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Eosinophilic Granulomatosis with Polyangiitis (EGPA)- A presentation of rapid progressive demyelinating polyneuropathy

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Abstract

A 79 year old female patient, presented with severe burning pain of bilateral palms and soles for 5 days duration which progressed rapidly over a duration of 2 months. She is a known case of allergic rhinitis and sinusitis with poorly controlled asthma since childhood, requiring MDI Seretide, Ventolin and Theophylline. She was diagnosed with diabetes mellitus 6 years ago where she is currently on Metformin. Examination revealed bilateral distal sensorimotor neuropathy with presence of occasional rhonchi on auscultation of the lungs. Blood investigations revealed anaemia with eosinophilia (64% eosinophils on differential leukocytes counts), positive anti-MPO antibody and significantly raised serum Ig E level. Myeloma screening and HIV, hepatitis B and hepatitis C screening were negative. Paraneoplastic screening was unremarkable. Proteinuria was presence with urine protein/creatinine ratio of 2.53 gram. However, sural nerve biopsy showed severe decrease density of myelinated fibers with active axonal degeneration and perivascular epineural inflammation, without any structural damage to the vessels to indicate vasculitis, which the underlying etiology was unable to be determined based on histology grounds. Two nerve conduction study were performed at 2-month interval which revealed rapidly progressive demyelinating polyradiculoneuropathy. She was initially treated as for diabetic neuropathy which the diagnosis was revised when she deteriorated rapidly within 2 months duration. In view of history of poorly controlled asthma, sinusitis, significant eosinophilia with extravascular manifestations (polyneuropathy and renal involvement) with complete resolution after immunosuppressants (normalisation of eosinophilia and urine protein/ creatinine ratio), and positive anti-MPO antibody, the diagnosis of EGPA was made.

Keywords

granulomatosis with polyangiitis; demyelinating polyneuropathy

Abbreviations

EGPA: Eosinophilic Granulomatosis with Polyangiitis; Anti-MPO antibody: Anti- Myeloperoxidase Antibody

Introduction

Eosinophilic granulomatosis with polyangiitis, which was previously known as Churg-Strauss syndrome (CSS), is a multisystem disorder characterized by chronic sinusitis, asthma, and peripheral

blood eosinophilia. EGPA classically presents with multiple different phases which known as prodromal phase, eosinophilic phase and vasculitic phase [2,3]. Asthma is the cardinal features in EGPA which account for 90% of the patients diagnosed with EGPA [4]. EGPA is often suspected in patients with poorly controlled asthma or in those who require long term systemic glucocorticoids to control their asthma. Nearly half of the patients diagnosed with EGPA would have underlying upper airway and ear involvement, namely recurrent sinusitis, otitis media and nasal polyposis [4,5]. Peripheral neuropathy is commonly seen and accounts for almost 75% of the diagnosed cases of EGPA [10]. Mononeuritis multiples is the commonest neuropathy presentation in patients with vasculitic neuropathy from EGPA [3,4,26,27]. Rarely, patient would present with painful neuropathy which progress to small fibers neuropathy or demyelinating polyneuropathy. Other systemic involvement like renal, skin, gastrointestinal tract and musculoskeletal involvements are not uncommon. The diagnosis of EGPA is suggested by the presence of asthma, rhinosinusitis, and eosinophilia and then confirmed by lung biopsy or biopsy of other clinically affected tissues (eg, skin, peripheral nerve). Systemic corticosteroid is the primary therapy for the treatment of EGPA. Immunosuppressive agent is typically added in patients with more advanced or refractory disease and in those whose disease flares with tapering of systemic glucocorticoids [3, 4].

Case Presentation

A 79 year old, Chinese lady, presented with 5 days history of severe burning pain of bilateral palms and soles, associated with minimal weakness of both lower limbs for 4 days duration. She had minimal walking difficulty where she needed to hold onto furniture while ambulating at home. Her condition deteriorated rapidly within 2 month period where she was unable to ambulate independently and became wheelchair bound while she was admitted to the hospital.

