Boomerang sign: Clinical significance of transient lesion in splenium of corpus callosum

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Abstract

Transient signal abnormality in the splenium of corpus callosum on magnetic resonance imaging (MRI) is occasionally encountered in clinical practice. It has been reported in various clinical conditions apart from patients with epilepsy. We describe 4 patients with different etiologies presenting with signal changes in the splenium of corpus callosum. They were diagnosed as having progressive myoclonic epilepsy (case 1), localization-related epilepsy (case 2), hemicrania continua (case 3), and postinfectious parkinsonism (case 4). While three patients had complete involvement of the splenium on diffusion-weighted image ("boomerang sign"), the patient having hemicrania continua showed semilunar involvement ("mini-boomerang") on T2-weighted and FLAIR image. All the cases had noncontiguous involvement of the splenium. We herein, discuss these cases with transient splenial involvement and stress that such patients do not need aggressive diagnostic and therapeutic interventions. An attempt has been made to review the literature regarding the pathophysiology, etiology, and outcome of such lesions.

Key Words

Boomerang sign, corpus callosum, diffusion-weighted imaging, epilepsy, hemicrania continua, measles, magnetic resonance imaging, splenium

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Introduction

Transient signal alteration in the splenium of corpus callosum on magnetic resonance imaging (MRI) has been reported in a variety of neurologic and nonneurologic conditions.[1-7] After the first observation in patients with epilepsy by Chason *et al*.,[8] the involvement of the splenium has been described by many authors in neurologic conditions of varied etiologies.[1-8] Splenial lesions are visualized as hyperintense lesions on T2-weighted images, fluid attenuated inversion recovery, and diffusion-weighted MR images. The images remain unaltered by gadolinium administration. Various pathophysiologic mechanisms have been put forth, but none is well proven.[2] It is a self-limiting phenomenon, which subsides over a period, once the underlying disease gets controlled. It may, sometimes, pose problems in the diagnosis and management of patients. Because of its benign nature and complete reversal without any specific treatment, aggressive diagnostic and therapeutic approaches are not needed. We describe 4 cases having different clinical scenario presenting with transient lesions of splenium on MRI.

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Case Reports

Case 1

A 21-year-old man with medically refractory epilepsy, constituted by partial, generalized, and myoclonic seizures for 4 years, presented to us with increase in myoclonic jerks and serial generalized seizures from 1 day. There was suggestion of cognitive impairment from the past 2 years and mild unsteadiness of gait. The patient was loaded with intravenous sodium valproate (30 mg/kg body weight) to which his seizures responded. MRI of the brain showed hyperintensity of the splenium of corpus callosum ("Boomerang sign") on diffusion-weighted image (DWI) [Figure 1d] with decreased apparent diffusion coefficient (ADC) values. T2-weighted image (T2WI), fluid attenuated inversion recovery (FLAIR), and T1-weighted image (T1WI) did not reveal any abnormal signals in splenium of corpus callosum and other areas of brain (except for an incidental cysticercus in left lentiform nucleus) [Figure 1a–c]. Currently the patient's medication regimen included valproic acid (1400 mg/day), levetiracetam (1000 mg/day), and clonazepam (1.5 mg/day). A follow-up MRI done after 6 months revealed disappearance of altered

signals in the splenium on DWI images [Figure 1e]. The routine hematologic and biochemical investigations were within normal limits.

Case 2

A 38-year-old man presented with multiple episodes of left partial seizures with secondary generalization, followed by Todd's palsy. After loading the patient with intravenous sodium valproate (30 mg/kg body weight), an equivalent oral dose of sodium valproate was started. MRI of the brain done next day after admission revealed a well-defined parafalcine space occupying the lesion with perilesional edema [Figure 2a–c]. Also evident was the uniform hyperintensity of the splenium of corpus callosum ("Boomerang sign") on DWI [Figure 2e] with low ADC values. T1WI and T2WI did not reveal any abnormal signals in the splenium of corpus callosum [Figure 2d]. A follow-up MRI done after a week depicted complete disappearance of altered signals in the splenium on DWI image [Figure 2f]. The patient was transferred to the Department of Neurosurgery for further management.

