm3: million / cubic millimeter. Carotid Doppler ultrasound of both upper limbs was performed to rule out vascular pathology. The results of the ultrasound were unremarkable. Negative ANA, negative blood cultures, and normal echocardiography ruled out systemic lupus erythematosus and infective endocarditis. A diagnosis of vasculitis was suspected based on raised ESR, background ILD, vasculitic skin lesion, and positive MPO-ANCA. The diagnosis was confirmed based on a biopsy of the ulcerated skin of the digits that showed leukocytoclastic angiitis with neutrophilic infiltrate in the capillaries of the dermis. The patient was counseled about her condition and was prescribed oral azathioprine 50mg BD, oral Co-amoxiclav 625 mg BD for seven days, oral hydroxychloroquine 200mg BD, oral prednisolone 15 mg TDS, and oral nifedipine 10mg BD. She was instructed to follow up after four weeks with a repeat complete blood picture, ESR, urine R/E, and ANCA

level. At four weeks of follow-up, her paresthesia and dyspnea showed improvement, though the skin lesions were present, and her MPO ANCA level was 60 AU. She was continued on the same treatment. However, her steroid dose was reduced to 30 mg daily.

DISCUSSION

Microscopic polyangiitis (MPA) is an idiopathic autoimmune disease primarily affecting small blood vessels. It is diagnosed using MPO-ANCA, although ANCA is only observed in 50-75% of MPA patients.MPA has also been shown to be associated with proteinase 3-ANCA (PR3-ANCA). Both MPO-ANCA and PR3-ANCA target parts of neutrophils, leading to neutrophil activation and subsequent release of inflammatory mediators, resulting in a cascade of endothelial cell damage. The disruption to vessel wall integrity can manifest as conditions such as crescentic glomerulonephritis in the kidneys or pulmonary capillaries in the lungs.[2,9] While renal involvement is the most common manifestation, occurring in over 80% of MPA cases, pulmonary and cutaneous manifestations are also commonly seen. Biopsies of affected organs reveal fibrinoid degeneration, neutrophil infiltration, and erythrocyte extravasation. Microscopic polyangiitis is believed to be a combination of environmental triggers and genetic factors. Among some genetic markers being researched, human leukocyte antigen (HLA) alleles may also play a role in developing susceptibility to ANCA-associated vasculitis like microscopic polyangiitis.[10] The rise in serum ANCA profiles in clinical practice has increased to MPA reports over the past 20 years.[9] Recent studies have suggested that MPO-ANCA may be connected to both the onset and progression of MPA, a condition characterized by necrotizing small-vessel vasculitis and no deposition of immune complexes at the affected site. Although ongoing research is investigating these possible associations, it is essential to emphasize that the pathophysiology of microscopic polyangiitis is complex, and the exact mechanisms influencing disease pathogenesis are still unknown.[11] MPA was previously described as a kidney-lung syndrome; however, in recent years, new manifestations, such as interstitial lung disease (ILD) and diffuse alveolar hemorrhage, have been observed. A pathological pattern of Usual Interstitial Pneumonia - ILD is often seen in CT imaging among patients with MPA ILD. Despite this, the prevalence of this type of lung disease among patients with MPA remains low. ANCA antibodies are seen at a rate of 8% - 36% in patients with Idiopathic Pulmonary Fibrosis (IPF).[12] However, ILD and a positive ANCA profile cannot confirm ANCA-associated vasculitis (AAV). Other clinical criteria must be met to diagnose a patient with an MPA. An updated categorization criteria for AAV (the 2021 ACR/EULAR criteria) was proposed by The European Alliance of Associations for Rheumatology (EULAR) and The American College of Rheumatology (ACR). The 2021 classification criteria for MPA are shown in Table 2. According to the guidelines, a patient score >5 indicates a positive diagnosis for MPA. A total score of more than five can classify MPA.[13] The patient exhibited a positive MPO-ANCA and ILD on imaging, qualifying as a positive MPA test.

Table 2: 2021 ACR/EULAR Classification Criteria for MPA 14

Predictor Variables	
pANCA- or anti-MPO ANCA-positive	+6
Pauci-immune glomerulonephritis	+3
Fibrosis or interstitial lung disease on chest imaging	+3
Serum eosinophil count => 1x 10^9/L	-4
Nasal bloody discharge, ulcers, crusting or sinonasal congestion	-3
cANCA- or anti-PR3 ANCA-positive	-1

In research published by Wurmann et al., clinical manifestations such as peripheral neuropathy, arthritis, fever, and skin involvement were suspected to be possible vasculitis. Only later were lung associations observed as essential clinical symptoms of MPA.[15] Another study by Arulkumaran et al. on 510 patients revealed that MPO-ANCA-positive MPA had a 2.7% association with ILD.[8] This case of MPA exhibits a distinct and atypical presentation characterized by prominent cutaneous involvement as the primary presenting symptom. The patient initially presented with a digital ulcer on the left hand, which raised suspicion of underlying vasculitis activity affecting the small vessels in the skin. The ulcer demonstrated features consistent with vasculitis, including erythema, necrosis, and impaired wound healing. The presence of a digital ulcer as the initial sign of the disease is extremely rare, further highlighting the novelty of this case. In addition to the cutaneous involvement, the patient also exhibited sensory abnormalities in the extremities, indicating peripheral neuropathy. The sensory disturbances in this case, such as paresthesia, numbness, and tingling sensations, suggest nerve damage due to vasculitic involvement. Moreover, concurrent respiratory symptoms and ILD were identified in this patient. Interstitial lung disease adds another layer of complexity to the presentation. Interstitial pneumonia in MPA can lead to lung fibrosis, resulting in impaired lung function and potentially significant morbidity. The combination of these diverse clinical features, including the digital ulcer, peripheral neuropathy, and ILD, in the absence of other primary symptoms (such as renal involvement) typically associated with MPA, makes this case highly distinctive and unusual. Such atypical presentations can pose

