

# Subacute sclerosing panencephalitis: Hyper acute variant

<sup>1</sup>Anupriya Arthur *MS (Ophthalmology)*, <sup>2</sup>RohithNinan Benjamin *DM (Neurology)*, <sup>2</sup>Prabakhar AppaswamyThirumal *DM (Neurology)*, <sup>3</sup>Pavitra Mannam *MD (Radiology)*, <sup>2</sup>Sanjith Aaron *DM (Neurology)*

<sup>1</sup>Department of Ophthalmology, <sup>2</sup>Neurology Unit, Department of Neurological Sciences, & <sup>3</sup>Department of Radiology, Christian Medical College & Hospital, Vellore, Tamil Nadu, India

## Abstract

Subacute sclerosing panencephalitis (SSPE) usually presents insidiously. Acute presentations with a fulminant course can occur. However hyper acute presentations with a non-progressive course have not been reported. Here we describe two cases that had hyper acute presentation with occipital involvement misdiagnosed initially as ischemic infarct. One case remained stable for 4 years and then had a fulminant course and patient succumbed; the other patient continued to remain stable at 2 year follow up. In countries where SSPE is prevalent, it is important to be aware of such a variant of SSPE.

**Keywords:** Sub-acute sclerosing panencephalitis, cortical visual impairment, stroke mimics

## INTRODUCTION

As the name implies, subacute sclerosing panencephalitis (SSPE) presents insidiously and progresses slowly. Rarely it can present acutely with a fulminant course.<sup>1</sup> However hyperacute presentations which remain non-progressive for years has not been reported. Such presentations can be mistaken for an acute ischemic stroke both clinically and radiologically. Here we present two cases of SSPE whose initial presentation was hyperacute impairment in visual functions due to occipital lobe lesions. Due to the acute presentation and the radiological findings both these patients were treated as having ischemic stroke. Moreover, after the initial symptoms, these patients had a stable course not exhibiting any other symptoms or signs of SSPE for the next few years.

## CASE REPORTS

### Case 1

A 26-year-old woman had sudden onset of reading difficulty an hour into a written examination; she suddenly noticed that she was unable to read the words on the question paper. She was able to see the paper outline, and the desk as well as other people sitting around her. She had deciphering single alphabets, but was able to write what she

wanted to although she could not read what she had just written. She required the help of the invigilator who read the question for her, and thus was able to complete the examination. She was able to catch a bus and return home by herself. By the same evening she could see single alphabets one at a time. She consulted an ophthalmologist who could not detect any abnormality and her symptoms were attributed to stress and fatigue. However, when her deficits persisted she was referred to a referral medical centre.

On clinical examination, her unaided visual acuity was 6/6 (J1); her colour vision was trichromatic, the anterior segment examination was normal and there was no relative afferent papillary defect. The cup-disc ratio was 0.3 with healthy neuroretinal rims and a normal macula. Evaluation of visual fields showed right homonymous hemianopia (Figure 1, Baseline). Optical coherence tomography of the retinal nerve fibre layer was normal. The macula showed normal foveal contour and thickness.

On visual field examination, she had right macular sparing homonymous hemianopia and simultanagnosia. She had inability to see and appreciate the meaning of the whole visual array but was able to see and recognize the individual parts. When shown a bottle with water, she had difficulty ascertaining the level of water in the bottle without intense concentration. She could