Case 3

A 34-year-old woman, diagnosed as a case of hemicrania continua, presented with progressively increasing headache and loss of complete responsiveness to indomethacin from a week. She was a vegetarian without any significant past history of chronic ailment or drug abuse. Apart from indomethacin (150 mg/day), she was taking 40 mg of verapamil twice daily. The clinical examination was noncontributory without any suggestion of an organic substrate. MRI of the brain was suggestive of a semilunar hyperintensity ("mini-boomerang") on T2WI and FLAIR image involving the posterior part of splenium of corpus callosum [Figure 3a–d]; there was no evidence of restriction on DWI [Figure 3e, f]. Magnetic resonance angiography was normal; however, magnetic resonance venography (MRV) showed lack of proper visualization of veins at the level of vein of Galen [Figure 3g, h]. Serum B12 was found to be low (132 pg/mL). The lady was prescribed a short course of prednisolone, starting with 60 mg/day for 3 days and reduced by 10 mg every fourth day, and the dose of verapamil was increased to 160 mg in two divided doses after checking for any rhythm disturbance. No vitamin supplementation or anticoagulants were prescribed. The lady responded well and follow-up MRI done after 3 months showed complete resolution of the splenial lesion [Figure 3i]; MRV did not reveal any change suggesting the anomaly to be a normal variant.

Case 4

A 10-year-old school boy presented with a history of high-grade fever, rash, headache, and vomiting 20 days before admission. The fever subsided in 7 days but the patient developed right-sided extrapyramidal symptoms in the form of tremor, rigidity, and bradykinesia predominantly involving the upper limb. The patient did not have seizures or altered sensorium. On examination, the patient had cog-wheel rigidity and

