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Case Report

An extraordinary pulmonary artery involvement in granulomatosis with polyangiitis

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ABSTRACT

Granulomatosis with polyangiitis (GPA) is an autoimmune mediated systemic disease and characterized by pauci-immune vasculitis mainly of small and medium vessels with typical necrotizing granulomatous lesions in the affected tissues. A 44 year old lady who was known to have GPA presented with unusual presentation of its category with extraordinary large vessels involvement including pulmonary arteries and her condition improved with immunosuppressive therapy. We reported this case, to improve the awareness about other overlapping categories of vessels vasculitis that may involve large vessels and main pulmonary arteries and to avoid misdiagnosing these patients with category of classical large vessels vasculitis.

Keywords: GPA, Pulmonary artery, Large vessels, Wegener's granulomatosis

INTRODUCTION

Vasculitides are uncommon disorders, in which vessels are affected by inflammatory cells and may lead to blood stream compromise or further complications. Generally, the vasculitis is classified based on the 2012 International Chapel Hill consensus conference on the nomenclature of systemic vasculitides (CHCC 2012) and categorized into large, medium, small and other vessels involvement categories. Among these, small vessel vasculitis category is subcategorized into antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) versus immune complex associated vasculitis. One of the AAV, GPA, formerly known as Wegener's granulomatosis, which is an autoimmune mediated systemic disease and characterized by pauci-immune vasculitis mainly of small and medium vessels with typical necrotizing granulomatous lesions in the affected tissues.[1-3] The common clinical presentations may involve most commonly otorhinolaryngologic symptoms as well as respiratory (upper and/or lower) airway, kidneys.[4,5] The respiratory involvement may include subglottic, tracheal stenosis pulmonary infiltrates, nodules, cavitation, alveolar capillaritis, pulmonary hemorrhage, hemoptysis, pleurisy.[4,5] Ozaki et al in a case series of 24 GPA patients having large vessels involvement, they found that most commonly affected vessel was the abdominal aorta (12 cases), thoracic aorta (6 cases), subclavian artery (4 cases) and internal carotid artery (4 cases).[6] In another case report, Clark et al reported one GPA patient with large vessels involvement in from of pulmonary artery stenosis.[7] The GPA diagnosis was established based on clinical assessment, serological tests and histological analysis, using a standardized criteria for example, American college of rheumatology research criteria for diagnosis of GPA. The GPA is treated based on different clinical presentations and disease extent using particular immunotherapy such as steroid, rituximab, cyclophosphamide.[8] This case report was published to

increase the awareness about rare GPA presentation like involvement of large vessels and main pulmonary arteries, to avoid misdiagnosing these patients with classical large vessels vasculitis category as per CHCC 2012 such as giant cell arteritis or Takayasu arteritis.

CASE REPORT

Our patient was a 44 year old lady who was known to have GPA, which was diagnosed in December 2016 based on hearing impairment, sinusitis, upper airway involvement, lung involvement, elevated C-ANCA and biopsy showing granulomatous inflammation from subglottic and nasopharyngeal areas in 2008. She also had recurrent subglottic stenosis since 2011 and underwent multiple surgical interventions. Also, she underwent tracheostomy insertion in 2015 secondary to recurrent stridor and was successfully de-cannulated in 2016. She was diagnosed with query tuberculosis on 2011, based on positive purified protein derivatives (PPD) with more than 20 mm induration, cervical and hilar lymphadenopathy, but there was neither documented AFB smears nor cultures. At that time, the lymph node biopsy showed necrotizing granuloma. And the patient was treated for active TB with anti-tuberculous medications for 1 year. She was had heart failure with reduced ejection fraction of 40-45% with impaired LV relaxation and mild to moderate global hypokinesia based on echo done in December 2016 and repeated ECHO a year and 3 years after showed normal ejection fraction.

Her relevant history of presenting illness related to the new presentation in November 2016, when she was admitted to hospital due to new persistent vomiting of food content with diffuse abdominal pain for the past 4 months and associated with weight loss, about 20 kg and loss of appetite. She also had night sweats, fatigue and lethargy. She also had progressive persistent dry cough and associated with shortness of breath (NYHA class 2-3) and was not aggravated or relieved by anything apart from physical activity. She denied any history of chest pain, orthopnea, paroxysmal nocturnal dyspnea, palpitation, smoking, wheezing/atopy symptoms, nor thromboembolic events. Also, there was no other findings in the systemic review such as history of constitutional symptoms, recent upper respiratory trat, genitourinary or gastrointestinal infection or any history suggestive of new connective tissue diseases (CTD) or vasculitis. She was not using any new mediations prescribed anywhere. And her family history was negative for CTD, vasculitis or respiratory illnesses. Also, she had negative travel history, contact with TB patient or social history. She was up to date on vaccinations.