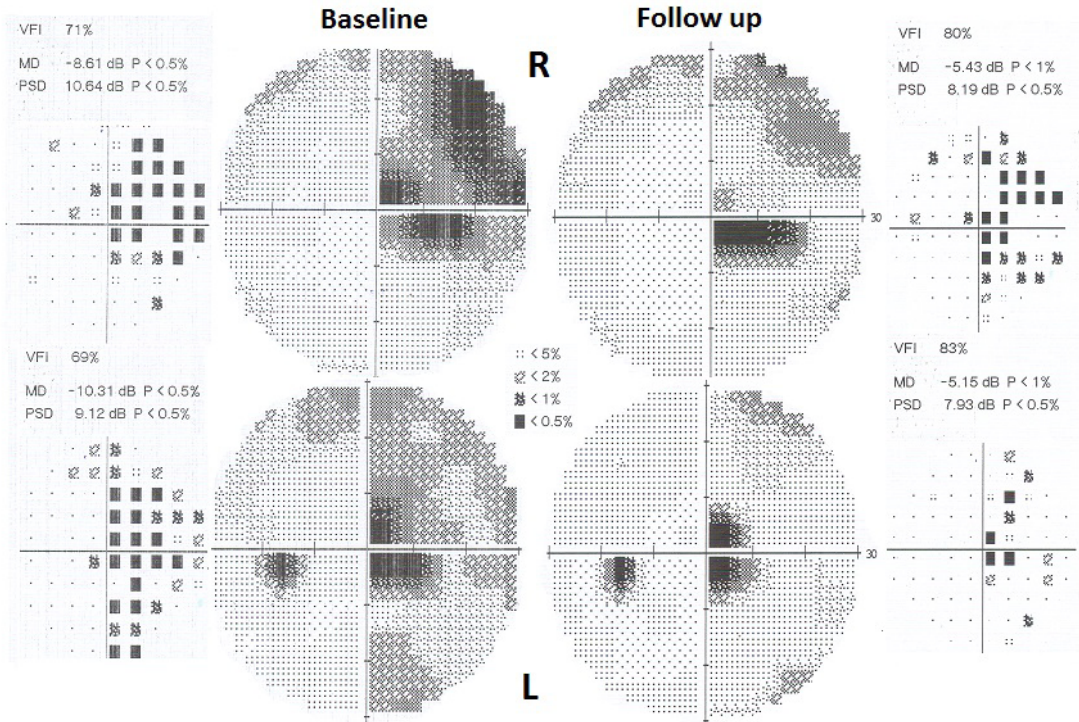


Figure 1. Case 1, visual fields at baseline showing a right homonymous hemianopia and at 4 years showing mild improvement in the same

not tell how many people were present in her room but could identify each individual. She had difficulty gauging the exact position of the objects, suggesting that she had optic ataxia. She had topographagnosia and difficulty remembering landmarks. She was able to draw a sketch of her neighbourhood and mark where her house was; but when shown a photo with the front view of her house taken from a distance with some of the nearby buildings, she was unable to find the house even when prompted to look at the grocery shop near her house. There were no findings to suggest visual agnosia, prosopagnosia, achromatopsia or akinetopsia. She was able to read only with intense concentration.

She reported mild impairment of memory, especially recent memory for visual recall. However, objective testing (Getman-Henderson-Marcus Test of Visual Recall) did not reveal any deficiency. The above deficits were localised to the lower and middle visual processing centres in the parietooccipital cortex. The presence of simultanagnosia suggested bilateral occipitoparietal disease. The initial MRI scan showed T2W hyperintense changes involving the occipital lobes, left more than right. These areas were hyperintense on FLAIR and DWI/

ADC sequences, suggestive of cytotoxic oedema. These changes were in the areas supplied by the posterior cerebral artery. (Figure 2A)

Due to the acute presentation and the imaging findings; stroke in the young was considered. Detailed investigations including transoesophageal echocardiogram, vasculitic and prothrombotic workups were negative.

Over the next 4 years she reported subjective improvement in her vision, and was able to read and write without any problem and there was no history of any field deficits. Objective testing with a repeat visual field mapping confirmed this (Figure 1, follow up)

A follow up MRI done after 4 years showed T2 hyperintensity and volume loss in the left occipital lobe; DWI and ADC maps showed low signal and high signals respectively. (Figure 2B,C,D)

A year later, she had multifocal seizures after a short febrile illness. Following which she developed altered sensorium and was unable to recognise her family members or to communicate. Her condition rapidly worsened. MRI showed signal changes into the left temporal and insular regions with swelling and hyperintensity that was seen also in the right occipital lobe (Figure 2E,F,G,H). Over the next 10 days she developed features of impaired frontal lobe function.

