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Dengue fever presenting with acute cerebellitis in an adult patient

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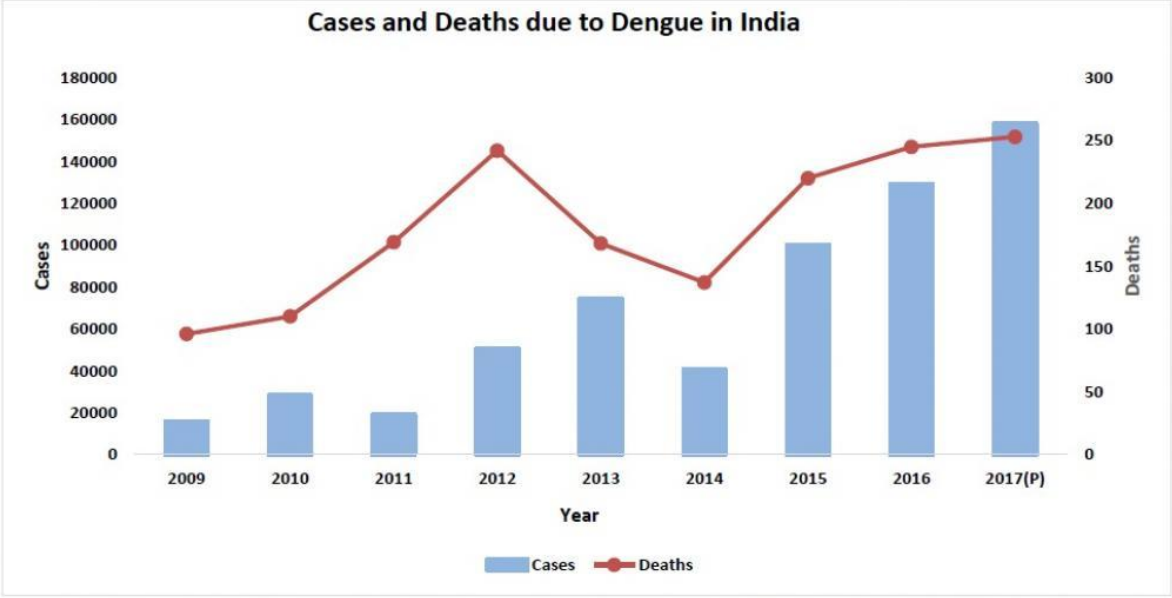
ABSTRACT
Acute cerebellitis is predominantly a disease of children with very few cases reported in adults. It is commonly caused by neurotropic virus and has rarely been reported with dengue virus. A 19-year-old male presented with 20 days history of headache, vomiting and unsteadiness of gait. Patient had a history of fever and arthralgia in the initial illness which resolved spontaneously after 4-5 days. On examination the patient had bilateral cerebellar signs. Magnetic resonance imaging (MRI) of the brain showed faint restricted diffusion in vermis and both cerebellar hemispheres suggesting acute cerebellitis. Lumbar puncture showed a leucocyte count of 10 cells/cumm, glucose 72 mg/dL and total protein 42.6 mg/dL; suggestive of resolving viral encephalitis. Blood serology was negative for IgM of CMV, HSV 1 & 2 and EBV. Dengue IgM antibodies by enzyme-linked immunosorbent assay (ELISA) were positive, confirming a recent dengue infection. He was managed conservatively. There was significant improvement in cerebellar symptoms in one week. We present a case of acute onset, MRI proven transient cerebellitis which was temporally associated with a recent dengue virus infection. Literature search showed only six reported cases of dengue associated cerebellitis in adults making it a rare complication of dengue fever.

Keywords: dengue, cerebellitis, ataxia

INTRODUCTION

Dengue is a viral infection, transmitted by *Aedes aegypti* mosquito with an incubation period of 5 – 6 days[1]. The incidence of dengue has grown dramatically around the world in recent decades. The number of cases reported worldwide increased from 2.2 million in 2010 to over 3.34 million in 2016[1].

