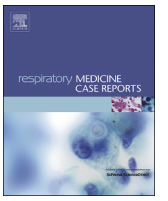
Respiratory Medicine Case Reports 52 (2024) 102122

Contents lists available at ScienceDirect

Respiratory Medicine Case Reports

journal homepage: www.elsevier.com/locate/rmcr



Case Report

Microscopic polyangiitis presenting as idiopathic pulmonary fibrosis

Brittany Duchene

Northeastern Vermont Regional Hospital, 1315 Hospital Drive, St. Johnsbury, VT, 05819, USA

ARTICLE INFO

Handling Editor: DR AC Amit Chopra

Keywords:
Microscopic polyangiitis
Idiopathic pulmonary fibrosis
Interstitial lung disease
ANCA-Associated vasculitis
Diffuse alveolar hemorrhage

ABSTRACT

The most detectable form of pulmonary fibrosis in MPA (microscopic polyangiitis) is UIP (usual interstitial pneumonia), occurring in 48 % of MPA patients with pulmonary fibrosis. In some cases, ILD (interstitial lung disease) is the initial clinical manifestation of MPA (22 % of cases). Here, we describe a patient diagnosed with IPF (idiopathic pulmonary fibrosis) who later developed pulmonary infiltrates on CT and hemoptysis, found to have diffuse alveolar hemorrhage on bronchoscopy and ultimately was diagnosed with MPA. There are no guidelines recommending routine screening of vasculitis in cases of suspected IPF, which may result in more misdiagnoses of vasculitides.

1. Introduction

Pulmonary fibrosis can present as the first clinical manifestation of vasculitis in 22 % of patients [1]. In fact, at the time of antineutrophil cytoplasmic antibodies (ANCA)-associated vasculitis diagnosis, some form of ILD is already detectable 66 % of the time. In patients with MPO (myeloperoxidase) positive vasculitis, UIP is the most common ILD pattern, occurring 48 % of the time [1]. UIP pattern fibrosis on CT imaging is also the pattern seen in IPF. The current ATS (American Thoracic Society) practice guidelines for diagnosis of IPF recommend using serological testing to exclude connective tissue diseases as potential causes of ILD, however there was not consensus on which tests to perform. That being said, there was consensus to routinely test for C-reactive peptide, erythrocyte sedimentation rate, antinuclear antibodies, rheumatoid factor, myositis panel, and anti-cyclic citrullinated peptide with a recommendation for other testing being performed on a case by case basis, but with no recommendation for routine ANCA testing [2].

2. Case presentation

A 65 year old man with a history of vitiligo and a former 21 pack year smoking history was referred to pulmonology clinic in October 2021 after a chest CT detected possible ILD in the setting of small volume hemoptysis, which was self-resolved. His chest CT was consistent with probable UIP (Fig. 1). He underwent serological testing for possible connective tissue diseases, which were unrevealing (Table 1). Given the probable UIP pattern of fibrosis, lack of other smoking related pulmonary findings, family history of pulmonary fibrosis (brother diagnosed with IPF) and the non-revealing connective tissue disease screening, he was given a diagnosis of idiopathic pulmonary fibrosis and started on nintedanib. His disease remained stable with no worsening of spirometry and no radiologic progression for 2.5 years (spirometry trends in Table 2).

In May 2024, he presented to the emergency department with coughing and scant hemoptysis, which was diagnosed as pneumonia based on a chest Xray. On exam he had bilateral crackles midway up his lung fields, normal heart sounds, no rashes, however vitiligo skin changes present. Complete blood count found no leukocytosis, but there was macrocytic anemia present (which had been

E-mail address: brittanyduchene@gmail.com.

https://doi.org/10.1016/j.rmcr.2024.102122
Received 1 June 2024; Received in revised form 26 August 2024; Accepted 25 September 2024
Available online 27 September 2024

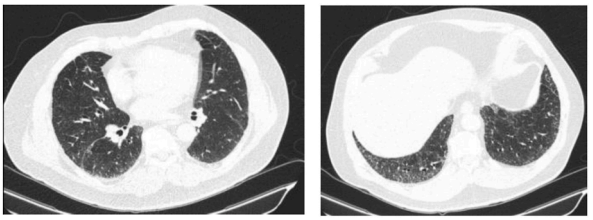


Fig. 1. Chest CT without contrast performed 9/15/21. Chest CT completed with thin cuts demonstrating peripheral and basilar reticular infiltrates with traction bronchiectasis, consistent with early usual interstitial pneumonia (UIP).