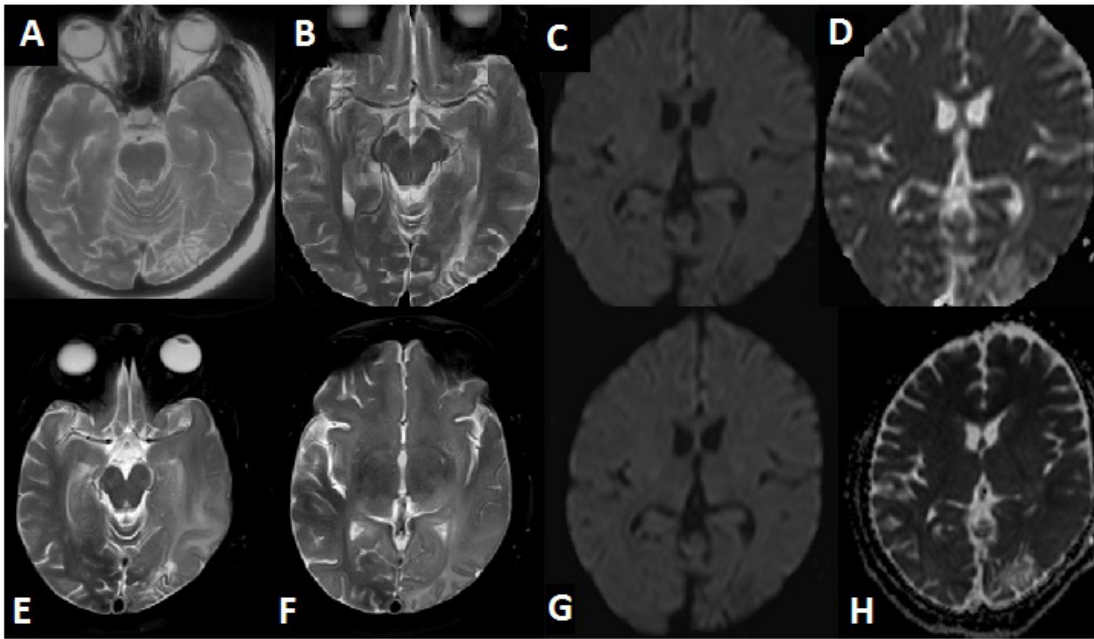


Figure 2. (A). MRI brain T2W imaging at the time of onset of symptoms of Case 1 showing left occipital lobe changes suggestive of an infarct. (B). Follow up imaging after 4 years showing T2 W image with hyperintensity and volume loss in the left occipital lobe (C, D). DWI and ADC imaging with low signal and high signal in the corresponding region respectively suggestive of a chronic infarct (E, F). Imaging done after another year when the patient developed neurological worsening; T2W Imaging showing progression in the areas of hyperintensity in the occipital lobe with spread of signal changes into the left temporal and insular regions, swelling and hyperintensity are also involving the right occipital lobe (G, H). The DWI and ADC of the corresponding regions show low signal on DWI and high signal on ADC, the new areas of involvement in the left temporal region do not demonstrate signal changes on either DWI or ADC

A full vasculitis work up was normal; cardiac evaluation did not show any valvular pathology or right to left shunt. Her blood cultures were negative. EEG showed bilaterally symmetrical, regular high voltage (300 mV) synchronous periodic complexes, occurring at 5 second intervals.

The CSF study showed 8 cells (98% lymphocytes). Oligoclonal bands were present with albumin quotient of 4.44 and IgG index of 3.21. Measles virus indirect immunofluorescence (IFA) was positive for IgG in both blood and CSF. The serum titre was 40 and CSF titre 14. The serum : CSF ratio was 10 (ratio < 64 is considered significant ). There was no history of measles infection and she had received measles vaccinations. She progressively worsened to decortication and was intubated for airway protection. She rapidly progressed to decerebrate responses, pupillary anisocoria and expired shortly after.