In India it is common in the post monsoon season (July, August, and September). In the last decade, the spike in cases of dengue was the highest in 2017, as per the data obtained from National Vector Borne Disease Control Programme (NVBDCP).(Figure 1) [2] With less than 20,000 cases in 2009, cases surged to 188,401 in 2017— more than a 300 per cent spike. When compared to 75,808 cases in 2013, it is more than a 250 per cent spike[2].



Source: Directorate of National Vector Borne Disease Control Programme, Dte.GHS, Ministry of Health & Family Welfare

Figure 1: Cases and deaths due to Dengue in India

Complications of dengue are potentially life-threatening and include dengue hemorrhagic fever, acute liver failure, acute kidney injury, and multi-organ failure. Neurological complications associated with dengue are rare which include aseptic meningitis, encephalitis, myelitis, intracranial hemorrhage and mono/polyneuropathies. Not much data are available to underline the pathophysiology of these neurological manifestations[3].

Acute cerebellitis is usually seen in paediatric age group. Patient usually presents with fever, headache, vomiting and cerebellar signs like nystagmus, ataxia and dysarthria. Complications observed are obstructive hydrocephalus, tonsillar herniation, cerebellar trunk compression, severe cerebellar atrophy[3].

Acute cerebellitis is majorly caused by neurotropic viral infections like Herpes simplex virus (HSV), Epstein Barr virus (EBV), cytomegalovirus (CMV) [4] and only a handful of cases are attributed to dengue virus. This has been a grey area in the ever expanding list of neurological complications of dengue fever. We report an adult patient from North India who presented with MRI proven acute cerebellitis as initial manifestation of dengue fever.

Case

A 19 year old male, from northern part of India, presented to the medical outpatient department of a Delhi based medical college with unsteadiness of gait. The patient was apparently well 20 days prior to admission when he developed high grade fever (39.4°C). It was continuous and associated with chills. Patient also experienced headache and 2-3 episodes of vomiting per day which started three days after the onset of fever. Along with that patient had difficulty in walking and he was swaying on either side. The patient was taken to a local practitioner for his symptoms and was given few oral medications. His fever resolved in five days but his headache and vomiting persisted and his unsteadiness of gait progressed.

After 20 days of his illness, the patient was referred to our hospital for his inability to walk and persistent headache and vomiting.

On admission, the patient was conscious and oriented with a Glasgow coma scale (GCS) score of 15/15. His pulse rate was 86 beats per minute; blood pressure was 118/82mmHg. There was no neck stiffness, skin rash or lymphadenopathy. On neurological examination, he had scanning speech and marked horizontal nystagmus with bilateral dysmetria checked by finger-nose and heel shin tests. Dysdiadokokinesia and incoordination was also