Table 1
Serological testing performed at time of initial pulmonary fibrosis diagnosis in 2021.

Serological Test	Result	Reference
Antinuclear antibody (titer)	1:160, homogenous, speckled	Negative
Cyclic Citrullinated Peptide (U/mL)	<2.5	<5.0
Rheumatoid Factor (IU/mL)	9.6	<12.0
Anti-double stranded DNA (IU/mL)	20.6	<30.0
Anti-SS-A Antibody (Units)	2.5	<20.0
Anti-SS-B Antibody (Units)	4.8	<20.0
Anti-Smith (Units)	5.5	<20.0
Scl 70 Antibodies, IgG (Units)	<0.2	<1.0
Anti-Jo-1 Antibody (Units)	<20.0	<20.0
Anti-PL-7 Antibody	Negative	Negative
Anti-EJ Antibody	Negative	Negative
Anti-OJ Antibody	Negative	Negative
Anti-SRP Antibody	Negative	Negative
Anti-Mi-2 Antibody	Negative	Negative
Anti-TIF-1gamma Antibody ((Units)	<20.0	<20.0
Anti-MDA5 Antibody (Units)	<20.0	<20.0
Anti-NXP2 Antibody (Units)	<20.0	<20.0
Anti-PM/Scl-100 Antibody (Units)	<20.0	<20.0
Anti-Ku Antibody	Negative	Negative
Anti-SSA 52kD Antibody (Units)	<20.0	<20.0
Anti-U1 RNP Antibody (Units)	<20.0	<20.0
Anti-U2 RNP Antibody	Negative	Negative
Anti-U3 RNP Antibody	Negative	Negative

Table 2
Spirometry testing trends since 2021. FEV1: forced expiratory volume in 1 second; FVC: forced vital capacity; LLN: lower limit of normal.

Date	FEV1/FVC	LLN	FEV1 (L)	%	LLN (L)	FVC (L)	%	LLN (L)
9/23/21	0.82	0.65	2.84	83	2.65	3.45	75	3.63
7/21/22	0.82	0.65	2.88	85	2.61	3.53	78	3.60
1/19/23	0.80	0.65	2.76	81	2.61	3.45	76	3.60
11/20/23	0.81	0.65	2.77	82	2.58	3.41	76	3.57

present previously). Coagulation panel was normal and a venous blood gas was as follows: pH 7.43, pvCO2 35, pvO2 42, venous saturation 79 %. On his complete metabolic panel, there was evidence of acute kidney injury with a creatinine of 1.4mg/dL (baseline 1.1mg/dL), BUN 26, and GFR of 55mL/min/1.73m^2. His urinalysis also found a large amount of blood present with 10–20 RBC/hpf. Pulmonary consulted and recommended a chest CT (Fig. 2) due to concern for a possible ILD flare and lack of history consistent with pneumonia. The chest CT did have significant ground glass opacities with underlying reticular infiltrates in the bilateral lower lobes,

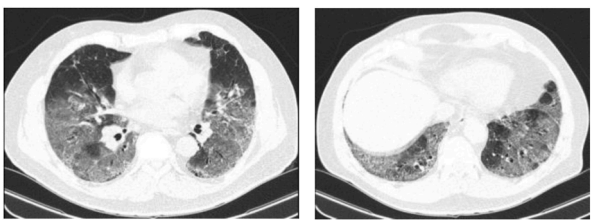


Fig. 2. Chest CT without contrast performed 5/6/24. Chest CT completed with thin cuts demonstrating extensive bilateral ground glass opacities involving the inferior portion of the bilateral upper lobes, right middle lobe, lingua and bilateral lower lobes with a background of pulmonary fibrosis.

