Case Report

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Guillain–Barré syndrome as the first presentation in a patient with systemic lupus erythromatous; case report

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Systemic Lupus Erythromatous (SLE) is an auto immune disease characterized by multi-organ affection, Guillain–Barré syndrome (GBS) is considered as an unusual and one of the least neuropsychiatric syndromes in SLE, this case report aiming to report a rare association of GBS as an initial presentation for an SLE in a female patient. A middle age female was presented with palpitation, shortness of breath and body weakness, she was admitted for four days and diagnosed with atypical GBS. She received Intravenous immunoglobulin (IVIG) for three days but no improvement was been noticed. The patient complained of dry cough, shortness of breath, palpitations and generalized weakness in association with back pain and paraesthesia of the fingers. General examination and lab workup were done and revealed a presence of SLE in relation to GBS. IVIG was then commenced 0.4 g/kg body/weight/day with Hydroxychloroquine 200mg tabs BID, Prednisolone 40mg, calcicare and Mycophenolatemofetil. Significant improvement was noted after receiving the above-mentioned medications and over a period of three months all her symptoms and complains were subside.

Keywords: guillain–barré syndrome • systemic lupus erythromatous • intravenous immunoglobulin • generalized weakness

Abbreviations: AIDP: Acute Inflammatory Demyelinating Polyradiculoneuro-Pathy; ACR: American College of Rheumatology; Anti-ccp: Anti-Cyclic Citrullinated Peptide; Anti-dsDNA: Anti-Double Stranded Dna; ANA: Antinuclear Antibody; Anti-Sm antibody: Anti-Smith Antibody; CSF: Cerebrospinal Fluid; ESR: Erythrocyte Sedimentation Rate; GBS: Guillain–Barré Syndrome; IVIG: Intravenous Immunoglobulins; RF: Rheumatoid Factor; S.C.P.K: Serum Creatinine Phosphokinase; SLE: Systemic Lupus Erythematosus

Introduction

Systemic Lupus Erythromatous (SLE) is multi-organ auto immune disease.The neuropsychiatric syndrome in SLE affects both central and peripheral nervous systems. The presentation of peripheral nervous system involvement in particular can be in form of acute demyelinating polyradiculneuropathy, Guillain–Barré Syndrome (GBS), mononeuropathy, polyneuropathy, myasthenia gravis, and others [1].

GBS is considered as a rare and one of the least neuropsychiatric syndromes in SLE [2]. There is no documented case in Sudan. Here we report the first and a rare case of GBS as an initial presentation of a female patient with SLE.

Case Report

On 16th of February 2020, a 45-year-old housewife from Eastern Sudan attended Alrayan private clinic and then referred to Haj-Elsafi hospital for admission and work up. She was first seen by a physician in kassala teaching hospital, where she was admitted for four days and diagnosed with atypical Guillain–Barré Syndrome (GBS) post infectious radiculopathy. She received a sub-dose of Intravenous Immunoglobulins(IVIG) for three days prior to reaching our hospital but did not notice much improvement.

Regarding her past medical history, she had dry cough, shortness of breath and palpitations for twenty days prior to the development of her weakness. The weakness was gradual in onset,

symmetrical, progressive, and ascending in nature, involving both upper and lower limbs starting distally and goes proximally until it reached its maximum intensity within three days. Her condition was associated with back pain and paraesthesia of the fingers, but there was no sensory loss. However, there was no sphincteric disturbance, symptoms suggesting cranial nerves involvement in the form of facial weakness, diplopia, change in speech, and difficulty in swallowing. She had no symptoms related to autonomic nervous system affection or symptoms of increase intracranial pressure.

Her systemic review revealed one month history of low-grade fever associated with multiple symmetrical pain involving small joints of her hands. It was non-migratory, non-progressive and not associated with morning stiffness, swelling, redness, hotness or deformity.There was no specific relieving or aggravating factors. Moreover, she denied skin, hair or nail changes. Sicca symptoms in the form of dry eyes, mouth and vagina were absent. Gynecological, gastrointestinal, urogenital and other systems were unremarkable. She has no history of trauma, recent vaccination, diarrheal disease or chronic illness.

On examination, she looked ill, afebrile and vitally stable. She was fully conscious and oriented. She moved around with a wheel chair. Upper and lower limbs examination showed no muscle wasting or fasciculation. However, power was found to be grade three in both lower limbs and grade four in both upper limbs. Hypotonia was also noticed in her four limbs while hyporeflexia was confined to her ankles and knees along with bilateral down going plantar reflex. Co-ordination was normal, and all modalities of sensation and cranial nerves were intact. There were no signs of respiratory distress.

Musculoskeletal examination showed tenderness in her right and left metacarpophalangeal, proximal and distal interphalangeal joints of her hands with no swelling or deformity. Skin, hair and nails were normal and no ulcers were found. Additionally, examination of other systems was normal.