## Case 2

A 22-year-old man presented with sudden onset of “blindness” while he was walking down the street in the afternoon. There was no difference in vision for near or far objects. He called out for help and was taken inside a nearby shop where he could only appreciate bright light. He was taken to a tertiary care hospital where an MRI was done and showed bilateral, near symmetric swelling and hyperintensity in the occipital lobes, the DWI sequence showed increased signal intensity and the ADC map showed pseudo-normalisation in the same regions. (Figure 3 A, B, C) He was treated as a case of young stroke with occipital infarcts, and occlusions of both the posterior cerebral arteries was suspected. A detailed ophthalmologic examination showed visual acuity of fingers counting at 1 metres in the right eye and finger counting at ½ metre in the left eye, with accurate projection in all quadrants. Colour vision was achromatic. The anterior segment examination was normal with no relative afferent papillary

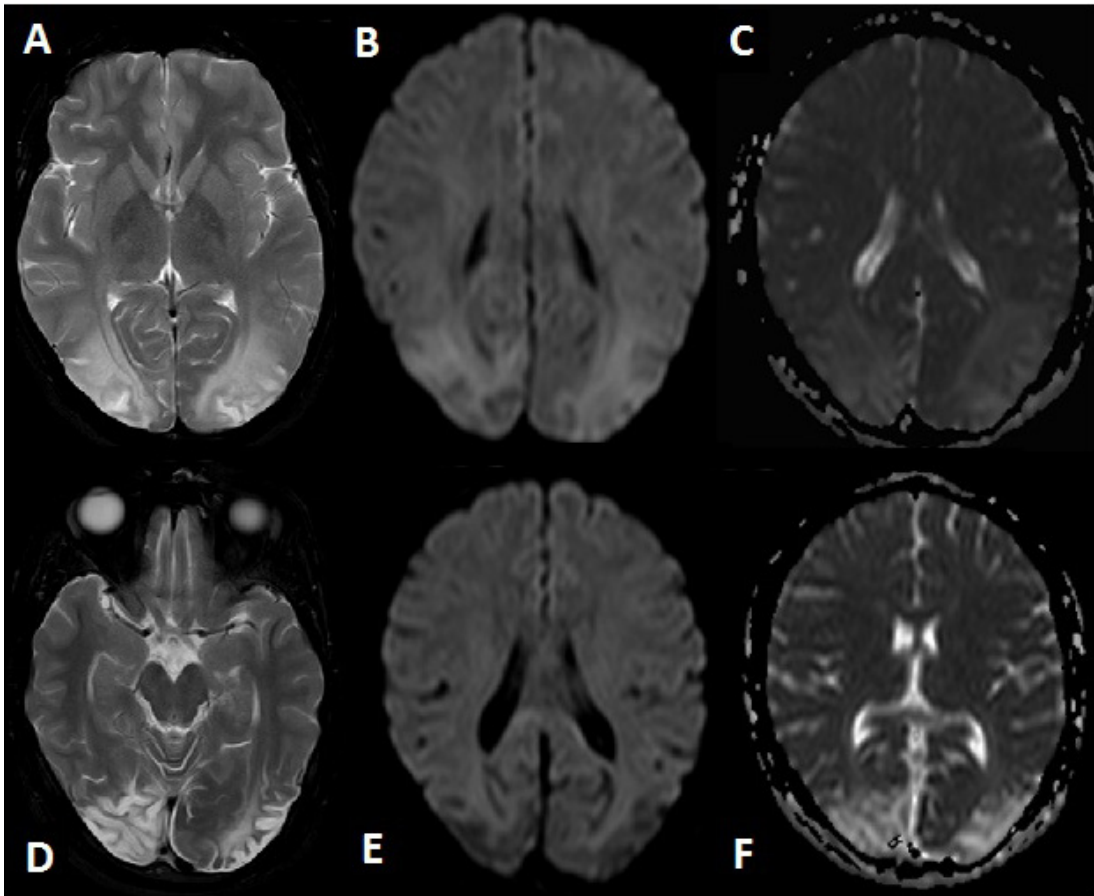


Figure 3. (A). T2 W image of Case 2 showing bilateral, near symmetric swelling and hyperintensity in the occipital lobes bilaterally. (B). DWI showing increased signal intensity in the corresponding areas of the occipital lobes. (C). ADC map showing pseudo normalisation in the same location. (D). Follow up imaging at 14 months interval; T2 W images show residual hyperintensity and mild volume loss in the occipital lobes bilaterally. (E). DWI and (F). ADC map showing low signal and increased signal respectively similar

defects. The fundal examination showed normal cup disc ratio (0.4) with normal macula. Optical coherence tomography of the retinal nerve fibre layer was normal. All investigations towards an aetiology for young stroke, including complete prothrombotic work up, genetic markers of thrombosis, and transcranial Doppler bubble study (using head frame) were found to be negative. CSF examination showed total WBC 13/cumm3 (98% lymphocytes and 2% 98% monocytes 2%), total RBC 2/cumm3, glucose 60 mg/dL, protein 64 mg%. Measles virus indirect immunofluorescence (IFA) showed positive IgG in both blood and serum with titre of 40 in serum and CSF titre of 2, with serum to: CSF ratio of 20 (ratio of < 64 is considered significant). The EEG (including a diazepam enhanced EEG recording) was normal.

He had history suggestive of measles in his childhood though his vaccination status was not

clear. The patient was started on isoprinosine (Inosiplex) and amantadine. At eight months follow up, the patient's vision was unchanged. There were no new symptoms and a repeat EEG was normal. MRI was repeated after 14 months with T2 weighted images showing residual hyperintensity and mild volume loss in the occipital lobes bilaterally, DWI and ADC maps showing low signal and increased signal respectively similar to that seen in chronic infarcts (Figure 3, D, E, F). This patient remained stable without any new symptoms after 2 years of follow up.