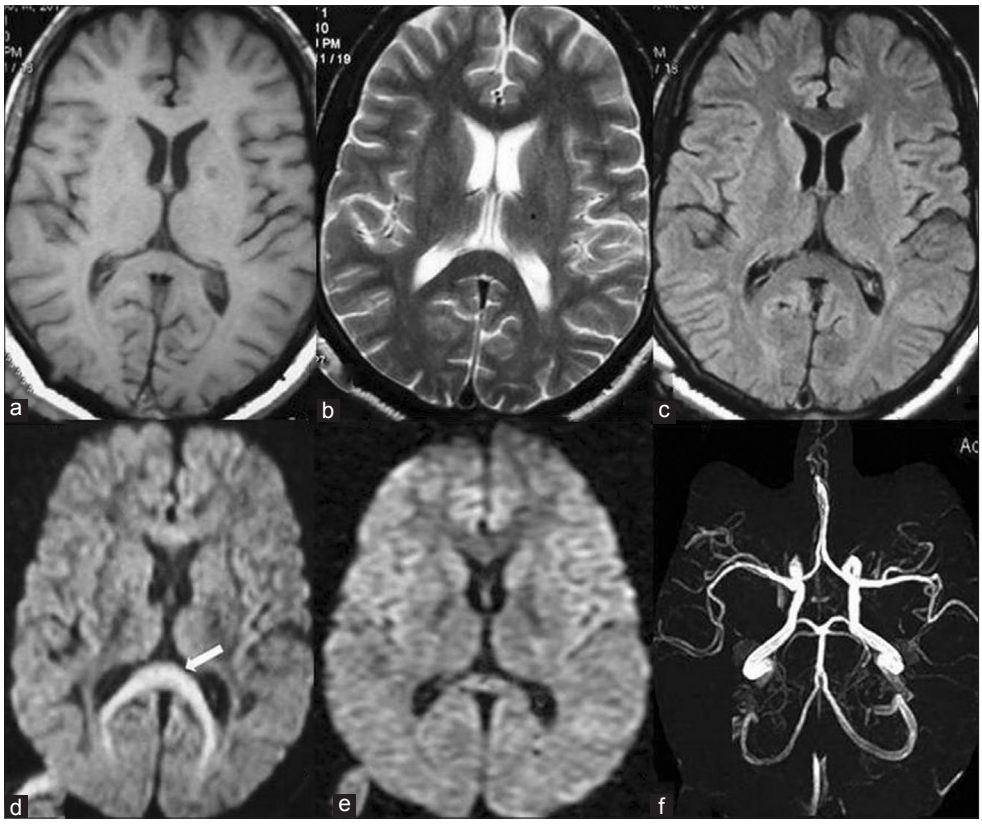

Figure 1: Magnetic resonance imaging and magnetic resonance angiography (Brain) of case 1, with refractory epilepsy, showing normal, axial, T1-weighted (a), T2-weighted (b) and fluid attenuated inversion recovery (c) images with increased signal intensity of the entire splenium of corpus callosum ("Boomerang sign") on diffusion-weighted image (d); repeat diffusion-weighted image (e), done at 6 months, showing complete resolution of abnormal signals involving the splenium. Magnetic resonance angiogram (f) did not reveal any abnormality

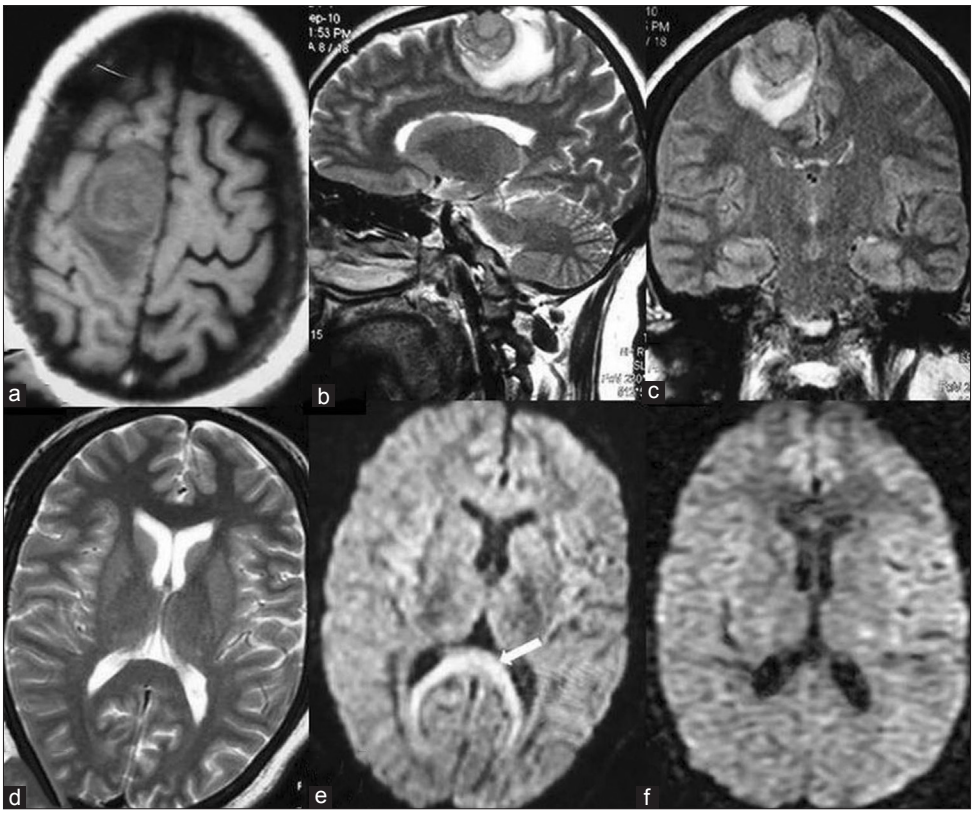

Figure 2: Magnetic resonance imaging (Brain) of case 2, with localization related epilepsy, showing a right-sided well defined parafalcine extra-axial space occupying lesion, with perilesional edema, in T1-weighted axial (a), T2-weighted sagittal (b) and coronal (c) images. T2-weighted image (d), axial section, focussing on the corpus callosum appears normal while a uniform hyperintensity of the splenium of corpus callosum ("Boomerang sign") on diffusion-weighted image (e) is evident. Follow up diffusion-weighted image (f), done at 1 week, depicts complete disappearance of altered signals in the splenium