Her laboratory investigations revealed an Erythrocyte Sedimentation Rate (ESR) of 80 mm/h; insufficient vitamin D level of 13.7 ng/mL for which cholecalciferol 60,000 IU weekly was commenced and slight decrease in Serum Creatinine Phosphokinase (S.C.P.K). Her complete blood picture showed slight increase in platelet count (480,000/mL) while other parameters were within the normal range, (**Table 1**).

Table 1. Lab investigations and results.

Date	Investigation	Result	Reference value
10-02-2020	Serum vitamin D3 level	13.7 ng/ml	30-100 ng/ml
	Blood urea	32 mg/dl	15-50 mg/dl
	Random blood sugar	112 mg/dl	<180 mg/dl
	Serum creatinine phosphokinase	24 u/l	26-140 u/l
	Total white blood cells	9200 cmm	7.5 ± 3.0
	Red blood cells	5230000 cmm	4.8 ± 1
	Blood hemoglobin	13.6 g/dL	14.0 ± 2.5 g/dL
	Mean corpuscular volume	82.6fl	86.0 ±10 fl
	Platelets	480000 cmm	32.5 ± 2.5 cmm
	ESR	80 mm/h	0.15 mm/h
17-02-2020	Rheumatoid factor IgM	29.2l U/ml	<20IU/ml=negative
			>20IU/ml=positive
	Cyclic citrullinated peptide	0.76	<1.0=negative
			>1.0 =positive
	ANA Profile	Positive for Ro-52	
	Anti dsDNA antibodies	Negative	
	Anti sm antibodies	Negative	
	Complements level	Normal	
06-04-2020	White blood cells	9300/µl	3000-7000 µl
	Lymphocytes	3.10×10^{3}/µl	1.5-4× 10^3/µl
	Neutrophils	5.50× 10^3/µl	2-7.5× 10^3/µl
	Red blood cells	5.35mill/µl	3.5-5 mill/µl
	Blood hemoglobin	13.2 g/dl	11.5-16 g/dl
	Mean corpuscular volume	75.3 fl	76-96fl
	Platelets	334×10^{3}/µl	$140\text{-}450\times10^{3}$/µl
	ESR	30 mm/h	5-20 mm/h

After further workup, Rheumatoid Factor (RF) was found to be positive while anti-cyclic citrullinated peptide (anti-ccp) was found to be negative. Moreover, Antinuclear Antibody (ANA) test and anti-Ro52 antibodies were found to be positive and therefore the diagnosis of Systemic Lupus Erythematosus(SLE) along with her symptoms was made (**Table 1**).

The diagnosis of GBS was done based on her clinical manifestations and nerve conduction studies.

IVIG was then commenced; 0.4 g/kg bodyweight per day, for 5 days along with Hydroxychloroquine 200 mg tabs BID, Prednisolone 40 mg tabs OD and Calcicare 500 mg tabs OD. Mycophenolatemofetil 500 mg tabs BID was also commenced after the chest infection was managed. After ten days significant improvement was noted after receiving the above-mentioned medications.

On her last follow up, all her symptoms subside. As she walk without support and the examination were normal with power grade five in all muscle groups.

Discussion

SLE is an autoimmune disease which is more common in female and affects many organ in the body such as joints, kidney, heart, central and peripheral nervous system, blood, skin and others [3]. Our patient is a female patient who presented with pain involving small joints of her hands and neurological manifestations.

Central nervous system manifestations in SLE are rare but commonly include vascular related manifestations (stroke, transient ischemic attack and venous thrombosis), cognitive (delirium and dementia), headache, psychiatric disorder (psychosis, mood disorder and anxiety), seizer, peripheral neuropathy and demyelination disorder [4,5]. In a study done by Hanly JG et al, 572 patients with SLE were reviewed for neuropsychiatric manifestations. 28% of them had at least single neuropsychiatric event within around 5 months of the diagnosis; however, only 19%-38% were attributed to SLE [6]. The prevalence of GBS in SLE is rare and it was estimated at less than 2%, but it can be fatal due to respiratory failure and autonomic disturbances [7]. GBS is an autoimmune demyelinatingpolyneuropathy affecting peripheral nerves and usually occurs after episodes of upper respiratory tract or gastrointestinal infections [8]. Campylobacter jejuni, mycoplasma pneumoniae, influenza virus, Epstein Barr virus, hepatitis, HIV and others organisms were found to be associated with GBS [9].