## DISCUSSION

In patients with acute cortical visual, the usual differentials considered are: (1) Top of the basilar syndromes with involvement of the paramedian visual cortices; (2) Posterior

reversible encephalopathy syndrome (PRESS) with white matter oedema, usually sparing paramedian brain parenchyma; (3) Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS); (4) Cerebral venous thrombosis causing haemorrhagic infarcts with edema; (5) Demyelinating diseases like acute disseminated encephalomyelitis (ADEM) and multiple sclerosis.

In both our patient the MR angiogram did not show any narrowing or beading to suggest vasculitis or PRESS. The MR venogram was not suggestive of any venous thrombosis. There were no white matter lesions to suggest any demyelinating diseases like MS, ADEM or PRESS. The lactate levels were normal and there was no sparing of the deep white matter, or MRI findings disappearing with improvement of clinical symptoms to suggest a mitochondrial disorder like MELAS.

When SSPE is clinically suspected in a patient with atypical presentation, early diagnosis may be difficult. The EEG may be normal in the early stage. The CSF analysis may not show any pleocytosis, and the CSF glucose and protein may be normal. However intrathecal synthesis of measles antibodies due to the persistence of measles virus in the central nervous system is reflected both in the CSF and serum. Measles antibody titres should be checked both in the serum and CSF. CSF globulin levels may be raised (> 20% of the total CSF protein). Anti-measles antibody titres greater than or equal to 1:4 or a ratio greater than or equal to 1:256 in serum is often the only diagnostic marker in the early stage.

Neurologic complications associated with measles include: (1) Measles encephalitis; usually occurring within the first 2 weeks of the rash with the CSF showing a lymphocytic pleocytosis; (2) Acute disseminated encephalomyelitis (ADEM), an autoimmune demyelinating disease against the myelin basic protein triggered by measles infection<sup>2</sup>; which usually occurs during the recovery phase; (3) Subacute measles encephalitis (SME)<sup>3,4</sup> or measles inclusion body encephalitis (MIBE), which is usually seen after 1 to 6 months after measles infection in children and immunocompromised adults. The condition has a fulminant course with refractive seizures and high mortality. The CSF picture is normal with no anti-measles antibodies detected; (4) Subacute sclerosing panencephalitis caused by long-term measles infection of the central nervous system.

