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Case Report

Syndrome of transient headache and neurological deficits with cerebrospinal fluid lymphocytosis mimicking dengue encephalitis in a child

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ABSTRACT

The syndrome of transient headache and neurological deficits with cerebrospinal fluid lymphocytosis (HaNDL) has been infrequently reported in children. This condition can mimic many serious conditions of the central nervous system, while actually being benign in nature. The authors present the report of an 8 year old developmentally normal female with family and personal history of migraine, which was initially suspected to have Dengue encephalitis. She had an episode of seizures, meningism and altered sensorium. Normal mental status and physical findings were observed intermittently. Detailed evaluation including analysis of blood, cerebrospinal fluid (CSF) and neuroimaging were done. Neuro-infections, vascular pathology and autoimmune disorders were ruled out prior to reaching a diagnosis of HaNDL. She responded well to symptomatic treatment and made a full recovery. She was discharged on migraine prophylaxis considering her history. Dengue as causation and the occurrence of seizures in HaNDL has not been reported previously.

Keywords: HaNDL, CSF Pleocytosis, Migraine, Headache, Meningism

INTRODUCTION

First described in the year 1981,[1] HaNDL has been reported infrequently in children below 10 years of age.[2-4] Its aetiology still remains obscure, with researchers implicating immunogenic responses[5,6] and viral infections[7] as probable causations.

HaNDL has been recently classified by the International headache society (IHS) in its 3rd (beta, 2013) version of the International classification of headache disorders (ICHD) under the seventh group, 'Headache attributed to non-infectious inflammatory disease' with the code of 7.3.5.[8]

HaNDL can mimic a variety of conditions including aseptic meningitis, meningo-encephalitis, migraine with aura, hemiplegic migraine or stroke, thus posing a diagnostic conundrum for the physician. Ruling out life threatening neuroinfections and vascular pathologies is necessary before arriving at a diagnosis of this benign, self-limiting condition.

CASE REPORT

An 8 year old developmentally normal south Indian female, H. was referred to us from an area endemic for Dengue during late 2014, as a case of probable Dengue encephalitis. She had moderate intermittent fever lasting for 10 days. She was initially treated with oral antibiotic (Cefixim), domperidone, paracetamol and mefanamic acid on out-patient basis for 7 days in her town by a local physician. She was observed to be increasingly irritable thereafter for a period of 3 days and complained of recurrent episodes of headache, abdominal pain, nausea and vomiting. Her appetite had decreased significantly necessitating intravenous fluid administration. Her blood workup was found to be positive for Dengue infection

(IgM), and hence was referred to our institution for intensive care. She had one episode of generalized seizures during transport, which lasted for 10 minutes.

We elicited a positive familial history of Migraine in H.'s mother, maternal aunt and elder sister. The mother and aunt had headaches since childhood, while only the mother had hemiplegic migraine at the age of 22 years- both received treatment for migraine. The 19 year old elder sibling C., who was a high achieving medical student, had history of recurrent abdominal pain and headaches since the age of 7 years. The severity of C.'s headaches had often caused her to avail frequent leaves of absence from her school and had also made her depressed. She had undergone laparoscopy as part of her evaluation for abdominal pain which failed to detect any abnormalities. During one of C.'s hospitalizations for headache at a local hospital, she was suspected to have tuberculosis meningitis. Both siblings had received Anti-tuberculosis treatment with for a period of 6 months. As C.'s headaches continued unabated, her parents had her evaluated by a neurologist and thereafter she was started on migraine prophylaxis with Flunarizine, Propranolol in addition to tricyclic antidepressants. C.'s condition showed gradual amelioration thereafter. We were able to ascertain that H. had started missing school since 1 year, in spite of her brilliant academic performance. She was often criticised for her headaches, which were assumed to be an excuse for truancy from school.

Course in the hospital

In the emergency medicine department, we encountered a highly irritable, drowsy H., who adopted a flexed posture, but was moving all limbs. She was euglycaemic, afebrile, had a Glasgow Coma Scale (GCS) score of 12/15 and had stable vitals. Neurological examination revealed hypertonia of lower limbs, exaggerated deep tendon reflexes, bilateral withdrawal plantar reflexes, positive brudzinskis sign, and terminal neck stiffness. One more episode of generalized seizures occurred. Her pupils and fundi were normal. Examination of other systems did not reveal any significant abnormalities.

H. was admitted to our Intensive care unit with a provisional diagnosis of acute meningoencephalitis. Her treatment consisted of intravenous fluids, antibiotics (Ceftriaxone and Amikacin), anticonvulsants (Fosphenytoin, Midazolam), Paracetamol, Pantoprazole and Ondansetron. No further seizures occurred and she continued to be stable.

CSF analysis revealed lymphocytic pleocytosis (18 cells) with mild elevation of protein (50 mg/dL). CSF culture, Gram and Zeihl Nielsen staining were negative. MRI brain and Chest X-ray were normal. Blood investigations revealed normal values for Haemoglobin (12.1 g/dL), total counts (4200 cells/uL), 38% Neutrophils, 55% Lymphocytes, Erythrocytic sedimentation rate (13mm/1st Hour), SGPT (16 IU/L), Creatinine (0.4 mg/dL), Sodium (138 mmol/L), and Potassium (3.9 mmol/L). Thrombocytopenia (84000 cells/uL) and a positive Dengue serology (IgM) were reported.

