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Mepolizumab efficacy in the treatment of patients with eosinophilic granulomatosis with polyangiitis – Case Report

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CASE STUDY

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ABSTRACT

Eosinophilic granulomatosis with polyangiitis (EGPA), is a rare necrotizing vasculitis predominantly involving small to medium size vessels with eosinophilia and necrotizing granulomatous inflammation involving the respiratory tract, mepolizumab is an anti-interleukin-5 monoclonal antibody that binds to interleukin-5 and stops it from interacting with its receptor on the surface of eosinophils. To demonstrate that, we present a case of young female known to have bronchial asthma and chronic sinusitis since childhood presented with shortness of breath, found to have EGPA, her condition deteriorated and finely she was treated with Mepolizumab, which showed that it has efficacy in treating patients with EGPA.

Key Words

Vasculitis, EGPA, Mepolizumab

Implications for Practice:

1. What is known about this subject?

Eosinophilic granulomatosis with polyangiitis (EGPA), is a rare necrotizing vasculitis predominantly involving small to medium size vessels.

2. What new information is offered in this case study?

Mepolizumab showed that it has efficacy in treating patients with EGPA.

3. What are the implications for research, policy, or practice?

Mepolizumab can be used as alternative therapy in the management of EGPA.

Background

Eosinophilic granulomatosis with polyangiitis EGPA, previously called Churg-Strauss syndrome, when they offer the initial prescription for the illness. It is a rare necrotizing vasculitis predominantly involving small- to medium-size vessels with eosinophilia and necrotizing granulomatous inflammation involving the respiratory tract. Moreover, patients with eosinophilic granulomatosis with polyangiitis have a potential therapeutic alternative to neutralize interleukin 5. Apart from this, mepolizumab (GlaxoSmithKline) is an anti-interleukin-5 monoclonal antibody that binds to interleukin-5 and stops it from interacting with its receptor on the surface of eosinophils. To demonstrate that, we present a case of a young female known to have bronchial asthma and chronic sinusitis since childhood presented with shortness of breath, found to have Eosinophilic granulomatosis with polyangiitis; her condition deteriorated, and finely she was treated with Mepolizumab (Nucala)

Case details

Twenty-three years old Saudi female patient's known case of bronchial asthma and chronic sinusitis since childhood. The condition started three years back when she was referred from the peripheral hospital complaining of progressive dyspnoea, wheezing chest, coughing blood-tinged mucous, basal crepitations, and lower limb edema. Also, she had a low-grade fever, purpura, skin ulcers, and near gangrene Left little toe. In addition to the deterioration of conscious level, weakness of the dorsiflexor muscles of

both lower limbs, more on the left side. The Chest infiltration was more on the right side. (Figure 1) Computerized Tomography (CT) brain showed hypodensity (Figure 2); Magnetic Resonance Imaging (MRI) Brain showed: Multiple focal areas with altered signal intensity Involving white matter in cortical, subcortical locations, and peri-ventricular. The High T2 and flair signals. (Figure 3) No lesion in the spinal cord. However, a Skin biopsy showed leukocytoclastic vasculitis with marked eosinophilia. At this time, the caregiver doctor gave intravenous antibiotics, and he sent the septic screen. Also, the primary doctor ordered a Methylprednisolone pulse at 500mg per day for three days, then oral prednisolone at 40mg daily, IVIG 0.4 g per Kilogram per day for 5days. Cultures returned negative then; cyclophosphamide started Low dose of 500mg per intravenous for two weeks for six doses, HQ 200mg per oral two times a day and pneumocystis jirovecii pneumonia (PCP) prophylaxis. Also, Rivaroxiban loading dose then started 20mg daily. After the second dose of Cyclophosphamide (CYC) she improved gradually. At that time, she was able to walk with support and was discharged home and continued in the outpatient department (OPD) with tapering of corticosteroid. Three months after the last dose of Cyclophosphamide (CYC), she started on Mycophenolate Mofetil (MMF) as maintenance therapy, and prednisolone reached only 5mg per oral once daily. Two months back, she presented with dyspnea, wheezy chest and shortness of breath, lower limb edema, Neuropathic pain in both lower limbs, and lower motor neuron weakness left foot (partial foot drop). White Blood Cells (WBCs):13.47, eosinophil's 20 Per cent, Hemoglobin (HG): 14.7, Platelet (PLT):421, Erythrocyte Sedimentation Rate (ESR): 37, C - reactive protein (CRP): 1.4. Normal renal function without proteinuria. Albumin 44, Aspartate Aminotransferase (AST): 12, Alanine Aminotransferase (ALT): 11, Cyclophosphamide (CYC) was restarted, and the dose of Mycophenolate Mofetil (MMF) was also increased with Rituximab. Also, a Methylprednisolone pulse was given, and the oral steroid dose Increased. Mepolizumab (Nucala), a Human monoclonal antibody (anti-interleukin-5), started at 300mg subcutaneously for four weeks. Three months after beginning Nucala: The dyspnea, wheezes, lower limb edema, weakness & paresthesia started to be relieved. Last Complete Blood Cell (CBC): White blood cells 7.80, eosinophils 1 Per Cent, Hemoglobin 13.9, Platelet 418, Erythrocyte sedimentation rate 11, C-reactive protein <0.4. Normal liver & renal function without proteinuria, with normal chest X-ray (Figure 4).

