
Neuro-ophthalmic complications in systemic lupus erythematosus: Case analysis and the literature review

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Abstract

SLE is an autoimmune connective tissue disease mostly occurs in women, affects various systems of the body with broad range of symptoms and complications. A 31 year old female was admitted in October 2013 with complaints of right lower limb weakness and inability to walk for 3 days and diagnosed to have systemic lupus erythematosus (SLE) remission. A detailed medical history revealed multiple admissions, initially with Parinaud's syndrome due to an upper midbrain tectal lesion in December 2004 when she was Primigravida at 32 weeks and she developed SLE at 37 weeks. In subsequent admissions she was diagnosed to have transverse myelitis along with steroid induced diabetes mellitus (2005), obsessive compulsive disorder (2008) and optic neuritis (2009). On every admission patient has treated successfully; visual acuity is improving leisurely. Reviewed literature shows the relationship between SLE and its neuro-ocular complications. All the conditions diagnosed in the patient are related directly or indirectly with etiology and/or treatment of SLE; so this case would be helpful to understand pathogenesis, diagnosis and management of such cases.

Keywords: Systemic lupus erythematosus, Parinaud's syndrome, Transvere myelitis, Optic neuritis, Diabetes mellitus, Obsessive compulsive disorder, dementia, Diabetes insipidus

1.Introduction

Diagnosis of different neuro-ophthalmic complications in systemic lupus erythematosus (SLE) is a challenging task for clinicians especially for rheumatologists and neurologists. Transverse myelitis, optic neuritis and obsessive compulsive disorder (OCD) in SLE are to be found as a rare combination. Hereby we present a case of 31 year old female who is suffering from complex of neuro-ophthalmic complications in SLE. We went through the literature and found very few cases reported such complications occurring in a SLE patient. Reviewed literature shows that the conditions diagnosed in the patient are related directly or indirectly with etiology and/or treatment of SLE. So this case would be helpful to understand pathogenesis, diagnosis and management of such cases.

2. Case Presentation

A 31 year old female was admitted in October 2013 with complaints of right lower limb weakness and inability to walk for 3 days, which was insidious in onset and gradually progressive. A detailed medical history revealed multiple admissions, initially with complaints of ptosis, giddiness and swaying diplopia in December 2004 when she was primigravida at 32 weeks. Based on Magnetic Resonance Venography (MRV) [figure 1] that showed bilateral transverse sinus thrombosis; she was diagnosed to have Parinaud's syndrome and treated with low dose aspirin and clopidogrel. At 37 weeks of pregnancy in January 2005, she was admitted for SLE with high grade fever, malaise and ANA +ve for which azathioprine 50 mg daily, prednisolone tapering therapy (50 mg daily for first week, 40 mg daily for next week and 30 mg daily for

continue as maintenance dose) were started and central diabetes insipidus (CDI) with polydipsia, polyurea and high ESR level for which desmopressin intranasal spray have prescribed for 4 weeks. In September 2005, she presented the complaints of back pain and on the basis of MRI spine she was diagnosed to have transverse myelitis (TM) (vascular origin) which was recovered by pulse steroid tapering therapy at 1 gram methylprednisolone for 3 days followed by 500 mg for 2 days intravenously. At the same time she presented steroids (given for SLE) induced diabetes mellitus; treated by metformin and glipizide. She came to hospital for evaluation of dyspnea and hiccough in July 2008. That time her parents were added that she drinks abnormal amounts of water from childhood and increased quantity/volume for last 15 days; 5-6 liter per day, on the basis of sign and symptoms psychiatry opinion declared obsessive compulsive disorder (OCD); predominantly compulsion which was successfully treated with clomipramine 50 mg twice daily for 4 weeks. In September 2009, she was admitted with loss of vision; ophthalmic consultation was taken that evaluated constriction by Goldman Field's Charting in right [figure 2] and left eyes. She was evaluated to have optic neuritis of right eye and started with prednisolone tapering therapy. On recent admission in October 2013 patient was conscious, co-operative and well oriented to time, place, space and person. Memory and cognition were normal. Physical examination of the limb revealed a reduction in the power of right hip (4/5), knee (3/5), and no power in right ankle (0/5) or toes (0/5) indicating loss of motor