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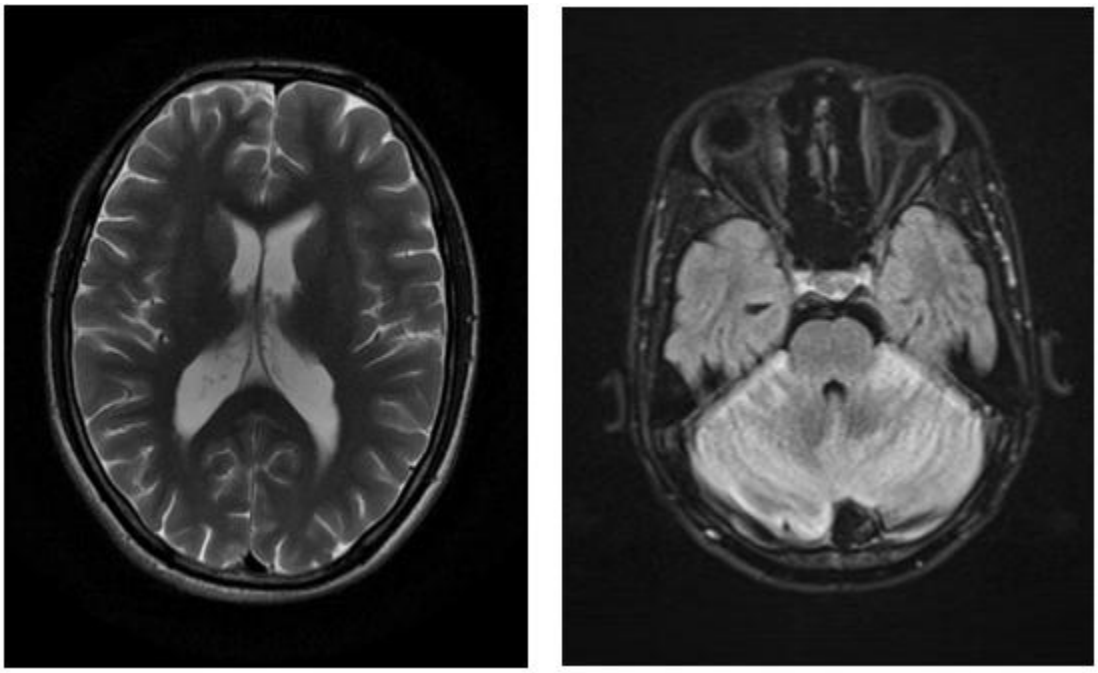
present which was equally observed on both sides. His gait was wide-based and ataxic with a tendency to fall on either side. The rest of the neurological examination including muscle tone, power, deep tendon reflexes and sensation was normal. A diagnosis of acute encephalitis leading to acute cerebellitis was kept provisionally and the patient was investigated for the same. The patient's fundus examination of both eyes was done which showed normal disc with no papilledema. The patient's hemoglobin was 11.7 g/dL (13 – 18 g/dL), hematocrit 44.2% (40 – 50%), total leucocyte count $6.7\times10^3/mm^3$ (4 - 11 $\times10^3/mm^3$), platelet count $314,000/mm^3$ (150,000 – 400, 000/ mm^3). Renal function, liver function, urine examination, blood glucose were normal. His vitamin B12 levels came out to be 1808 pg/mL (190 – 950pg/mL).

Magnetic resonance imaging (MRI) brain showed diffusely increased signal intensity on FLAIR (Figure2 a) and T2W images in bilateral cerebellar hemispheres and cerebellar vermis with corresponding low signal intensity on T1WI. These areas also showed marked diffusion restriction on Diffusion Weighted (DW) images. There was mild mass effect on 4^{th} ventricle with mild dilatation of both lateral (Figure 2 b) and 3^{rd} ventricles. These findings were compatible with cerebellitis with hydrocephalus. The chest X-ray and ultrasound abdomen were normal.



- Image 2 (a): T2 weighted axial image obtained at the time of presentation showed dilatation of bilateral lateral ventricles (arrows pointing to bulging walls of ventricles).
- Image 2 (b): FLAIR axial image at the time of presentation at the level of 4th ventricle shows diffuse hyperintense signal intensity (Arrow) in cerebellum suggestive of cerebellitis.

His cerebrospinal fluid (CSF) examination revealed a total leucocyte count of 10 cells/ mm^3 (0-5 cells/mm^3), all lymphocytes with glucose level 72 mg/dL (45 – 80mg/dL) and total protein levels 42.6 mg/dL (15 – 60 mg/dL). Viral polymerase chain reaction (PCR) in CSF for HSV 1 and 2, CMV, Japanese encephalitis virus (JEV), EBV, adenovirus, varicella zoster and parechovirus were all negative. Serological tests for CMV IgM, HSV 1 & 2 IgM and IgG, EBV IgM were all non-reactive. His CMV IgG and in EBV profile, VCA gp 125 IgG and EBNA 1 IgG were positive denoting remote infection from these virus. Serological tests for human