Patient is a known case of asthma diagnosed since childhood, with average asthmatic attack of once in every 3 months, currently on Seretide and ventolin inhaler, as well as Theophylline for asthma control. She has been having recurrent allergic rhinitis and sinusitis requiring symptomatic treatment from the general practitioner. Patient has been suffered from diabetes mellitus for 6 years, where she is currently on Metformin, with latest Hba1c on admission was 6.7%. General examination was unremarkable. Her vitals parameters were normal.

Respiratory examination revealed occasional rhonchi. Nervous system examination revealed symmetrical minimal weakness of all 4 limbs, generalised hypo-reflexia as well as reduced in pin-rick sensation in glove and stocking distribution. Other system examinations were unremarkable.

She was initially treated as for diabetic peripheral neuropathy in view of the clinical presentation and nerve conduction study which showed demyelinating polyneuropathy with symmetrical involvement of her symptoms. However, her condition deteriorated rapidly over 2 month period where she deteriorated clinically and neurophysiologically. The diagnosis of diabetic neuropathy was reconsidered and re-evaluated to look for any other possibilities of demyelinating polyneuropathy which could rapidly progressed, for instance vasculitic neuropathy, paraneoplastic neuropathy, paraproteinaemia or infectious related neuropathy in a patient with HIV and hepatitis B or C infections.

Blood investigations revealed normochromic normocytic anaemia (9.9 g/dL), Total Leukocytosis

(13.5 mmol/L), eosinophilia (Absolute eosinophil 14.32 x 10^{9}/L), Serum Ig E 887 IU/ ml, and Anti-Myeloperoxidase Antibody (Anti MPO Ab) positive. Myeloma screening was negative with no evidence of paraproteinaemia. HIV, hepatitis B and hepatitis C screening were negative as well as negative paraneoplastic screening. Her Urine protein/ creatinine ratio was 2.53 g, suggestive of renal involvement, which resolved (0.50 g) after initiation of immunosuppressive therapy. CT scan of the chest showed mild bilateral apical scarring, with small calcified granuloma over the left lower lobe apical segment. No obvious mass detected from the CT scan of the thorax, abdomen and pelvis region.

Two nerve conduction studies were performed (May 2014 and July 2014), revealed demyelinating polyradiculoneuropathy which then rapidly progressed to severe sensorimotor polyneuropathy (Table 1 and Table 2). Sural nerve biopsy showed severe decrease density of myelinated fibers, with active axonal degeneration. Individual collections of perivascular epineural inflammation is noted. However, no structural damage to the vessels to indicate vasculitis. The etiology of the underlying process cannot be determined from this histology grounds.

She was treated with intravenous hydrocortisone 100mg every 8 hourly, intravenous immunoglobulin for total of 5 days duration and oral cyclophosphamide 50mg daily. Physiotherapy in the ward was started and patient had been doing well with significant improvement in her functional status. She was able to walk with a walking stick after the initiation of the treatment. No recurrence of the symptoms since 6 months of follow up and she improved well. Patient remains clinically and functionally stable while she is on Oral Prednisolone and Azathioprine. Repeated eosinophils counts revealed significant improvement with resolution of eosinophilia from the peripheral blood counts. (1.4% eosinophils on differential leukocytes counts), as well as resolution of proteinuria from the repeated urine protein/ creatinine ratio.

Discussion

EGPA, or formerly known as Churg-Strauss syndrome, is a rare systemic small and medium-sized vessel vasculitis, which distinguishes itself from other small-sized-vessel vasculitis by the presence of severe asthma, and blood and tissue eosinophilia. This patient was diagnosed with EGPA based on the 4 criteria that were presence: Eosinophilia, Asthma, Sinusitis and polyneuropathy. We report that there were delay in the diagnosis of the patient. She presented with sensory complaint, which the nerve conduction study showed early demyelinating polyradiculoneuropathy. She was treated symptomatically and the neurological symptoms were attributed to diabetes mellitus. However, patient again re-presented with rapid worsening of her neurological function affecting her daily activity of livings. Hence, the diagnosis of EGPA based on American College of Rheumatology criteria is crucial for early diagnosis of EGPA in order to prevent serious complication from the disease at the later stage.