bradykinesia. MRI of brain done at the onset of extrapyramidal symptoms revealed T2WI hyperintense signals involving bilateral substantia nigra more pronounced on left side [Figure 4a] without restriction on DWI. Also noted was the uniform hyperintensity of the splenium of corpus callosum ("Boomerang sign") on DWI [Figure 4d] with low ADC values. T1WI and T2WI images denoted normal signals in the splenium of corpus callosum [Figure 4b, c]. The serology for various viruses, including Japanese Encephalitis virus in blood and cerebrospinal fluid was ordered. The serological test for measles virus was positive in blood with raised IgM antibody titers. The extrapyramidal symptoms of patient improved with pramipexole. Follow-up MRI performed 10 days after the previous one, revealed complete disappearance of altered signals in splenium [Figure 4e]. The T2 hyperintensities involving bilateral substantia nigra, however, persisted [Figure 4f].

Discussion

Corpus callosum is the largest commissural white matter bundle in the brain containing 200–250 million interhemispheric fibers.[9] Major portion of the corpus callosum receives its arterial supply from the carotid system except for splenium, which is supplied by the vertebrobasilar system.[3] Several pathologic conditions, such as multiple sclerosis, Marchiafava–Bignami disease, tumors, ischemia, leukodystrophy, and HIV-related encephalopathy, may affect the corpus callosum, producing permanent changes.[2]

Various transient peri-ictal abnormalities on MRI have been documented in the literature with or without involvement of splenium of corpus callosum.[10] Transient peri-ictal signal abnormality involving solely the splenium of corpus callosum on MRI is not frequently encountered in clinical practice. So, the treating physician might be tempted to subject the patient to unnecessary diagnostic and therapeutic interventions. The occurrence of this abnormality was first described by Chason *et al*. as a transient post-ictal focal edema denoting transhemispheric propagation of seizure through the corpus callosum.[8] Since then, various etiologic factors have been associated with the transient hyperintensities of the splenium [Table 1].

As mentioned earlier, several hypotheses have been put forward to explain transient changes in splenium. The association of these changes with epilepsy is complex. Breakdown of the blood–brain barrier (BBB), producing transient focal edema has been implicated by some authors in patients having seizures.[8,11] In contrast, Kim *et al*. attributed it to "possible anti-epileptic drug (AED) toxicity induced reversible demyelination".[12] Mirsattari *et al*. and Gurtler *et al*. suggested the role of cytotoxic edema brought on by ischemia related to abrupt cessation of long-term AED.[13,14] They postulated that sudden cessation of AED could lead to alteration of the arginine–vasopressin (AVP) system, resulting into hydric imbalance. Apart from carbamazepine, several antiepileptic drugs have been found to interfere with the AVP system.[15]

Table 1: Clinical conditions associated with transient splenial hyperintensity

Possible causes	References
Epilepsy	
Seizures	5, 8, 10-15, 19
AED overdose	
Abrupt drug withdrawal	
Infections	
Encephalitis	1, 3, 4, 16, 17, 18, 23
Salmonella	
Malaria	
Rota virus infection	
Demyelinating	
ADEM	2, 24
SLE	
Metabolic	
Hypoglycemia	1, 2, 6, 17
Hypo-/hypernatremia	
Renal failure	
Vascular	
Cerebrovascular disease	20*, 21*, 25
Post-cardiac arrest	
Hypertensive encephalopathy	
Pre-eclampsia	
Posterior reversible encephalopathy syndrome	
Migraine with aura	
Miscellaneous	
Malnutrition-Vitamin B12 deficiency	5, 7, 26
Drug toxicity–cyclosporine, fluorouracil, metronidazole	
High-altitudinal cerebral edema	
Trauma–axonal injury	

ADEM = Acute disseminated encephalomyelitis; AED = Antiepileptic drugs; SLE = Systemic lupus erythematosus. *Studies reporting the involvement of entire splenium ("Boomerang sign"); focal involvement was observed in the rest.