This patient presented with a previous history of pain affecting small joints of her hands. Later, her investigations have revealed high ESR and ANA titers. She was positive for anti-Ro52 antibodies. The diagnosis of SLE is based on both clinical features and laboratory results. Positive anti-dsDNA antibodies anti-Sm antibodies and low complement levels are part of the immunological criteria of American College of Rheumatology (ACR) for diagnosis of SLE, while ANA titer is used for screen and a negative result will help to exclude SLE as a diagnosis [10]. Anti-Ro52 antibodies were found to be positive in many autoimmune diseases such as SLE, Sjögren's syndrome, undifferentiated connective tissue disease and rheumatoid arthritis [11,12]. The patient also has a positive rheumatoid factor result. Rheumatoid arthritis could be a differential diagnosis for her joints pain but her anti CCP antibodies level was insignificant. In addition, theinvolvement of the distal interphalangeal joint is not common in rheumatoid arthritis and usually suggests other diagnosis [13]. In this case the patient has no ulcer, skin manifestation, hair or nail changes, serosal involvement, and no renal or cardiovascular symptoms. Arthritis in SLE can be the first manifestation even months before diagnosis, which is no deforming and associated with significant pain and less swelling as in this case [14].

The prevalence ofGBS was found to increase with age [15]. Our patients presented with symptoms suggestive of GBS at the age of 45. She had experienced symmetrical ascending muscle weakness involving both upper and lower limbs. It was gradual and reached the maximum on the third day. Her condition associated with back pain and fingers paresthesia; however, there were no sensory loss, sphincteric symptoms or cranial nerves involvement. Her examination was consistent with findings suggestive lower motor neuron lesion. Few similar cases have been reported among SLE patients [16-19].

Acute Inflammatory Demyelinating Polyradiculoneuro-Pathy(AIDP) is the most common subtype of GBS which is the same for our case[9]. Involving cranial nerves only in a form of Miller-Fisher (MFS) variant was also reported, whoever our patients had no cranial nerves symptoms [18].

The pathogenesis of GBS in SLE is not clear yet. Gao Z etal.reported many factors which can play a role in developing GBS in SLE patients; such as: vascular occlusion of small vessels, cytokines (interferon-α and interleukin-6) and various autoantibodies including anti cardiolipin antibodies and lupus anticoagulant that damage myelin components [20]. Also, the fact that SLE patients have suppressed immunity due to treatment

of the disease might increase the risk of infection with Campylobacter jejuni and hence developing GBS [21].

A similar case was reported by Fazio RM et al, in which a 44 years old female was presented with a one week history of progressive lower extremities weakness associated with loss of reflexes. Her investigations were consistent with GBS and underlying SLE for the first time [22].

Diagnosis of GBS is clinical and supported by many investigations including Cerebrospinal Fluid (CSF) analysis; in which protein level will be elevated with normal cell count (Cytoalbuminologic dissociation), but it can be negative in the first week in about half of patients.Another diagnostic features are signs of polyneuropathy or polyradiculopathy on nerve conduction studies [23,24]. The diagnosis of the current case was made based on the clinical symptoms and examination findings.

Regarding the treatment, it is worth mentioning that the patient received initially a sub dose of IVIG only, but without improvement. Then another course of IVIG (0.4 g/kg bodyweight per day) was given for five days. Additionally, Hydroxychloroquine 200 mg tabs BID, Prednisolone 40 mg tabs OD and Mycophenolatemofetil 500 mg tabs BID were started. This treatment was effective and her condition had improved significantly with power grade 5 in all limbs during her follow up visit.

Similarly, In many cases the treatment of GBS in SLE was effective using IV immunoglobulin and plasmapheresis [18,25]. In some cases corticosteroid and cyclophosphamide were used as effective first line of treatment [17,20,26]. Y Santiago-Casas reported a 20-year old female who was diagnosed with GBS. Plamapheresis was done in the first 12 days, but without improvement. Subsequently she received IV immunoglobulin (400 mg/kg/day) for five days without response. Furthermore, after the diagnosis of SLE, she received cyclophosphamide and methylprednisolon which resulted in significant improvement [21].

In the same way of inadequate initial response to the treatment with IVIG, HC Okoh et al, described a similar situation where GBS was the first presentation of SLE in a 41-years- old female. Her condition failed first to respond to IVIG and plasmapheresis; however, she had an improvement after a second course of IVIG [18].

Conclusion

GBS is a rare manifestation of SLE.Our patient was diagnosed with SLE and GBS. Her condition had significantly improved with the use of IVIG, hydroxychloroquine and corticosteroids.

Limitations

Lumbar puncture was not done.