Vision can be affected in SSPE and the

pathology can be anterior or posterior. Anterior visual symptoms can occur due to chorioretinitis or optic neuritis.<sup>5,6</sup> Cases of sudden loss of vision bilaterally have been described due to chorioretinitis preceding neurological symptoms.<sup>7</sup> Posterior visual loss can occur in SSPE as a result of occipital lobe involvement. In their series, Khadilkar *et al.*<sup>8</sup> reported 40% cases of SSPE presented with uncommon features like vision loss, seizures, and behavioural disturbances. Parieto-occipital involvement was a common cause of their visual symptoms. In SSPE, the parieto-occipital region of the brain is most severely affected. Later on, the pathology spreads to involve the anterior portions of cerebral hemispheres, subcortical structures, brainstem, and spinal cord. In the early stages there can be extensive demyelination resulting from viral attack on the oligodendrocytes with subsequent neuronal degeneration and cortical atrophy.<sup>9</sup> There are case reports of SSPE presenting with acute visual loss only, due to occipital lobe involvement. However in 2 of them<sup>10,11</sup> other neurological manifestations of SSPE were noted within 3 months and in one, radiology showed that other areas were already involved at presentation.<sup>12</sup> In both our patients, their clinical conditions remained stable for years after the initial hyperacute presentation. Both did not have any of the features to classify them even as modified Jabbour classification Stage I<sup>13</sup> (Table 1)

Ten percent of SSPE patients have a fulminant course.<sup>14</sup> However, in this rapidly evolving subset of patients, acute visual loss due to occipital lobe involvement is uncommon. Our patients do not fall in the fulminant subgroup of SSPE which is described in patients developing at least 66% neurologic disability (as measured by the neurologic disability index) in the first three months or death within six months.<sup>15</sup>

In patients with adult onset SSPE; where the initial symptom of SSPE manifest after 18 years of age, visual symptoms are known to occur early and often is the initial manifestation. Some of this adult onset SSPE cases have a protracted course. In a retrospective study from India<sup>16</sup>, 2

#### **Table 1: Modified Jabbour classification**

- Stage I: Mental and behavioral changes, forgetfulness, irritability and lethargy
- Stage II: Myoclonic jerks, dyskinesia, choreoathetosis, ataxia
- Stage III: Decerebrate rigidity and decorticate rigidity.
- Stage IV: Severe loss of all cortical function, flexion posturing of limbs and mutism.

out of 39 adult onset SSPE cases presented with impaired vision. In another series Singer *et al.*<sup>17</sup> noted ophthalmological symptoms as the first complaint in 8/13 (61%) cases of SSPE. In another retrospective analysis<sup>18</sup> of 34 patients presented with visual symptoms, however, in none of them a hyperacute presentation was noted. Except for a longer interval between measles infection and the presence of the ophthalmic symptom, other clinical and radiological profiles were similar to those of childhood onset SSPE.

Verma *et al.*<sup>1</sup> reported two patients in whom the symptoms were precipitated by viral infections. In one patient, the neurological symptoms developed after dengue infection and in other after varicella zoster. Concurrent viral illness may have suppressed the immunity unmasking the SSPE.

In conclusion, we described two cases of adult onset SSPE, where the initial symptoms were visual. Both our cases were unique since unlike the usual adult onset SSPE; (1) the onset of symptoms were very abrupt and after the onset, (2) the clinical course was relatively non-progressive for years. (3) Even years after their initial symptoms, they did not have any features to classify them as Stage I on modified Jabbour classification for SSPE. Clinicians need to be cognizant of such hyper acute and relatively non-progressive variant of sub-acute sclerosing panencephalitis and should include it in the differential diagnosis of acute cortical visual loss.