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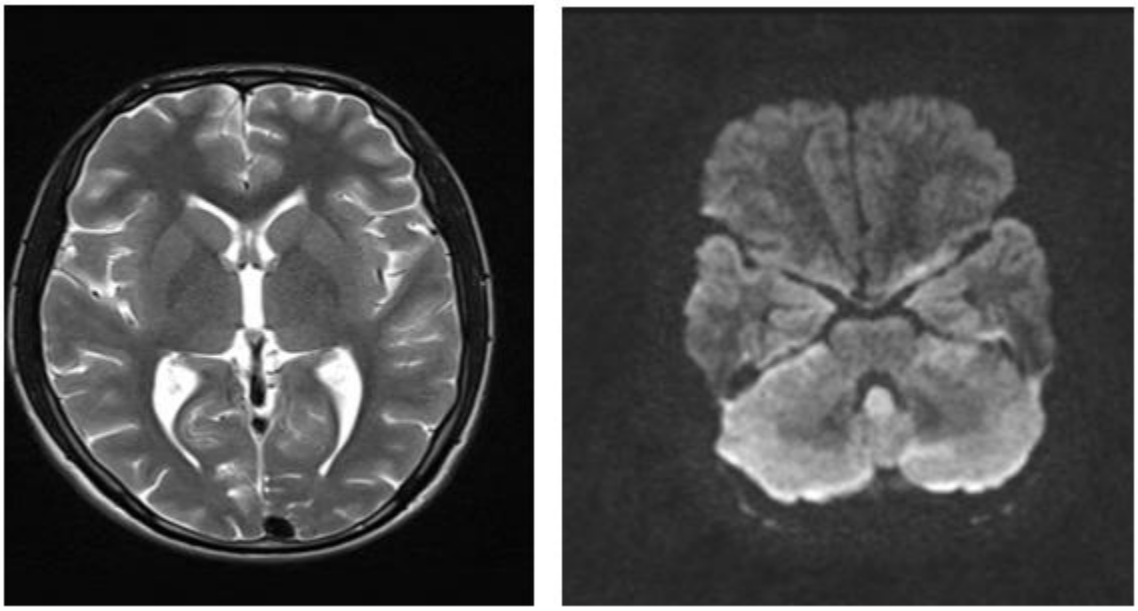
immunodeficiency virus (HIV) and hepatitis B and C were negative.

The dengue IgM antibody test by enzyme-linked immunosorbent assay (ELISA) was positive on the next day of the admission which was 21 days since onset of illness. A final diagnosis of "Acute viral encephalitis with acute cerebellitis with hydrocephalus as sequelae of dengue fever" was made. He was managed with injection mannitol followed by oral acetazolamide for his hydrocephalus with supportive therapy like pantoprazole, ondansetron and intravenous fluids. On day 3 of the admission, his headache and vomiting resolved completely; however cerebellar symptoms and signs persisted, although reduced. His platelet counts were normal throughout his hospital stay.

Follow up was done after 2 weeks. The patient was able to walk without support but still there was slight unsteadiness in his gait. He did not have any constitutional symptoms. Follow up MRI brain revealed markedly reduced cerebellar hyperintensities on FLAIR images. Residual mild diffusion restriction persisted, particularly in vermis (Figure 3a). Hydrocephalus showed near total resolution (Figure 3b). After four weeks, the patient's gait unsteadiness improved further indicating a good prognosis.



- Image 3 (a): Follow up scan reveals resolved hydrocephalus (arrow points at smooth contour of ventricular walls).
- Image 3 (b): Follow up scan also revealed regression in FLAIR Hyperintensity with mild residual diffusion restriction in vermis (arrow) on DW images.

Discussion

Cerebellitis is a disease of pediatric age group and till now only 36 cases (caused by different viruses) have been reported in adults so far[5]. Majorly cerebellitis is caused as a complication of acute viral encephalitis. The common virus associated with viral encephalitis and cerebellitis are varicella zoster virus, EBV, measles, mumps, rubella, HIV, HSV and coxsackie virus[4]. Pathologically, involvement of the afferent and efferent cerebellar pathways including spinocerebellar and frontopontocerebellar directly by the virus can be one explanation of the cerebral ataxia[6]. One study has demonstrated dengue antigen in brain of some patients with dengue encephalitis suggesting a direct tropic effect of the virus[7]. Alternatively it could be an immune system mediated reaction induced by the virus leading to disruption of these pathways[7].