Discussion

The anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAVs) are a group of disorders that includes severe, systemic, small-vessel vasculitis, is characterized by the presence of autoantibodies to the neutrophil proteins, proteinase 3 (PR3-ANCA) or myeloperoxidase (MPO-ANCA). There are three AAV subgroups: granulomatosis with polyangiitis (GPA), microscopic polyangiitis, and eosinophilic granulomatous polyangiitis (EGPA), all are defined according to clinical presentation[1]. EGPA is a rare necrotizing vasculitis predominantly involving small- to medium-size vessels with eosinophilia and necrotizing granulomatous inflammation involving the respiratory tract. Almost always, asthma is present. Allergic rhinitis is also a typical presentation, but Mortality and morbidity are frequently associated and caused by cardiac involvement. There may also be gastrointestinal, cutaneous, and neurological manifestations[2]. Management is divided into the induction and maintenance of remission. Remission can happen by a combination of high-dose glucocorticoids and cyclophosphamide. IV immunoglobulin, mycophenolate mofetil, or biological agents such as infliximab and rituximab may be used[3]. Also, a combination of methotrexate and glucocorticoid is a less toxic alternative to cyclophosphamide and can use for induction with non-organ-threatening or non-life-threatening conditions. For maintenance of remission, a combination of low-dose glucocorticoids plus azathioprine, leflunomide, or methotrexate is sufficient. Recent research has indicated that activation of the complement system, particularly the alternative complement system, plays a significant role in the pathogenesis of ANCA-associated vasculitis[4]. Therapies that target the alternative pathway and the anaphylatoxin C5a have developed because of the identification of the complement's function in AAV[5]. Interleukin-5, a cytokine that controls eosinophil proliferation, maturation, and differentiation, is more prevalent in those who have eosinophilic granulomatosis with polyangiitis. (6) Patients with eosinophilic granulomatosis with polyangiitis have a potential therapeutic alternative to neutralize interleukin 5. An anti-interleukin-5 monoclonal antibody called mepolizumab (GlaxoSmithKline) binds to interleukin-5 and stops it from interacting with its receptor on the surface of eosinophils[7-9]. In 2017, Expanded FDA approval for mepolizumab (Nucala) in treating adults with eosinophilic granulomatosis with polyangiitis[10].A multicentre, double-blind, parallel-group, phase 3 Randomized control trial, mepolizumab led to noticeably more weeks in remission

and a more significant percentage of remission than did placebo, enabling a decrease in the need for glucocorticoids [11]. In our study, our patient received Mepolizumab (Nucala) 300mg SC/4 weeks after a trial of multiple medications; she improved significantly clinically and lab-wise with no apparent side effects or complications.

Conclusion

Mepolizumab is a treatment that has resulted in a consistent reduction in the absolute eosinophil count, with concomitant clinical improvement in patients with other eosinophilic disorders, such as severe eosinophilic asthma. Our study showed that Mepolizumab has efficacy in treating patients with eosinophilic granulomatosis with polyangiitis. More studies are needed.

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PEER REVIEW

Not commissioned. Externally peer reviewed.