## DISCLOSURE

Financial support: None

Conflicts of interest: None

## REFERENCES

1. Verma R, Sharma P, Kumar D, Vidhate MR. Acute fulminant subacute sclerosing panencephalitis in two patients: Dual viral hit hypothesis. *Ann Trop Med Public Health* 2012;5:605-8
2. Johnson RT, Griffin DE, Hirsch RL, *et al.* Measles encephalomyelitis--clinical and immunologic studies. *N Engl J Med* 1984; 310:137.
3. Freeman AF, Jacobsohn DA, Shulman ST, *et al.* A new complication of stem cell transplantation: measles inclusion body encephalitis. *Pediatrics* 2004; 114:657-60.
4. Mustafa MM, Weitman SD, Winick NJ, *et al.* Subacute measles encephalitis in the young immunocompromised host: report of two cases diagnosed by polymerase chain reaction and treated with ribavirin and review of the literature. *Clin Infect Dis* 1993; 16:654-60
5. Johnston HM, Wise GA, Henry JG. Visual deterioration as presentation of subacute sclerosing panencephalitis. *Arch Dis Child* 1980;55:899-901.
6. Tandon R, Khanna S, Sharma MC, Seshadri S, Menon V. Subacute sclerosing panencephalitis presenting as optic neuritis. *Indian J Ophthalmol* 1999;47:250-2
7. Sharma S, Chanana B, Gulati S, Venkatesh P and Singh S. Acute Bilateral Vision Loss as the Presenting Feature of Subacute Sclerosing Panencephalitis. *Indian J Pediatr* 2009; 76 (9):952-3.
8. Khadilkar SV, Patil S G, Kulkarni K S. A study of SSPE: early clinical features. *J Pediatric Neurol* 2004; 2(2):73-7.
9. Allen IV, McQuaid S, McMahon J, *et al.* The significance of measles virus antigen and genome distribution in the CNS in SSPE for mechanisms of viral spread and demyelination. *J NeuropatholExpNeurol* 1996;55:471-80.
10. Kabra SK, Bagga A, Shankar V. Subacute sclerosing panencephalitis presenting as cortical blindness. *TrpDoct* 1992;22:94-5.
11. Sharma S, Sawhney IM, Lal V, Gupta SK. Subacute sclerosing panencephalitis presenting as cortical blindness. *J Assoc Physicians India* 1995;43:434.
12. Dundar NO, Aralasmak A, Gurer IE, Haspolat S. Subacute sclerosing panencephalitis case presenting with cortical blindness: early diagnosis with MRI and MR spectroscopy. *ClinNeuroradiol* 2014;24(2):185-8.
13. Jabbour JT, Duenas DA, Severe JL, Krebs H, Horta-Barbosa L. Epidemiology of subacute sclerosing panencephalitis. *JAMA* 1972; 220:959-62.
14. Risk WS, Haddad FS. The variable natural history of subacute sclerosing panencephalitis: a study of 118 cases from the Middle East. *Arch Neurol* 1979;56:610-4.
15. PeBenito R, Naqvi SH, Arca MM, Schubert R. Fulminant subacute sclerosing panencephalitis: Case report and literature review. *ClinPediatr (Phila)* 1997;36:149-54.
16. Prashanth LK, Taly AB, Ravi V, Sinha S, Arunodaya GR. Adult onset subacute sclerosing panencephalitis: Clinical profile of 39 patients from a tertiary care centre. *J NeurolNeurosurg Psychiatry* 2006;77:630-3.
17. Singer C, Lang AE, Suchowersky O. Adult onset subacute sclerosing panencephalitis: case reports and review of the literature. *MovDisord* 1997;12:342-53
18. Jagtap SA, Nair MD, Kambale HJ. Subacute sclerosing panencephalitis: A clinical appraisal. *Ann Indian AcadNeurol* 2013;16(4):631-3.