Physical examination

On her physical examination, she looked anxious, but conscious and oriented to time, place and persons. She was afebrile, heart rate of 106 and blood pressure of 140/96 mmHg, respiratory rate of 20 per minute and oxygen saturation 98% on room air. She had strong proximal and distal pulses, with no bruits.

The ENT exam showed bilateral tender maxillary sinuses, and hearing impairment. No ophthalmological involvement. Her cardiovascular system exam showed that her JVP was not elevated, normal heart sound and no murmur or rub. Her respiratory exam showed bilateral vesicular breathing, no add sounds. Her abdominal exam was generally unremarkable and no lower limbs edema or lymphadenopathy. Her upper and lower limbs exam was unremarkable and no skin rash, purpura, nodules or ulcers. There were no findings of neurological deficits.

Laboratory investigations

The laboratory investigations requested in the current presentation are summarized in the following (Table 1).

Table 1: Laboratory investigations.

Tests	Results/comments
Hb: 103 g/l	Low
MCV: 84 fl	Normal
MCH: 30 pg	Normal
WBCs: 5.54×109 /l	Normal
Platelet: 390×109 /l	Normal
Urea: 2.5 mmol/l	Normal
Creatinine: 59 umol/l	Normal
Hepatic profile	Normal
CRP: 9.2 mg/l	Normal
ESR: 55 mm/hr	High
C-ANCA (PR3): 246.2 units	High, (146 units)
ANA, anti-GBM, RF, IgG-subclasses levels	Normal
Thrombophilia screen	Negative
Protein/creatinine ratio: 8.50 mg/mmol	Normal
Respiratory, urine and blood cultures	Negative
Respiratory viral multiplex	Negative
Acid fast bacilli culture ×3: negative	Negative
Aspergillus galactomannan: 0.08	Non-reactive
Fungitell: <31 pg/ml	Non-reactive
Viral screen including hepatitis, HIV, CMV and EBV	Unremarkable

Imaging

CT chest with contrast on December 2016 demonstrated a significant inflammatory process identified in the mediastinum surrounding the great vessels as well as significant narrowing of the left main stem bronchus as well as at least 40% narrowing of the right main pulmonary artery identified. No significant luminal stenosis however identified in the intra parenchymal pulmonary vessels.

These processes extending in the peri-bronchial distribution (Figure 1). CT chest with contrast on March 2017 demonstrated small consolidation involving the left upper lobe surrounded by ground glass halo likely represent fungal infection. CT paranasal sinuses without contrast on March 2017 demonstrated minimal mucosal disease of the anterior ethmoid air cells and maxillary sinuses. No evidence of acute sinusitis.

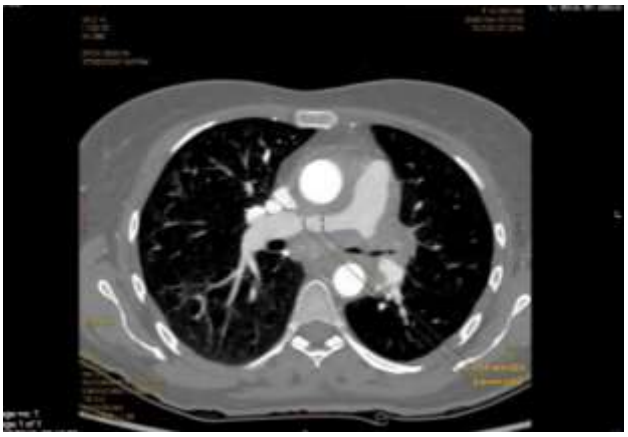

Figure 1: A CT chest with contrast showing a significant inflammatory process identified in the mediastinum surrounding the great vessels as well as significant narrowing of the left main stem bronchus as well as at least 40% narrowing of the right main pulmonary artery identified.

Hospital course during 1st admission

Flare of granulomatosis with polyangiitis

She received pulse steroid for 4 days as 500 mg IV methylprednisolone then tapering steroids and also, started on cyclophosphamide in December 2016 and received 6 consecutive doses (last dose was in May 2017) as well as bactrim prophylaxis.

Left upper lobe consolidation surrounded by ground-glass opacity

CT chest showed left upper lobe lesion surrounded by ground glass halo suggesting fungal infection. CT was done after a CXR revealed a new nodule in the left upper lobe in January 2017. While she was prepared to undergo CT-guided biopsy, CT revealed regression of the above-mentioned lesion from about 1 cm to 0.5 cm. Thus, biopsy was cancelled.

And as per infectious disease recommendations to repeat CT chest after 2-4 weeks and to consider biopsy or BAL if it was worsening. In addition, as fungal screen including *Fungitell* and *Aspergillus galactomannan* were non-reactive. The possibility of fungal infection was very unlikely, based on regression of the lesion (by 50%) on repeated imaging and indicating her response to prednisone, it had been agreed that the most likely lesion was related to her disease activity.

She was improving symptomatically and by imaging and was discharged home to be seen in the day medial unit and the outpatient clinics.