Fig. 3. Bronchoalveolar lavage (BAL) performed 5/7/24. Subsequent saline aliquots of 60 cc performed. BAL return found progressive bleeding with subsequent aliquots diagnostic for diffuse alveolar hemorrhage. Aliquots labelled 1–3.

right middle lobes and lingula, again initially raising concerns for an ILD flare. A bronchoscopy was performed the following day, which unexpectedly found diffuse alveolar hemorrhage (Fig. 3). The patient required more oxygen support so was admitted to the ICU post-bronchoscopy due to high flow nasal cannula needs. Due to the diffuse alveolar hemorrhage diagnosis, further serologic testing was performed: anti-IgA 135 U/mL, cold agglutinin titer <2, p-ANCA positive, c-ANCA negative, proteinase 3 (PR3) <0.2 U, myeloperoxidase >8.0 U, glomerular basement membrane IgG <0.2 U, complement C1q component 12 mg/dL, complement C4 9 mg/dL and complement C4 function 40 U/mL. He was diagnosed with microscopic polyangiitis based on his laboratory findings, serological testing, clinical picture and bronchoscopy results. His nintedanib was held given the active bleeding. He was treated with pulse dose steroids (1 g per day for 3 days) followed by a high dose prednisone taper (and sulfamethoxazole-trimethoprim prophylaxis). On consultation with rheumatology as an inpatient, he was planned for initiation of rituximab. He dramatically improved with this and was able to be discharged home without any oxygen needs 8 days after initial presentation.

3. Discussion

Microscopic polyangiitis is an idiopathic systemic vasculitis. MPA is a small vessel vasculitis and is typically ANCA-associated [3]. It routinely can affect both the pulmonary and renal systems and is defined by necrotizing vasculitis of small vessels. MPA should be suspected in patients who present with constitutional symptoms, signs of glomerulonephritis, upper or lower respiratory tract involvement or multiple mononeuropathy. Serological ANCA testing increases the likelihood of MPA as 55–65 % of cases are associated with a positive test [4]. A negative ANCA test does not exclude the diagnosis, as at least 10 % of patients with clinical MPA may have negative serological studies. The diagnosis of MPA should be confirmed with a tissue diagnosis when possible. In settings of an extremely high probability of MPA, treatment can be initiated without tissue confirmation. Typically, the biopsy site is the skin or kidneys, whereas transbronchial biopsies are thought to be less helpful as the typical histopathological finding is

acute and chronic inflammation with pulmonary capillaritis [5]. There have been attempts to standardize the classification and diagnostic criteria for small vessel vasculitides, with the most common being the International Chapel Hill Consensus Conference nomenclature which provides disease definition but not a classification criteria [6]. The American College of Rheumatology/European Alliance of Associations for Rheumatology classification criteria for MPA does provide a criteria [7], however this is primarily used for research purposes.

When the pulmonary system is afflicted in MPA, the most likely manifestations are ILD and diffuse alveolar hemorrhage [9]. With the most common ILD pattern seen in MPA being UIP, often times when this is the first sign of MPA (as occurs in 22 % of patients [1]), it is misdiagnosed as IPF [8]. Up to 25 % of patients with MPA-ILD can progress to clinical MPA, thus monitoring for occult hematuria may be reasonable [9]. The official ATS/ERS/JRS/ALAT clinical practice guidelines do recommend serological testing in all patients with newly detected ILD who are clinically suspected of having IPF [4]. The purpose is to rule out connective tissue disease as the cause of the ILD. In all patients there is a recommendation for testing C-reactive protein, erythrocyte sedimentation rate, antinuclear

antibodies, rheumatoid factor, myositis panel and anti-cyclic citrullinated peptide. There is a recommendation for adding specific tests for scleroderma, Sjogrens and vasculitis if there is suspicion of these [4]. As discussed, ILD may be the first manifestation of vasculitis, which if misdiagnosed as IPF may lead to unnecessary anti-fibrotic therapy and delayed diagnosis and treatment of the true underlying issue. In fact, MPA patients with UIP patterned fibrosis can present with the fibrosis 6–108 months earlier than systemic MPA disease [10]. Being aware of the manifestation of ILD in vasculitides and screening of appropriate patients at ILD diagnosis onset is appropriate.