functionality. The weakness was progressive as during the course of admission, patient developed weakness in left lower limb as well. Neurological examination revealed no meningeal irritation however, ataxic gait was observed to the right side. Magnetic resonance imaging of whole brain with and without contrast was found to be normal. Magnetic resonance imaging of spine showed hyperintense T₂ images extending from T₁-T₉ indicative of Syringomyelia or edema. Laboratory investigations found slightly elevated post prandial blood glucose, C – Reactive protein <6mg/L and low Complement C4 level. Visual acuity of both eyes found to be decreased too. Optic examination by Goldman Field's Charting showed constriction of fields in right and left eyes. Neurological examination was assessed by Brainstem Evoked Response Audiometry (BERA), Visual Evoked Potential (VEP), and Somatosensory Evoked Potential (SSEP) which were all found to be normal. Other neurological examinations were found to be normal. On the basis of sign, symptoms and investigations she was diagnosed to have recurrent optic neuritis with optic atrophy of both eyes and suspected multiple sclerosis but the absence of plaques on MRI brain ruled out the multiple sclerosis. Now azathioprine 50 mg daily was added to existing prednisolone therapy with supportive drugs. The patient improved symptomatically and power in both limbs improved. Visual acuity is improving leisurely. Patient was discharged in last week of November and was advised to follow up every month.

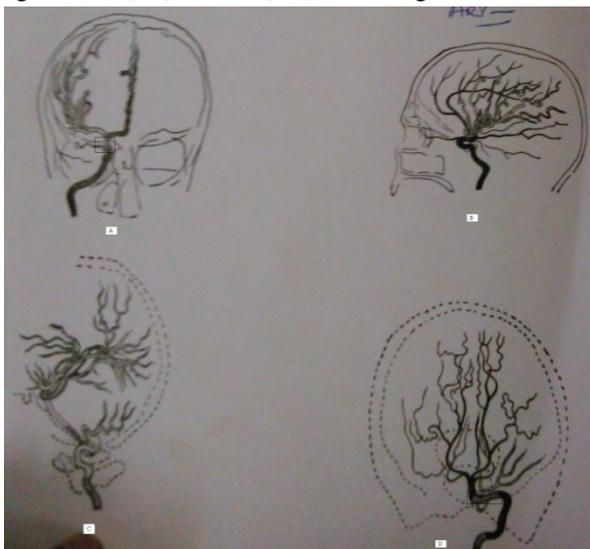


Figure 1: Magnetic Resonance Venography (MRV) (December, 2004) showing the bilateral transverse sinus thrombosis in part A and D indicated by rectangle.

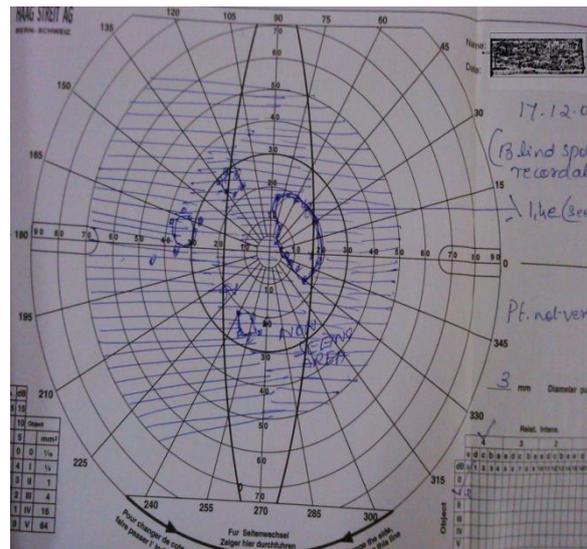


Figure 2: Goldman Field's Charting (September, 2009) showed loss of vision in right eye.