Hospital course during 2nd admission

In August 2017, the patient presented to rheumatology clinic with progressive facial, peri-orbital and neck swelling for last 2-3 months that was associated with shortness of breath of NYHA class 3 for the last one week.

Flare of granulomatosis with polyangiitis/extensive vascular thrombosis

She underwent a CT head-neck (ENT) w/contrast in early days of August 2017 and demonstrated significant involvement by granulomatosis with polyangiitis including diffuse infiltration of the aerodigestive tract, involvement of the nasal cavities and bilateral involvement of the skull base, no enhancing lesions in the imaged portions of the brain parenchyma; short segment thrombosis of the proximal cervical right internal jugular vein with poor flow in the right sigmoid venous sinus, secondary to the infiltrative disease at the skull base. There was also thrombosis of a short distal segment of the left internal jugular vein, left brachiocephalic vein and left subclavian vein at the venous confluence.

After that, she underwent a helical CT scan of the chest, and demonstrated mediastinum and pulmonary parenchyma: interval progression of the infiltrative soft tissue mass lesion of the mediastinum, with interval progression of the right and left pulmonary artery stenosis with most stenotic portion that measures 3.7 mm in the right pulmonary artery and was 10.2 mm and the most stenotic area in the left pulmonary artery that measures 4.8 mm and was 11.8 mm. Interval progression of the narrowing the left main bronchus. There was a new severe stenosis of the lower SVC and moderately of the right subclavian vein. There was a thrombosis of the left brachiocephalic vein extending to the lower internal jugular vein. Multiple venous collaterals in the right sided chest wall. And interval progression of the soft tissue masses infiltrating in the trachea with tracheal stenosis of shortest diameter that measured of 3.7 mm and was 6.6 mm.

Also, she underwent PET-CT whole body in late days of August 2017 and demonstrated significant metabolic improvement in inflammatory disease process involving and surrounding mediastinal vessels and the left lung main trunk. The anatomical soft tissue infiltration in the mediastinum and chest seen/described on recent contrast enhanced CT was not as apparent/easily seen on our non-contrast CT (Figure 2 a and b).

Figure 2: (a and b) PET-CT whole body showing significant metabolic improvement in inflammatory disease process involving and surrounding mediastinal vessels and the left lung main trunk.

During that admission, as reported by radiology, her findings were consistent with GPA, with major vessels involvement and there was no evidence of any significantly worsening mediastinal mass. They advised to do PET-CT and then to consider CT-guided biopsy if feasible. A PET-CT scan was done and it was suggestive of a focus seen at the origin of the left main stem bronchus may be a reasonable target for biopsy. Pulmonary service was consulted and suggested that there was no need for bronchoscopy or biopsy at that time and to recommended to repeat imaging after 6 weeks of GPA and anticoagulation therapies, in a multidisciplinary meeting. After that, she was treated with therapeutic dose of enoxaparin and she was also received pulse steroid therapy for 4 days as 500 mg of IV methylprednisolone. Over few days, her shortness of breath and facial and neck swellings were improving with her regimen, based on her clinical assessment, laboratory investigations as well as radiological imaging. She was discharged home to be seen in ambulatory settings with close follow up. After three months on December 2017, she was re-evaluated in the clinic and she was clinically better without dyspnea and improving neck swelling. A recent CT showed complete resolution of the right and left pulmonary artery narrowing.

DISCUSSION

GPA has wide variety of presentations, mainly related to small to medium vessels vasculitis. This case report presentation on a rare presentation of GPA such as involvement of large vessels including very rare involvement of pulmonary arteries. Upon reviewing the literature, Ozaki et al in a case series of 24 GPA patients having large vessels involvement, they found that most commonly affected vessel was the abdominal aorta (12 cases), thoracic aorta (6 cases), subclavian artery (4 cases), and internal carotid artery (4 cases).[6] In another case report, Clark et al reported one GPA patient with large vessels involvement in from of pulmonary artery stenosis.[7] As in any organ or life-threatening rheumatologic presentation of vasculitis, that appropriate diagnosis and aggressive immunosuppressive therapy including pulse steroid in combination with either cyclophosphamide or rituximab, was an important cornerstone in the outcome of GPA patients.[8] On our patient, the combination of pulse steroid therapy with cyclophosphamide, yielded complete remission and resolution of patient symptoms.

CONCLUSION

After presenting this case report, we emphasize on the importance of knowing various, different and rare presentations of systemic diseases including atypical presentations of systemic diseases such as vasculitis. In addition, this case reported to improve the awareness about other overlapping categories of vessels vasculitis that may involve large vessels and main pulmonary arteries and to avoid misdiagnosing these patients with classical large vessels vasculitis category as per CHCC 2012 such as giant cell arteritis or Takayasu arteritis. As well as, to show the role of combination with either cyclophosphamide or rituximab, as an important cornerstone in the outcome of GPA. Definitely, the ongoing researches on GPA will provide better understanding of its various presentations and management in the future.

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