Apart from epilepsy, the transient signal alterations in splenium of corpus callosum have been described in patients with encephalitis/encephalopathy due to various organisms, including recent reports from tick-born and H1N1 encephalitis.[16-18] Tada *et al*. studied reversible splenium lesion in 15 patients with encephalitis/encephalopathy.[3] He speculated that viral antigens or receptors on the antibodies induced by the antigens had specific affinities for receptors on splenial axons, leading to raised inflammatory cytokines, such as interleukin-6, causing inflammation of splenium. Hackett *et al*. reported signal alterations in splenium in patients affected by high-altitudinal cerebral edema.[7] He strongly suggested the role of vasogenic edema involving predominantly the white matter. An explanation for this pathogenic mechanism may be a BBB alteration due to a cerebral capillary hydrostatic pressure increase, which is commonly observed in conditions, such as hypertensive encephalopathy, preeclampsia, posterior reversible encephalopathy syndrome, seizures, and toxic effects of cyclosporine. In contradiction, Oster *et al*. questioned the role of both, AEDs and vasogenic edema, in the development of transient splenial hyperintensities after seizures.[19] He demonstrated increased signal on DWI with low ADC values, which were inconsistent with vasogenic edema as the cause. The changes in splenium were attributed to transient disturbance of energy metabolism and ionic transport in reversible myelin vacuolization or intramyelinic edema. This transient disturbance of energy metabolism and ionic transport was speculated as a result of repeated excessive activity of commissural projections during seizure propagation. The similar mechanism explains the transient hyperintensity of splenium in cases 1 and 2 following serial seizures.

We would like to emphasize an important aspect that is evident from our case 2. Although the space occupying lesion (seizure focus) was also in proximity to the anterior commissural fibers, that is, genu and rostrum of corpus callosum, it was characteristically spared on MRI. We propose that the unique anatomical and physiological property of fibers of splenium of corpus callosum makes it susceptible for transient signal alterations on MRI after seizure propagation. This can be likened to reversible posterior leukoencephalopathy syndrome involving specifically the posterior parts of brain, especially if we consider the blood supply of this area.

The splenium involvement appears hyperintense on T2WI and FLAIR image and iso- or hypointense on T1WI. The changes in DWI appear earlier than the changes in T2WI and FLAIR, as reported by Oster *et al*.,[19] as observed by us in case 1. Involvement of the splenium, based on signal changes, can be divided into two types according to its shape and extent: Oval, circumscribed, with well-defined borders usually located in the middle; or wider, with less regular borders and involving the entire splenium ("Boomerang sign"). In most of the previous case series, the focal involvement of splenium has been documented in MRI done after seizures.[5,11-15] Involvement of entire splenium is occasionally reported, mainly due to hypoxic injury of corpus callosum.[20,21] It's noteworthy to mention that cases 1 and 2 had uniform involvement of splenium of corpus callosum after serial seizures.

Disappearance of signal abnormalities in the splenium of corpus callosum has been documented by various authors and the timing of follow-up MRI performed ranges from 3 days to 1 year.[3,5,11] Conti *et al*. subjected 6 patients with isolated signal changes in splenium of corpus callosum to serial MRIs at 4, 8, and 12 weeks and demonstrated complete disappearance of lesions in 4 patients.[2]

As the changes are transient, the timing of MRI study is very crucial to pick up these abnormalities in splenium and may thus explain the rarity of occurrence in routine MRIs.

We would also like to share our experience of incidental semilunar hyperintensity ("mini-boomerang") involving predominantly the posterior part of splenium on MRI in case 3 [Figure 3a–i]. Such transient signal changes have not been reported in patients of hemicrania continua. Whether the abnormality is a sequel of the basic disease process or is attributable to subtle deviation in MRV with associated low serum B12 in case 3 cannot be said with certainty. Since the response was seen without the use of anticoagulants and vitamin supplementation, this does give a suggestion that some unknown pathophysiological mechanism might be