On the morning of day 2, we observed a co-operative, conversant and alert H., who sat by her mother's side, interacted well and was accepting food. Neurological examination was normal except for terminal neck rigidity. In a span of 1 hour, we saw a marked change in her demeanour. H. complained of excruciating right sided orbito-fronto-temporal throbbing pain, and had two episodes of vomiting. She preferred being held by her mother and was averse to bright lights, was irritable and cried. After administration of intravenous paracetamol, her complaints subsided within 1 hour, and thereafter she slept for an hour. At this juncture, we strongly considered the possibility of Migraine-like headache, and planned to initiate a combination of Ibuprofen and Paracetamol in her treatment after improvement in platelet counts.

H. was transferred to the wards and continued to be monitored intensely. She had five more episodes of similar headache in spite of avoiding most common triggering foods in a span of 48 hours. We advised her parents to maintain a diary of events with a record of time of headache, meals, complaints and immediately preceding events, which was dutifully done. H. was also told to avoid bright flickering lights and television viewing. We reviewed the diary after a day, and noted that H. was able to predict her oncoming headache episodes at least half an hour before occurrence. Ibuprofen and Paracetamol were started after observing a satisfactory rise in platelet counts, and this resulted in a rapid reduction in the frequency of headaches. By day 5, she had only one episode in 24 hours, and her appetite had also improved significantly. We consulted the neurologist, who suggested ruling out neuroinfections and seizure disorders prior to starting antimigraine prophylaxis.

CSF-PCR was negative for infectious agents (JE Virus, Dengue 1-4, HSV, Measles, Mumps, Chikungunya, West Nile Virus, Toxoplasmosis, Pneumococcus, H. influenza, meningococcus, Cryptococcus, M. Tuberculosis and Filamentous fungi). No CSF Oligoclonal Bands were seen. A repeat CSF routine analysis still showed persistent lymphocytic pleocytosis (15 cells) with elevated proteins (71mg/dL). Electroencephalogram (EEG) showed intermittent posterior predominant alpha with frontal predominant beta activity along with frequent slowing to theta range in the mid temporal leads bilaterally. No focal slowing or epileptiform discharges were recorded. Mantoux test, CRP and Anti-nuclear antibody assays were negative. Our diagnosis was revised to HaNDL after reviewing existing literature on migraine like headaches with CSF lymphocytosis. We stopped her anticonvulsant medication (Phenytoin), and continued Ibuprofen and paracetamol for one more week. We also started treatment with Funarizine and Propranolol. H.'s parents and class teacher were counselled. Our patient

was discharged on day 7 after being headache-free for 36 hours; her neck stiffness had also disappeared. She was followed up after a week, and then monthly. Only 2 episodes of relatively milder headache were reported in an 8 month period, which were well controlled with Ibuprofen and Paracetamol. She has since resumed her academics, and is cheerful.

DISCUSSION

HaNDL was most frequently encountered in young adults (15-40 years), with male predominance.[9] Reports on children are rare, and may be due to alternate presumed diagnoses. Children are mostly unable to communicate the exact nature of their headaches, and the neurological manifestations of HaNDL may often be interpreted as arising due to severe intracranial infection or systemic illness. Ruling out other conditions requires expensive investigations, which are mostly avoided and empirical treatment is often administered based on CSF reports and initial clinical findings.

Our patient, a female and of relatively younger age does not fit into the typical HaNDL patient demography. The presence of CSF lymphocytic pleocytosis and meningism would have prompted management along the lines of viral meningoencephalitis or tuberculosis meningitis in most hospitals. The single episode of seizures in our patient was the only event that could be considered as a 'transient neurological deficit', although no other literature specifies such an occurrence. Regular observation enabled us to study our patient during her episodes of headache and during periods of normalcy. The marked difference in her general condition at these instances observed with consistency, and the fact that she could predict the oncoming headaches, helped us reach the diagnosis. An underlying migraine in H. was also considered a strong possibility. We thereby avoided subjecting the child to un-necessary long term treatment with anticonvulsants or anti-tubercular drugs. We observed that the combination of Ibuprofen and Paracetamol worked better in controlling her headaches than Paracetamol alone.

Patients with Dengue encephalitis and meningitis may have CSF pleocytosis and elevated protein, but the course of illness in them is prolonged and complicated.[10] The rapid amelioration of our patient's complaints with the administration of appropriate drugs, her stable hemodynamic and absence of significant deterioration or deficits allowed us to rule out serious neuroinfection or vasculitis. This was supported by investigations including imaging studies and normal CSF-PCR. The patient's EEG also did not reveal any focal slowing, a finding contrary to other studies,[6] although theta range waves were seen. Generalized slowing on the EEG during acute stage has been reported.[11,12] In H.'s case; the CSF did not show any dramatic changes on samplings during the initial presentation, and on recovery.

The strong family history of migraine was confounding, yet the history of migraine-type headaches in our patient, which is also an uncommon occurrence,[6,12] for over a year prior to her hospitalization, prompted us to administer migraine prophylaxis. Our review of prior literature revealed the use of Propranolol,[11] Valproic acid,[13] Acetazolamide and systemic Steroids[14] in treatment.

CONCLUSION

A diagnosis of HaNDL is arrived at after excluding other serious conditions with similar clinical features. The course of illness in children may have differences compared to adults, and pose a diagnostic challenge. Meningism, history of seizures etc. may be present. The value of good history elicitation and observation of a patient with headache during and after the episodes needs to be emphasized. Reliance on CSF reports alone may be confounding and lead to unnecessary treatment, and hence it has to be taken in conjunction with imaging studies and detailed regular physical examination. HaNDL in migraneurs, although reported infrequently, may occur. In such patients, administration of migraine prophylaxis is warranted unless contraindications exist. Maintenance of a headache diary serves as an extremely useful aid for diagnosis. Physicians need to familiarize themselves with HaNDL and its mimicking of other serious conditions.

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