We reported the rare presentation of polyneuropathy seen in this patient, which progressed rapidly within 2 months interval. The initial nerve conduction study showed typical picture of bilateral symmetrical demyelinating polyradiculoneuropathy, evidence by absent of bilateral H reflexes, reduced conduction velocities in both upper limbs and lower limbs, as well as prolonged F waves in all 4 limbs. The neuropathy rapidly worsened after 2 months without any treatment instituted. The typical neuropathy seen in EGPA are mononeuritis multiplex or polyneuropathy, whereas in our case, we reported the classical picture of demyelinating polyradiculoneuropathy from the nerve conduction

study.

In our case, the patient was started with intravenous hydrocortisone and at the same time, she was given intravenous immunoglobulin, for a total of 5 days duration. Patient's condition improved dramatically which she became more independent in her daily activity of living, as well as her functional status. She is currently on Prednisolone 10mg daily and Azathioprine 50mg daily, with complete back to her normal daily function.

Table 1: May

(Sensory Conduction Study)

Nerve: Stimulation/ Recording Site	Latency (msec)	Amplitude (uv)	Conduction Velocity(msec)
R Median: wrist/ 2nd digit	4.6	18	28.3
L Median: wrist/ 2nd digit	3.6	6.5	36.1
R Ulnar: wrist/ 5th digit	2.7	14	40.7
L Ulnar: wrist/ 5th digit	2.3	9.5	47.8
R Radial: forearm/ 1st interspace	1.85	27	54.1
L Radial: forearm/ 1st interspace	1.88	25	53.2
R Sural: leg/ ankle	3.4	14	35.3
L Sural: leg/ ankle	3.8	9.7	31.6
R Saphenous nerve: leg/ ankle	3.7	7.6	32.4
L Saphenous nerve: leg/ ankle	3.3	7.6	36.4

H Reflex

Nerve: stimulation site/ recording site	Latency (msec)	Amplitude
R Tibial: popliteal fossa/ soleus	Absent	
L Tibial: popliteal fossa/ soleus	Absent	

Motor Nerve Conduction

Nerve; Stimulation/Recording site	Latency (msec)	Amplitude (mv)	Conduction Velocity (M/sec)	F wave latency (msec)
R Median: wrist/ APB	Absent	-	-	-
L Median: wrist/ APB	Absent	-	-	-
R Ulnar: Wrist/ ADM Above elbow/ ADM Erb's/ ADM	2.8 7.9 13.0	7.1 5.9 5.7	Above elbow/ wrist: 49.0 Erbs'/ Above elbow: 62.7	26.7
L Ulnar: Wrist/ ADM Above elbow/ ADM Erb's/ ADM	2.7 7.5 12.5	7.3 6.6 5.7	Above elbow/ wrist: 58.3 Erbs'/ Above elbow: 60.0	26.2

R Radial: Forearm/ Extensor Indices Arm/ Extensor Indices Erb's/ Extensor Indices	2.7 4.6 7.8	10.2 8.9 8.3		
L Radial: Forearm/ Extensor Indices Arm/ Extensor Indices Erb's/ Extensor Indices	2.4 4.4 7.9	8.2 8.0 7.1		
R Tibial: Ankle/ AH Popliteal Fossa/ AH	5.0 14.1	4.1 3.0	Popliteal fossa/ ankle: 38.5	68.5
L Tibial: Ankle/ AH Popliteal Fossa/ AH	4.8 12.4	3.8 1.2		71.3
R Peroneal: Ankle/ EDB Below Fibular Head/ EDB Above Fibular Head/ EDB	 4.1 12.5 14.5	 3.4 2.9 3.1	Below fibular head/ ankle: 34.5 Across fibular head: 37.5	52.8
L Peroneal: Ankle/ EDB Above Fibular Head/ EDB	 4.5 15.6	 1.8 1.8	Above fibular head/ ankle: 33.3	55.5
R Peroneal: Below Fibular Head/ TA Above Fibular Head/ TA	 3.5 4.9	 5.0 5.0	Across fibular head: 42.9	
L Peroneal: Below Fibular Head/ TA Above Fibular Head/ TA	 3.4 5.2	 5.2 4.9	Across fibular head: 44.4	

Table 2: July (2 months later)