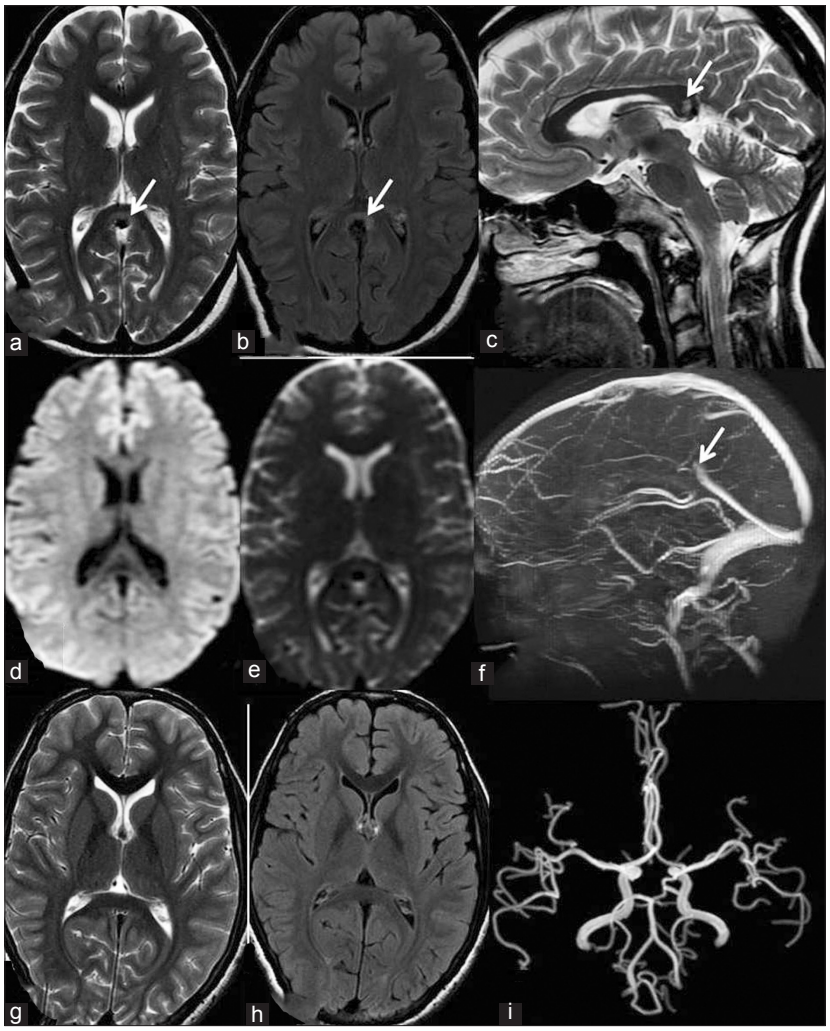

Figure 3: Magnetic resonance imaging, magnetic resonance angiography and magnetic resonance venography (Brain) of case 3, with hemicrania continua, showing semilunar hyperintensity ("mini-boomerang") on axial T2-weighted (a) and fluid attenuated inversion recovery (b) images with a focal hyperintensity on sagittal T2-weighted image (c); there was no evidence of restriction on diffusion-weighted image (d) and the apparant diffusion coefficient map (e) was normal. Lack of proper visualization of veins at the level of vein of Galen was evident on magnetic resonance venogram (f). Repeat T2-weighted image (g) and fluid attenuated inversion recovery image (h) at 3 months showing complete resolution of the abnormal signals in splenium. Magnetic resonance angiogram (i) did not reveal any abnormality

responsible for the occurrence of transient splenial lesion in this patient.

As observed in case 4, the T2 hyperintense signals in the splenium of corpus callosum disappeared in contrast to persistent T2 hyperintensities in substantia nigra on follow-up MRI. This interesting finding points toward different pathogenic mechanisms possible for two abnormalities after measles infection. One of the pathogenic mechanisms discussed above, especially that given by Tada *et al*. after encephalitis/encephalopathy, is more likely responsible for transient changes in splenium.[3] Mito *et al*. reported transient round signal change in the splenium of corpus callosum in 1 of 2 patients with measles encephalitis.[22]