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Dengue, although not a neurotropic virus, but rarely can present with neurological complications like cerebellitis in this case. One study quoted the occurrence of neurological complications in dengue infection is 0.5-6.0% [8]. Previously, the association of dengue with cerebellar syndrome in adults has been reported in only six instances. (Table 1) [3, 9, 10, 11] In all these reports, the cerebellar symptoms started from two days to two weeks after the onset of fever. In our case also the cerebellar symptoms appeared three days after the onset of his fever. The patient, however presented to our hospital after 20 days of his illness. By then his fever had subsided and ataxia was the only prominent symptom that remained. So this case report emphasizes that dengue should be a part of investigative work up for all cerebellitis patients, especially if patient comes in post monsoon season of a tropical country when dengue cases are at a surge, even if patient is afebrile and shows no signs and symptoms of a current dengue infection. Another interesting thing about this case is that MRI scan of the brain showed hyperintensities on T2/FLAIR sequences in cerebellum bolstering up our clinical diagnosis of cerebellitis. In six previously reported cases, an abnormal MRI was found in two cases [3, 9] while it was normal in the others.

Our patient had mild lymphocytic leucocytosis in his CSF with normal protein and sugar levels. However this CSF study was done after 20 days of his illness. This probably indicates the resolving phase of viral encephalitis. In terms of prognosis and course of acute cerebellitis, it usually is self-limiting in children[12]. However in adults even after adequate treatment the patient needs rehabilitation to maximize his potential of fully recovering from the sequelae of cerebellar manifestations[5]. In just one month of follow up our patient was able to walk without support though still mildly ataxic, showing a favorable outcome.

Table 1

Cases	Age	Sex	Phase of presentation	Cerebellar signs	Dengue serology	Brain MRI	CSF Analysis	Duration of complete recovery
Withana et al. (3)	45	Female	Febrile	Scanning dysarthria, horizontal nystagmus, bilateral dysmetria, dysdiadochokinesia more prominent on the right, ataxia, tendency to fall to the right	NS 1 Antigen and IgM Positive (serum)	Normal	Not done	17 days

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Khoo (9)	60	Male	Recovery	Nystagmus in all directions, bilateral dysmetria more prominent on the left, ataxia	IgM positive (serum); PCR Negative (CSF) – taken on D9 of illness	Hyperintense signals in the right corona radiata and left frontal lobe suggestive of his previous stroke	Normal	34 days
Weeratunga et al. (10)	40	Female	Critical	Dysarthria, bilateral nystagmus, bilateral limb and gait ataxia	IgM positive (both serum and CSF)	Normal	Normal	2 months
Weeratunga et al.(10)	28	Male	Post recovery	Bilateral vertical and horizontal nystagmus, gait ataxia	IgM positive (both serum and CSF)	Normal	Normal	1 week
Weeratunga et al.(10)	25	Male	Febrile	Bilateral nystagmus, dysmetria, severe ataxia	IgM positive (both serum and CSF)	Bilateral and symmetrical T2 hyperintense lesions in the cerebellum	Normal	2 weeks
Karunarathne et al.(11)	43	Male	Recovery	Dysarthria, bilateral limb and gait ataxia	IgM positive (serum), IgG positive (both serum and CSF) [EBV IgM positive	Bilateral diffuse hyperintense areas in cerebellar hemispheres	Viral infection [10 cells/µl (9 lymphocytes, 1 neutrophil) Proteins 0.88 g/dL	2 weeks

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					(serum)]		Sugar 55.8 mg/dL]	
Jain et al. (present study)	19	Male	Febrile	Scanning dysarthria, horizontal nystagmus, bilateral dysmetria, bilateral dysdiadochokinesia, ataxia, tendency to fall to either side	IgM positive (serum	Hyperintense signals in bilateral cerebellar hemispheres and cerebellar vermis, mild hydrocephalus	Viral infection [10 cells/µl (all lymphocytes) Protein 42.6 mg/dL Glucose 72 mg/dL]	4 weeks

Table 1: Summary of seven cases with dengue cerebellitis

Conclusion

Dengue is a very common disease especially in tropical countries. Incidence is increasing exponentially with each passing year. Though neurological complications are not common but considering the massive disease burden and escalating trend, even rare complications are important. This case highlights a very rare but potentially serious neurological complication of dengue that is acute cerebellitis. Although acute cerebellitis is a self resolving condition, still it leads to high morbidity due to ataxia associated with it.

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