3. Discussion

Parinaud's syndrome is an ophthalmic condition described by abnormalities of eye movements and pupils dysfunction. It also known as dorsal midbrain syndrome; caused by lesion of the upper midbrain stem, characterized by paralysis of upgaze, convergence –retraction nystagmus, eyelid retraction and mid dilated pupils with some neurologic symptoms like “settings sun sign”. Patient history revealed ptosis, giddiness and oscillopsia (classical symptoms of midbrain dorsal syndrome) and MRI imaging was shown upper midbrain tectal lesion.[1] Classically Parinaud's syndrome is associated with young women with multiple sclerosis and cerebral arteriovenous malformations (AVMs) in their 20s-30s. AVMs are the dissociation between arteries and veins in human brain; commonly parental origin.[2] In this case AVMs might lead to cerebral hemorrhage as main risk which cause midbrain tectal lesion (Parinaud's syndrome). This non-traumatic and non-hypertensive midbrain hemorrhage is also the uncommon reason of the dorsal midbrain syndrome. Treatment is directed towards etiology; upgaze palsy, retraction nystagmus and convergence movements can be alleviate with bilateral inferior rectus recessions.

The patient was diagnosed to have SLE with symptoms and ANA positive status when she was primigravida at 37 weeks. SLE is an autoimmune connective tissue disorder affects various systems of body with broad range of symptoms. Pathogenesis of SLE shows apoptosis flaw and production of auto-antigen by both apoptotic cells and necrotic cells. Above process leads to activation of T cells and B cells; their antigens drive immune system that produces SLE symptoms. Various factors are associated with SLE development; association between development of SLE and pregnancy is not so clear. Several evidences suggest that hormones play a role in SLE pathophysiology; childbearing age is circumstantially evidenced. Hormonal changes (increasing estrogen level) promote physiological and immunological alterations that can be associated with increased lupus activity.[3] Pregnancy in lupus have a greater risk of intrauterine growth restriction, preterm delivery, fetal death, preeclampsia and spontaneous miscarriage. Vitamin supplements and corticosteroids (mostly prednisolone) therapy has strong supportive evidences for treatment of SLE in pregnancy; azathioprine can be added.

Patient was also diagnosed to have central diabetes insipidus (CDI) with the symptoms of excessive thirst and polyurea. CDI presents the arginine vasopressin (also known as anti diuretic hormone) deficiency in the body. Leventhal (1991)

and Scolari (1993) suggested that syndrome of inappropriate anti diuretic hormone secretion (SIADH) and CDI appears in SLE because of increased lupus activity; measured by high erythropoietin sedimentation rate (ESR) value and high dsDNA.[4] CDI responds to desmopressin which is prescribed as intranasal spray or oral tablets.

Patient developed transverse myelitis in October 2005 with chief complaints of back pain and weakness in right lower limb with inability to walk. Transverse myelitis is a rare and serious complication of SLE; occurred about 2-3% of patients. Connective tissue disorders like SLE, antiphospholipid antibody syndrome and demyelinating disorders can cause TM. Pathogenesis of TM in SLE is not so clear but literature described immune complex mediated vasculitis or cross-reaction between spinal cord phospholipids and antiphospholipid antibodies or ischemic spinal lesions due to thrombosis.[5] Magnetic Resonance imaging is an important investigation to identifying and characterizing CNS abnormalities in SLE. For this patient MRI of spine showed hyperintense T₂ image extending from T₁-T₉, indicative of possible ischemic etiology. Treatment options are intravenous steroids and plasma exchange with symptomatic therapies depends upon severity. She was initially started on IV prednisolone; later switched to oral therapy.

After 9 months of prednisolone treatment for SLE patient developed diabetes mellitus. 20% to 40% patients without history of diabetes mellitus developed hyperglycemia with long term corticosteroid treatment. Steroids enhance glucose production in liver and impede in peripheral glucose uptake; resulting insulin resistance and hyperglycemia.[6] Condition was treated with metformin and glipizide successfully.

Women with SLE commonly affected by neuropsychiatric manifestations (NP) associated with corticosteroids (CS) therapy after 6 weeks of treatment. Obsessive compulsive disorder (OCD), psychosis, insomnia and dementia cases have been reported; known as CS induced neuropsychiatric disorders (CIDP) or NP-SLE if the symptoms found in SLE patients.[7] Risk of CIDP increased with dose (when daily dose of prednisolone is ≥ 40 mg daily) has been observed in most of the cases. Prednisolone 40 mg daily was prescribed for the patient; but reduced to 30 mg daily she developed CS induced DM and stopped when she diagnosed to have OCD in 2008. Prevalence of OCD increases 10 to 15 folds in SLE patients. OCD is a psychiatric disorder which presents several medical conditions like obsession and compulsion. Compulsion is known as repetitive and ritualistic behavior of patient; they inexplicably

feel they have to; psychiatry consultation explains that she had compulsion predominantly. Selective serotonin reuptake inhibitors are the effective agents used to treat OCD, this patient treated with clomipramine a tricyclic antidepressant which have the better safety and tolerability profile in present conditions.[8]