Here, we present a rare case of a patient who had held an IPF diagnosis for 2.5 years prior to presenting with hemoptysis and ground glass opacities on chest CT. Bronchoscopy revealed diffuse alveolar hemorrhage which prompted a vasculitis work up, at which point he was found to be anti-MPO ANCA positive. Based on available diagnostic criteria, he was diagnosed as having MPA. This is an example of a vasculitis misdiagnosed as IPF resulting in years of anti-fibrotic therapy (with associated side effects) and a delayed diagnosis of his underlying vasculitis. Anti-fibrotic medications would be indicated in MPA-ILD with clear signs of progression, however it is possible the prompt treatment of vasculitis may negate the need for this. As part of the IPF work up, including vasculitis screening in select patients may prevent this from occurring in the future.

4. Conclusion

In the initial work up of clinically suspected IPF, adding an ANCA screen to the other serologic tests in patients with a history of hemoptysis or renal insufficiency may prevent an IPF misdiagnosis and delayed vasculitis diagnosis. In pulmonary fibrosis patients who are found to have ANCA positivity and no systemic manifestations, routine urinalysis to assess for microscopic hematuria may lead to more prompt rheumatologic involvement and systemic treatment.

CRediT authorship contribution statement

Brittany Duchene: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Data curation, Conceptualization.

Declaration of competing interest

No known competing financial interests.

References

[1] A. Masiak, Z. Zdrojewski, R. Peksa, et al., The usefulness of histopathological examinations of non-renal biopsies in the diagnosis of granulomatosis with polyangiitis, Rheumatologia 55 (5) (2017) 230.
[2] A. Greco, A. De Virgilio, M.I. Rizzo, et al., Microscopic polyangiitis: advances in diagnostic and therapeutic approaches, Autoimmun. Rev. 14 (9) (2015) 837–844.
[3] C. Shao, R. Chen, H. Huang, Zhao Yang, et al., Microscopic polyangiitis initially presenting with idiopathic pulmonary fibrosis: a case report, Front. Med. 24 (10) (2023).
[4] G. Raghu, M. Remy-Jardin, J. Myers, et al., Diagnosis of idiopathic pulmonary fibrosis: an official ATS/ERS/JRS/ALAT clinical practice guideline, Am. Thorasis Soc. Doc. 198 (5) (2018) e44–e68.
[5] G.E. Thompson, U. Specks, Update on the management of respiratory manifestations of the antineutrophil cytoplasmic antibodies-associated vasculitides, Clin. Chest Med. 40 (3) (2019) 573–582.
[6] J.C. Jennette, Overview of the 2012 revised international Chapel Hill consensus conference nomenclature of vasculitides, Clin. Exp. Nephrol. 17 (5) (2013) 603–606.
[7] R. Suppiah, J.C. Robson, P.C. Grayson, et al., American College of rheumatology/European alliance of Associations for rheumatology classification criteria for microscopic polyangiitis, Annal. Rheumatol. Dis. 81 (3) (2022) 321–326 2022.
[8] A.R. Kitching, H.J. Anders, N. Basu, et al., ANCA-associated vasculitis, Nat. Rev. Dis. Prim. 6 (1) (2020) 71.
[9] Casares M. Fernandez, A. Gonzalez, M. Fielli, et al., Microscopic polyangiitis associated with pulmonary fibrosis, Clin. Rheumatol. 34 (7) (2014) 1273–1277.
[10] A. Manfredi, G. Cassone, R. Izzo, et al., Interstitial lung disease in microscopic polyangiitis and granulomatosis with polyangiitis: demographic, clinical, serological and radiological features of an Italian cohort from the Italian Society for Rheumatology, Clin. Exp. Rheumatol. (2023) 821–828.