COMMENTARY

GRANULOMATOSIS WITH POLYANGIITIS: A 17 YEAR EXPERIENCE FROM A TERTIARY CARE HOSPITAL IN PAKISTAN

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Granulomatosis with Polyangitis (GPA) is an uncommon immunologically mediated necrotizing vasculitis affecting the small and medium sized systemic blood vessels. We previously reported our experience with this condition and herein, we document our study findings and compare them to the clinical and radiological findings of various studies from around the world. By doing so we hope to further create awareness of this condition afflicting not only our part of the population but is part of a larger global phenomenon.

Keywords: Vasculitis; Granulomatous Diseases; Lung

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INTRODUCTION

Granulomatosis with polyangitis (GPA) is an uncommon, immunologically mediated necrotizing vasculitis affecting the small and medium sized systemic blood vessels[1] Its characteristic feature is glomerulonephritis, vasculitis and respiratory tract lesions 1. The acronym ELK is used to describe involvement of the ear, nose and throat (ENT); lungs and kidneys.[1]

The differentials of GPA can be broadly classified into 2 subtypes of granulomatous lung diseases: Infectious lung diseases and Noninfectious lung diseases. Infectious lung diseases include Tuberculosis, whilst noninfectious lung diseases include Eosinophilic granulomatosis with polyangiitis, Microscopic polyangiitis (MPA), Sarcoidosis, Henoch-Schonlein purpura (HSP) and Systemic Lupus Erythematosis (SLE).[2]

We previously reported our experience with this condition and herein, we document the findings of our study[3] and compare it to the clinical findings and radiological features of our studies around the world. We hope that by doing so, we will be able to further create awareness of this condition afflicting not only our population but is part of a larger global phenomenon.

CLINICAL FEATURES

The most common organ system affected by GPA in our study was the respiratory system (80.4%) followed by renal (54.9) and ENT (49%).[3] This also lies in contrast with the findings of Shoba et al where the renal system was involved most frequently (70%) followed by the respiratory system (63%).[4] Sharma *et al* however showed a different result compared to ours with the ENT system being affected in 79 % of patients in their study followed by the kidney in 68% of patients.[5] Holle *et al* from Germany and Stone *et al* also reported ENT predominance in their respective studies.[6,7]

Based on these results, we can infer that within Pakistan, patients with GPA tend to have the respiratory system most frequently affected followed by ENT in contrast with similar studies from around the world. In our case, the manifestations of ENT involvement were expressed as hearing loss and epistaxis, which is similar to the findings of Stone *et al*, in whose study the most common presenting symptom was epistaxis as well.[7]

As noted above there are some conditions are similar in clinical presentation with GPA and will be discussed briefly here. In developing Countries, infectious diseases are the most common differentials of GPA. Within Pakistan, tuberculosis is the major differential diagnosis of GPA, especially given the prevalence of the disease in the country. Pakistan has the world's fifth highest Tuberculosis prevalence and the fourth highest multidrug resistant TB prevalence in the world and this grave situation results in other pathologies like GPA being pushed into the background.[8] Clinical Features suggestive, but not specific, of tuberculosis are prolonged cough, fever, weight loss, night sweats and lymphadenopathy.[2]

Eosinophilic granulomatosis with polyangitis (EGPA, Churg–Strauss syndrome) is a common differential and differs from GPA by having asthma, prominent gastrointestinal and cardiac involvement.[9] Microscopic polyangiitis (MPA) is another common differential of GPA that must also be considered. It differs from GPA in that there is usually an absence of upper respiratory tract features in the disease.[9] Henoch-Schonlein purpura (HSP; IgA vasculitis) must also be noted as a differential in patients with GPA. HSP often follow an upper respiratory tract infection but do not present with those features. Lung involvement however is uncommon.[9]

Sarcoidosis is another major differential of this condition. Clinically, the differentiating features of sarcoidosis are Erythema nodosum, Uveitis, Lymphadenopathy and Splenomegaly. The presence of these features will strongly favor against a diagnosis of GPA.[9] Other differentials are Systemic Lupus

Erythematosis (SLE) and other connective tissue diseases (CTDs). They differ from GPA in that patients with SLE suffer from photosensitive rashes, alopecia and Raynaud phenomenon which help to separate this pathology from GPA.[9]

RADIOLOGICAL AND SEROLOGICAL INVESTIGATIONS

In our study patients with respiratory system involvement were predominant, hence it is imperative to evaluate the findings on the radiological investigations done in these patients. About 31.4% of patients had pulmonary infiltrates, in the form of consolidation, in our study. This is similar to the results obtained by Shoba *et al*, in whose study infiltrates were found in 50% of the population.[4] Keller *et al* reported infiltrates present in 34% of patients with lung involvement.[10]

Likewise, the results demonstrated by Stone *et al* showed nodules or cavities as the predominant radiological finding.[7] We can therefore note that like the rest of the studies done on this subject, pulmonary infiltrates are a major finding in patients with suspected GPA and this reaffirms the American College of Rheumatology's criteria.[1]

Radiologically and/or serologically, there are certain features that help us differentiate some of the differentials listed above from GPA. Radiological features of TB include fibrosis with bronchiectasis, hilar and mediastinal lymph node enlargement, small nodular lesion and pleural effusions as well as upper lobe infiltrates.[2] Serologically, TB is diagnosed by the detection of Mycobacterium Tuberculosis in sputum, gastric secretions or bronchoscopic lavage.[2]

The characteristic features of EGPA is a significant (Defined as greater than 10% of peripheral WBC count) peripheral eosinophilia or tissue eosinophilia.[9] Another differential, MPA, differs from GPA on the basis of a biopsy of the affected organ system which shows a lack of granulomatous inflammation.[9] IgA deposition are seen on immunofluorescence of skin or renal biopsy in HSP but not in GPA.[9] In sarcoidosis, chest imaging has hilar adenopathy well-formed noncaseating granuloma without vasculitis on tissue biopsy.[9]

Lastly, GPA can be differentiated from SLE and other CTDs serologically as in SLE and other CTDs, in that SLE and the other CTDs display leukopenia and thrombocytopenia on the complete blood count but this phenomenon is not the case in GPA.[9] ANCA testing has been employed as diagnostic criteria for GPA at our institution. Anti-neutrophilic cytoplasmic antibody (ANCA) is a sensitive and specific test in 80–90% of patients with systemic disease, but sensitivity drops to 60% in localized disease.[11]

CONCLUSION

By comparing our results of our study with similar studies around the world and also comparing the differentials, we hope to bring some perspective to clinicians guiding them into being better able to effectively manage this rare but very debilitating condition. The most common differentials of GPA that must be considered include infectious causes like Tuberculosis and non–infectious causes like EGPA, MPA, HSP, sarcoidosis and SLE as well as other CTDs. (1100 words exc. references)

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