In September 2009 she experienced sudden significant decrease of vision in her right eye and diagnosed to have optic neuritis. Optic neuritis is an uncommon complication of SLE; occurs in approx 1% of patients. In SLE patients; optic neuritis related progressive visual loss is commonly associated with anterior or posterior ischemic optic neuropathy, a vaso-occlusive disease of optic nerve.[9,10] Histopathological evidences suggested that the focal ischemic lesion occurs due to lupus vasculitis; patient also has possible ischemic etiology. Optic neuritis associated with SLE responds to steroids dramatically or immunosuppressive agents (commonly cyclophosphamide) can be used as alternatives.[11] She was treated with tapered dose of prednisolone (50 mg daily for first week, 40 mg daily for next week and 30 mg daily for continue as maintenance dose) with supportive therapies. In recent admission she diagnosed to have remission SLE and recurrent optic neuritis with optic neuropathy for which azathioprine was added to existing steroids with supportive therapy. Patient was improved symptomatically and vision is improving slowly so she advised to come every month for follow up.

Key Points

1. Transverse myelitis, optic neuritis and OCD together in SLE are to be found as rare combination.
2. All the conditions diagnosed in this patient are related directly or indirectly with etiology, pathogenesis and/or treatment of SLE.
3. Ptosis, giddiness and oscillopsia are the classical symptoms of midbrain dorsal syndrome.
4. Increased estrogen level promotes physiological and immunological alterations with lupus activity.
5. Prednisolone tapering therapy has the strong supportive evidences for the treatment of SLE in pregnancy, azathioprine can be added.

References

- [1] Parinaud H. Paralyse des mouvements associés des yeux. *Archives de neurologie*, Paris, 1883, 5: 145-172.
- [2] MayoClinic.org. *Brain AVM (arteriovenous malformation) Symptoms - Diseases and Conditions - Mayo Clinic*. [Online] Available from: <http://www.mayoclinic.org/diseases-conditions/brain-avm/basics> [Accessed 2 Apr 2014].
- [3] D'Cruz DP, Khamashta MA, Hughes GRV. Systemic lupus erythematosus. *Lancet*. 2007; 369 (9561):587-596.
- [4] Leventhal L, Kobrin S, Callegari P. Systemic lupus erythematosus and the syndrome of inappropriate secretion of antidiuretic hormone.. *The Journal of rheumatology*. 1991; 18 (4): 613-616.
- [5] Schulz S, Shenin M, Mehta A, Kebede A, Fluerant M, Derk C. Initial presentation of acute transverse myelitis in systemic lupus erythematosus: demographics, diagnosis, management and comparison to idiopathic cases. *Rheumatology international*. 2012; 32 (9): 2623-2627.
- [6] Clore J, Thurby-Hay L. Glucocorticoid-induced hyperglycemia. *Endocrine Practice*. 2009; 15 (5): 469-474.
- [7] Bhangle S, Kramer N, Rosenstein E. Corticosteroid-induced neuropsychiatric disorders: review and contrast with neuropsychiatric lupus. *Rheumatology international*. 2013; 33 (8): 1923-1932.
- [8] Stein D. Obsessive-compulsive disorder. *The Lancet*. 2002; 360 (9330): 397--405.
- [9] Hackett E, Martinez R, Larson P, Paddison R. Optic neuritis in systemic lupus erythematosus. *Archives of neurology*. 1974; 31 (1): 9.
- [10] Lin Y, Wang A, Yen M. Systemic lupus erythematosus-associated optic neuritis: clinical experience and literature review. *Acta ophthalmologica*. 2009; 87 (2): 204-210.
- [11] Singh A, Khera K, Inam S, Hande H. Herpes simplex keratitis-induced endophthalmitis in a patient with AIDS with disseminated tuberculosis. *Case Reports*. 2014; 2014(feb27 1):bcr2013202804-bcr2013202804.