challenges in early diagnosis and management, as they may be initially misinterpreted as other conditions. There are no particular therapy recommendations for MPA-ILD patients. They are currently managed similarly to those with MPA without ILD manifestations. Further studies should be conducted to ascertain the prognosis of MPA-ILD patients treated with standard recommendations and whether they would benefit from supplemental medications.[16]

CONCLUSIONS

This unique case highlights the need to consider MPA even when clinical signs are atypical. Lung involvement with skin manifestations warrants a vasculitis workup; early immunosuppressive therapy is crucial for preventing late skin manifestations. Further research is necessary to understand MPA's diverse clinical presentations and prognostic implications.

CONFLICT OF INTEREST: None

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REFERENCES

1. Kallenberg CGM, Heeringa P, Stegeman CA. Mechanisms of Disease: pathogenesis and treatment of ANCA-associated vasculitides. Nat Clin Pract Rheumatol [Internet]. 2006;2(12):661–70.
2. Gu Y, Ting, Peng M, Shi J. Juhong. Medical Sciences Journal [Internet]. 2022;37(4):293–302.
3. Saraya T, Ogawa Y, Nakamoto K, Fujiwara M, Ishii H. Pulmonary involvement in microscopic polyangiitis: Computed tomography findings in 55 patients with analysis of risk factors for recurrence. Cureus [Internet]. 2022;
4. Chung SA, Seo P. Microscopic polyangiitis. Rheum Dis Clin North Am [Internet]. 2010 [cited 2024 Jun 3];36(3):545–58.
5. Uysal C, Yilmaz T, Kocyigit H, Akgun H, Sipahioglu MH. An unusual form of kidney injury without glomerulonephritis in microscopic polyangiitis: a case report. BMC Nephrol [Internet]. 2023;24(1).
6. Guillevin L, Durand-Gasselin B, Cevallos R, Gayraud M, Lhote F, Callard P, et al. Microscopic polyangiitis: clinical and laboratory findings in eighty-five patients. Arthritis Rheum [Internet]. 1999;42(3):421–30.
7. Adu D, Howie AJ, Scott DG, Bacon PA, McGonigle RJ, Micheal J. Polyarteritis and the kidney. Q J Med. 1987;62(239):221–37.
8. Arulkumaran N, Periselneris N, Gaskin G, Strickland N, Ind PW, Pusey CD, et al. Interstitial lung disease and ANCA-associated vasculitis: a retrospective observational cohort study. Rheumatology (Oxford) [Internet]. 2011;50(11):2035–43.
9. Chen M, Kallenberg CG. The pathogenesis of ANCA-associated vasculitis. Immunological Reviews [Internet]. 2010;233(1):158–71.
10. Wolfe F. Sleep problems and risk of fibromyalgia—untenable conclusions: Comment on the article by Mork et al. Arthritis Rheum [Internet]. 2012;64(5):1692–3.
11. Jennette JC, Falk RJ, Bacon PA, Basu N, Cid MC, Ferrario F, et al. 2012 revised international Chapel Hill consensus conference nomenclature of vasculitides. Arthritis Rheum [Internet]. 2013;65(1):1–11.
12. Nozu T, Kondo M, Suzuki K, Tamaoki J, Nagai A. A comparison of the clinical features of ANCA-positive and ANCA-negative idiopathic pulmonary fibrosis patients. Respiration [Internet]. 2009;77(4):407–15.
13. Pyo JY, Lee LE, Park Y-B, Lee S-W. Comparison of the 2022 ACR/EULAR classification criteria for antineutrophil cytoplasmic antibody-associated vasculitis with previous criteria. Yonsei Med J [Internet]. 2023;64(1):11.
14. Chung SA, Langford CA, Maz M, Abril A, Gorelik M, Guyatt G, et al. 2021 American College of Rheumatology/Vasculitis Foundation guideline for the management of antineutrophil cytoplasmic antibody–associated vasculitis. Arthritis Care Res (Hoboken) [Internet]. 2021;73(8):1088–105. Available from: https://assets.contentstack.io/v3/assets/bltee37abb6b278ab2c/blt9e4b7f8c646447ec/6331de84763d011cd3e9310e/anca-associated-vasculitis-guideline-2021.pdf
15. Wurmann P, Sabugo F, Elgueta F, Mac-Namara M, Vergara K, Vargas D, et al. Interstitial lung disease and microscopic polyangiitis in chilean patients. Sarcoidosis Vasc Diffuse Lung Dis [Internet]. 2020;37(1):37–42.
16. Yates M, Watts RA, Bajema IM, Cid MC, Crestani B, Hauser T, et al. EULAR/ERA-EDTA recommendations for the management of ANCA-associated vasculitis. Ann Rheum Dis [Internet]. 2016;75(9):1583–94.

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