Sensory Nerve Conduction

Nerve: Stimulation/ Recording Site	Latency (msec)	Amplitude (uv)	Conduction Velocity (msec)
R Median: wrist/ 2nd digit	Absent	-	-
L Median: wrist/ 2nd digit	Absent	-	-
R Ulnar: wrist/ 5th digit	Absent	-	-
L Ulnar: wrist/ 5th digit	Absent	-	-
R Sural: leg/ ankle	Absent	-	-
L Sural: leg/ ankle	Absent	-	-
R Superficial Peroneal nerve: leg/ ankle	Absent	-	-
L Superficial Peroneal nerve: leg/ ankle	Absent	-	-

Motor Nerve Conduction

Nerve; Stimulation/Recording site	Latency (msec)	Amplitude (mv)	Conduction Velocity (M/sec)	F wave latency (msec)
R Median: wrist/ APB	Absent	-	-	-
L Median: wrist/ APB	Absent	-	-	-
R Ulnar: Wrist/ ADM Above elbow/ ADM	6.1 11.9	0.1 < 0.1	Above elbow/ wrist: 43.1	-
L Ulnar: Wrist/ ADM Above elbow/ ADM	5.0 10.7	< 0.1 < 0.1	Above elbow/ wrist: 42.1	-
R Tibial: Ankle/ AH	Absent	-	-	-
L Tibial: Ankle/ AH	Absent	-	-	-
R Peroneal:Ankle/EDB	Absent	-	-	-
L Peroneal:Ankle/ EDB	Absent	-	-	-
R Peroneal:Below Fibular Head/ TA	Absent	-	-	-
L Peroneal:Below Fibular Head/ TA	Absent	-	-	-

Conclusion

From the case above, we conclude that EGPA complicated frequently with rapid, severe form of polyneuropathy, which could potentially worsened drastically if the treatment was not started early. Remission depends on early aggressive immunosuppressive therapy and physiotherapy. Overall prognosis of a treated patient appear good with good functional recovery with adequate treatment.

References

1. Jacob Churg; Lotte Strauss (March–April 1951). "Allergic granulomatosis, allergic angiitis, and periarteritisnodosa". The American Journal of Pathology. 27 (2): 277–301.

2. Lanham JG, Elkon KB, Pusey CD, Hughes GR. Systemic vasculitis with asthma and eosinophilia: a clinical approach to the Churg-Strauss syndrome. Medicine (Baltimore) 1984; 63:65.

3. Pagnoux C, Guillevin L. Churg-Strauss syndrome: evidence for disease subtypes? Curr Opin Rheumatol 2010; 22:21.

4. Comarmond C, Pagnoux C, Khellaf M, et al. Eosinophilicgranulomatosis with polyangiitis (Churg-Strauss): clinical characteristics and long-term followup of the 383 patients enrolled in the French Vasculitis Study Group cohort. Arthritis Rheum 2013; 65:270.

5. Chumbley LC, Harrison EG Jr, DeRemee RA. Allergic granulomatosis and angiitis (Churg-Strauss syndrome). Report and analysis of 30 cases. Mayo Clin Proc 1977; 52:477.

6. Della Rossa A, Baldini C, Tavoni A, et al. (November 2002). "Churg-Strauss syndrome: clinical and serological features of 19 patients from a single Italian centre". Rheumatology. Oxford. 41 (11): 1286–94.

7. Hattori N, Ichimura M, Nagamatsu M, et al. Clinicopathological features of Churg-Strauss syndrome-associated neuropathy. Brain 1999; 122 (Pt 3):427.

8. Santos YA, Silva BR, Lira et al. Eosinophilicgranulomatosis with polyangiitis (formerly known as Churg-Strauss syndrome) as a differential diagnosis of hypereosinophilic syndromes. Respir Med Case Rep. 2017 Mar 8;21:1-6.

9. Xu XL, Song W, Sui X et al. Radiological and Clinical Features of Eosinophilic Granulomatosis with Polyangiitis. Zhongguo Yi Xue Ke Xue Yuan Xue Bao. 2016 Oct 10;38(5):617-620.