Disclosure of conflict of interest

No conflicts of interest

References

1. Yu C, Gershwin ME, Chang C *et al.* Diagnostic criteria for systemic lupus erythematosus: a critical review. *J. AutoImmunity* 48, 10–13(2014).
2. Unterman A, Nolte JE, Boaz M *et al.* Neuropsychiatric syndromes in systemic lupus erythematosus: a meta-analysis. *Semin. Arthritis. Rheum.* (2011).
3. Lahita RG. The clinical presentation of systemic lupus erythematosus. *Syst. Lupus. Eryth*. 525–539 (2011).
4. Liang MH, Corzillius M, Bae SC*et al.* The American College of Rheumatology nomenclature and case definitions for neuropsychiatric lupus syndromes. *Arthritis. Rheum.* 42(4), 599–608(1999).
5. Muscal E, Brey RL. Neurological manifestations of systemic lupus erythematosus in children and adults. *Neurol. Clinics.* 28(1), 61(2010).
6. Hanly J, Urowitz M, Sanchez-Guerrero J *et al.* Neuropsychiatric events at the time of diagnosis of systemic lupus erythematosus: an international inception cohort study. *Arthritis. Rheum.* 56(1), 265–273 (2007).
7. Nadri Q, Althaf MM. Guillian-Barre syndrome as the initial presentation of systemic lupus erythematosus–case report and review of literature. *Ann. Saud. Med.* 35(3), 263–5 (2015).
8. Kuwabara S. Guillain-barré syndrome. *Drugs.* 64(6), 597–610 (2004).
9. Jasti AK, Selmi C, Sarmiento-Monroy JC *et al.* Guillain-Barré syndrome: causes, immunopathogenic mechanisms and treatment. *Expert. Rev. Clin. Immunol.* 12(11), 1175–1189 (2016).
10. Kuhn A, Bonsmann G, Anders H-J *et al.* The diagnosis and treatment of systemic lupus erythematosus. *Dtsch. Arztebl. Int.* 112(25), 423 (2015).
11. Malik F, Cahill J, Breese M *et al.* 202. Isolated anti-Ro52 antibodies: clinical significance in routine practice. *Rheumatol.* 53(suppl_1), i134–i5 (2014).
12. Murng SH, Thomas M. Clinical associations of the positive anti Ro52 without Ro60 autoantibodies: undifferentiated connective tissue diseases. *J. Clinical. Pathol.* 71(1), 12–9 (2018).
13. Venables P, Maini RN. Diagnosis and differential diagnosis of rheumatoid arthritis. (2014).
14. Cojocaru M, Cojocaru IM, Silosi I *et al.* Manifestations of systemic lupus erythematosus. *Maedica.* 6(4), 330 (2011).
15. Hughes RA, Rees JH. Clinical and epidemiologic features of Guillain-Barré syndrome. *J. Infect Dis*. 176(Supplement_2), S92–S8 (1997).
16. Vaidya S, Jasin HE, Logan J *et al.* Systemic lupus erythematosus and Guillain-Barre syndrome. *J. Clin. Rheumatol*. 5(6), 349–53 (1999).
17. Van Laarhoven HW, Rooyer FA, van Engelen BG *et al.* Guillain-Barre syndrome as presenting feature in a patient with lupus nephritis, with complete resolution after cyclophosphamide treatment. *Nephrol. Dial. Transplant. 16(4), 840–842 (*2001).
18. Okoh HC, Lubana SS, Langevin S *et al.* A case of systemic lupus erythematosus presenting as Guillain-Barré syndrome. *Case. Reports. Rheumatol*. 2015, (2015).
19. Chandrashekhar S, De Sousa E. Guillain-Barre Syndrome as a Rare Initial Presentation of Systemic Lupus Erythematosus. *AAN. Enterprises*. 447, (2018).
20. Gao Z, Li X, Peng T *et al.* Systemic lupus erythematosus with Guillian–Barre syndrome: A case report and literature review. *Medicine.* 97(25), (2018).
21. Santiago-Casas Y, Peredo R, Vilá L *et al.* Efficacy of low-dose intravenous cyclophosphamide in systemic lupus erythematosus presenting with Guillain-Barre syndrome-like acute axonal neuropathies: report of two cases. *Lupus.* 22(3), 324–327 (2013).
22. Fazio RM, Chen I, Somal N *et al.* Guillain-Barré syndrome as first presentation of systemic lupus erythematosus: a rare manifestation complicated by IVIg-induced splenic infarct. *Case. Reports*. 2015, bcr2015211598 (2015).
23. Van Doorn PA. Diagnosis, treatment and prognosis of Guillain-Barré syndrome (GBS). *La. Presse. Médicale.* 42(6), e193–e201 (2013).
24. Van Den Berg B, Walgaard C, Drenthen J *et al.* Guillain–Barré syndrome: pathogenesis, diagnosis, treatment and prognosis. *Nat. Rev. Neurol*. 10(8), 469–482 (2014).
25. Li X, Wang Y. Systemic lupus erythematosus with acute inflammatory demyelinating polyneuropathy: a case report and review of the literature. *J. Cli. Med. Res.* 8(7), 555 (2016).
26. Karmani J, Athar S. Guillain-Barre Syndrome as the Presenting Feature in a Patient with SLE. *World. J. Clin. Case. Rep. Case.* Ser. 1(1), 1001 (2020).