Other possible differential diagnoses of splenial lesions include ischemia, posterior reversible encephalopathy syndrome, diffuse axonal injury, multiple sclerosis, Marchiafava–Bignami disease, lymphoma, and extrapontine myelinolysis.[9] The most important clues to differentiate transient splenium involvement from others are absence of symptoms of hemispheric disconnection (apraxias of the left hand, pseudoneglect, alien left hand, agraphia, alexia, visual apraxias, and so on) and reversibility after control of underlying disease. The importance of clinical setting cannot be overemphasized. Also most other etiologies show paramagnetic contrast enhancement, which is very rarely present with transient splenium involvement.[2]

In summary, transient signal changes in the splenium of corpus callosum appear to be the nonspecific end result of different disease processes of various etiologies with varied pathogenic mechanisms. These lesions may be encountered incidentally while looking for some organic substrate in systemic disorders or most commonly in the post-ictal phase. The predilection for only the splenial part of corpus callosum, with sparing of other parts, needs to be looked into in detail. These lesions of

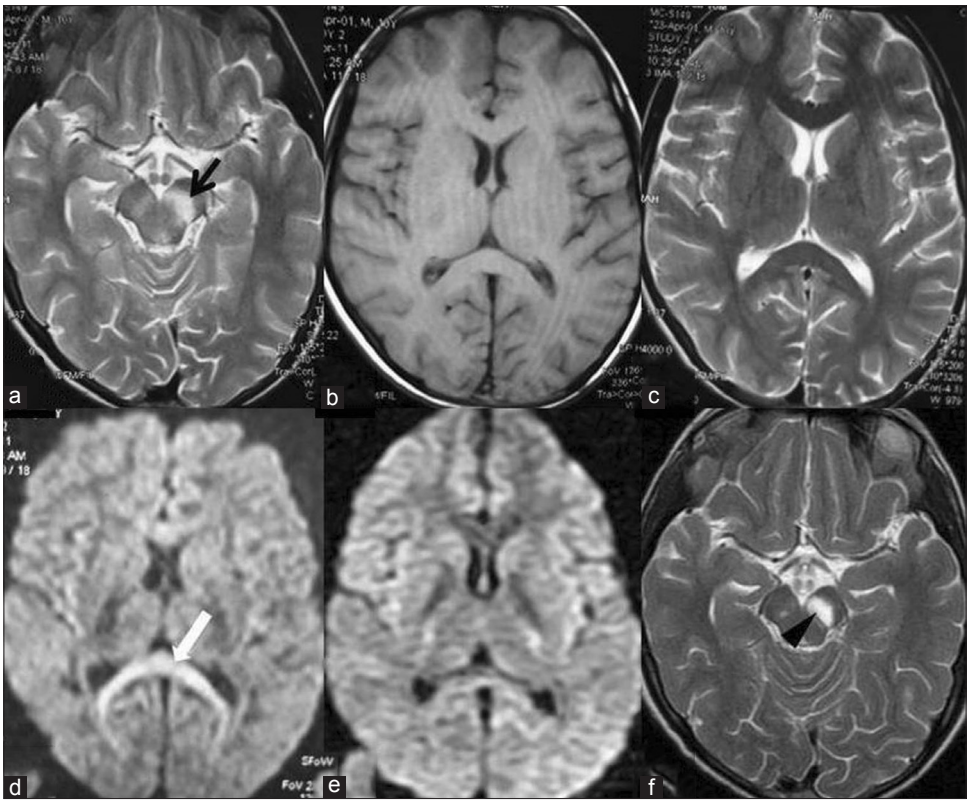

Figure 4: Magnetic resonance imaging (Brain) of case 4, with post-infectious parkinsonism, showing hyperintense signals in bilateral substantia nigra on axial T2-weighted image (a), more pronounced on left side; T1-weighted (b) and T2-weighted (c) images, axial section, focussing on the corpus callosum appear normal while a uniform hyperintensity of the splenium of corpus callosum ("Boomerang sign") on diffusion-weighted image (d) is evident. Repeat diffusion-weighted image (e), done after 10 days, depicting reversibility of lesion involving the splenium of corpus callosum; the hyperintense signals involving the substantia nigra on axial T2-weighted image (f) decreased in size

splenium carry a good prognosis due to their reversibility and should not be confused with serious pathologies.

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