CONFLICTS OF INTEREST

On behalf of all authors, the corresponding author states that there are no conflicts of interest.

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PATIENT CONSENT

The study was approved by the Ethics Committee of King Salman Armed Forces Hospital (KSAFH), Written informed consent was obtained from the patient for the publication of this case and any accompanying images.

Figures and Tables

Table 1:

Basic lab	Value	Range
Total WBC count	25 x103	4.5 – 11 x103
Percentage of Eosinophils	62 Per Cent	1.0-6.0 Per Cent
Hb Concentration	14 g/dL	13 – 17.5 g/dL
Platelet Count	106 x103/uL	150 - 450 x103/uL
BUN	4.9	3.2 – 8.2 mmol/L
Cr	80	62- 115 umol/L
CRP	6.6	<0.4 mg/dl
ESR	63	21-Jan

Table 2:

Advance	Value
ANA, DNA & ANCAc/p.	–ve
RF	+ve
C3 C4	normal
Immunoglobuline E 1550	1550
APS abs	–ve

Table 3:

Other	
ECG	Sinus tachycardia ST depression, T wave inversion & high troponin level.
Echo	Moderate to severe mitral & tricuspid regurgitation, marked apical hypertrophy & global hypokinesia.

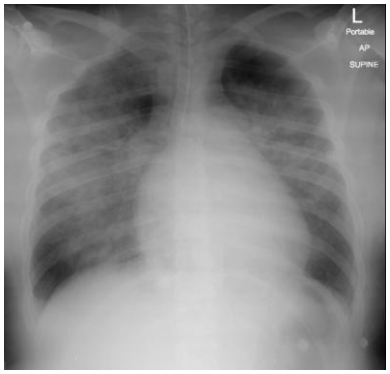

Figure 1: Computerized Tomography (CT) brain showed hypodensity.

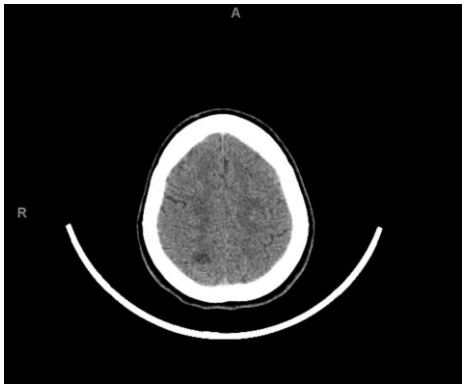

Figure 2: Multiple focal areas with altered signal intensity Involving white matter in cortical, subcortical locations, and peri-ventricular

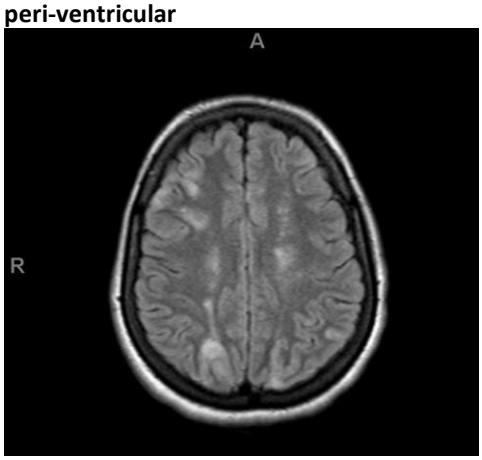

Figure 3: The High T2 and flair signals

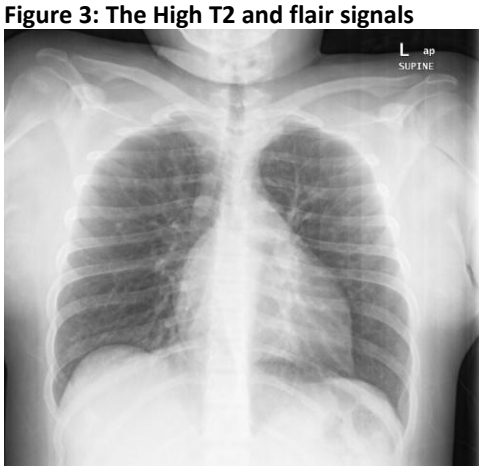

Figure 4: Normal chest X-ray

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