10. Mouthon L, Dunogue B, Guillevin L et al. Diagnosis and classification of eosinophilic granulomatosis with polyangiitis (formerly named Churg-Strauss syndrome). J Autoimmun. 2014 Feb-Mar;48-49:99-103.

11. Mahr A, Moosig F, Neumann T, et al. Eosinophilic granulomatosis with polyangiitis (Churg-Strauss): evolutions in classification, etiopathogenesis, assessment and management. Curr Opin Rheumatol. 2014 Jan;26(1):16-23.

12. Holle JU, Gross WL, Latza U, Nolle B, Ambrosch P, Heller M, et al. Improved Outcome in 445 Patients With Wegener's Granulomatosis in a German Vasculitis Center Over Four Decades. Arthritis and rheumatism. 2011;63(1):257-66.

13. Roubaud-Baudron C, Pagnoux C, Meaux-Ruault N, Grasland A, Zoulim A, Le Guen J, et al. Rituximab Maintenance Therapy for Granulomatosis with Polyangiitis and Microscopic Polyangiitis. Journal of Rheumatology. 2012;39(1):125-30.

14. Thiel J, Hässler F, Salzer U, Voll RE, Venhoff N. Rituximab in the treatment of refractory or relapsing eosinophilicgranulomatosis with polyangiitis (Churg-Strauss syndrome). Arthritis Res Ther. 2013 Sep 24;15(5):R133.

15. Greco A, Rizzo MI, De Virgilio A et al. Churg-Strauss syndrome. Autoimmun Rev. 2015 Apr;14(4):341-8.

16. Guillevin, L, Cohen, P, Gayraud, M et al. Churg-Strauss syndrome: clinical study and long-term follow-up of 96 patients. Medicine. 1999; 78: 26–37.

17. Chen, KR, Ohata, Y, Sakurai, M, and Nakayama, H. Churg-Strauss syndrome: report of a case without pre-existing asthma. J Dermatol. 1992; 19: 40–47.

18. Yamashita, Y, Yorioka, N, Taniguchi, Y et al. Nonasthmatic case of Churg-Strauss syndrome with rapidly progressive glomerulonephritis. Intern Med. 1998; 37: 561–563.

19. Martin, RM, Wilton, LV, and Mann, RD. Prevalence of Churg-Strauss syndrome, vasculitis, eosinophila and associated conditions: retrospective analysis of 58 prescription-event monitoring cohort studies. Pharmacoepidemiol Drug Safety. 1999; 8: 179–189

20. Watts, RA, Gonzalez-Gay, MA, Lane, SE, Garcia-Porrua, C, Bentham, G, and Scott, GI. Geoepidemiology of systemic vasculitis: comparison of the incidence in two regions of Europe. Ann Rheum Dis. 2001; 60: 170–172

21. Kinoshita, M, Shiraishi, T, Koga, T et al. Churg-Strauss syndrome after corticosteroid withdrawal in an asthmatic patient treated with pranlukast. J Allergy ClinImmunol. 1999; 103: 534–535.

22. Le Gall, C, Pham, S, Vignes, S et al. Inhaled corticosteroids and Churg-Strauss syndrome: a report of five cases. Eur Respir J. 2000; 15: 978–981.

23. Chumbley, LC, Harrison, EG, and DeRemee, RA. Allergic granulomatosis and angiitis (Churg-Strauss syndrome). Mayo Clin Proc. 1977; 52: 477–484.

24. Solans, R, Bosch, JA, Perez-Bocanegra, C et al. Churg Strauss syndrome: outcome and long term follow up of 32 patients. Rheumatology. 2001; 40: 763–771.

25. Clutterbuck, EJ, Evans, DJ, and Pusey, CD. Renal involvement in Churg-Strauss syndrome. Nephrol Dial Transplant. 1990; 5: 161–167.

26. Della Rossa A, Baldini C, Tavoni A, et al. Churg-Strauss syndrome: clinical and serological features of 19 patients from a single Italian centre. Rheumatology (Oxford) 2002; 41:1286.

27. Solans R, Bosch JA, Pérez-Bocanegra C, et al. Churg-Strauss syndrome: outcome and long-term follow-up of 32 patients. Rheumatology (Oxford) 2001; 40:763.

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