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Probable Human Bocavirus meningitis in a child

"Case report and review of literature"

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ABSTRCT

Human bocavirus (HBoV; family Parvoviridae; genus Bocavirus) was discovered in 2005 and was distributed worldwide (1). HBoV has gained considerable clinical relevance since its discovery. It has been detected in respiratory specimens, and when it causes disease, it seems to have a broad spectrum of signs and symptoms. Our patient was a five years old girl admitted to the Royal Hospital in Oman, on March 2019. Presented with headache, vomiting, fever, phonophobia and significant irritability. HBoVS virus was detected in this patient's BAL (Bronchoalveolar Lavage). This paper is reporting a rare case of probable HBoV meningitis.

Abbreviations: CSF = cerebrospinal fluid , CRP = C-reactive protein, CT = computed tomography, HBoV = human bocavirus, HMPV = human metapneumovirus, PCR = polymerase chain reaction, RSV = respiratory syncytial virus

INTRODUCTION

HBoV has been detected worldwide in nasopharyngeal aspirates collected for screening (2). Large-scale studies showed that HBoV can be detected in children with signs and symptoms of respiratory tract infection. Studies have detected HBoV in 9% and 19.3% of all sample indicating that it is the second or third most commonly detected virus ,in RVP(Respiratory Viral Panel) after Respiratory Syncytial Virus(RSV) and rhinovirus (3).

There is a high chance that the active and serious pneumonia that in fact was deduced to the HBoV mono-infection was linked to the neurological symptoms directly or indirectly, thus the case strongly supports the request for further cohort studies that systematically and controlled address the question if a correlation between the HBoV infection and neurological disorders exists(4). There are few case reports worldwide with proven Bocavirus meningoencephalitis(7,8).Most recently, a further atypical case of HBoV infection was observed that was associated with encephalopathy,(5) thus further confirming that at the present stage neurological side effects of respiratory HBoV infections cannot be excluded, although the causative relation has to be further investigated.

PRESENTING CONCERNS:

The patient was a 5 years old girl, previously healthy. She was admitted to on March 2019 in Royal Hospital in Oman , which is the biggest tertiary hospital. The Mother gave a history of abdominal pain and vomiting for seven days. The vomiting was worsening over time and became more significant for around nine times per day which required intravenous fluid hydration in a local health center. Few days prior to her

emergency visit, she started to have non-specific headache, phonophobia, photophobia and bodyache. The mother was concerned regarding child behavior changes as she became unusually aggressive.
In emergency department, she was febrile 39.7C with clinical signs suggestive of meningitis. Therefore, CT head was done and CSF was collected. She received acyclovir, ceftriaxone and vancomycin immediately. While admitted to pediatric ward, she was in the admission of Pediatrics ward, she was spiking fever and complaining of neck pain, headache, abdominal pain and she was unable to walk because of bodyache and lower limbs pain. She was not communicating with her parentslike before, and not cooperative on examination. Therefore we could not assess her communication and interaction in proper way.
She had a normal bowel habit and no urinary symptoms with no rash or joint pain. She hada runny nose, so RVP was done and antiviral oseltamivir was started.

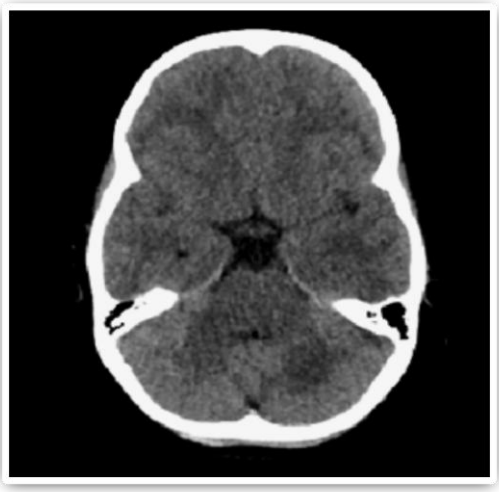
CLINICAL FINDINGS:

On physical examination, high mental function was intact with normal limbs power, tone and reflexes. CSF sample showed a WBC OF 30/uL mainly lymphocyte accounts for 80% and polymorphonuclear 20% ,and RBC <2/uL . Bacterial antigens in CSF were negative. CSF culture was negative for bacterial growth after 2 days and CSF viral PCR was not done as it is not a validated test in the national viral referral laboratory.
Respiratory viral panel (PCR) revealed Boca virus was positive, and all others viruses in our screening were negative .Laboratory tests revealed a leukocyte count of 14.3 10^9 /liter, Neutrophils 10 10^9/L , lymphocytes 3.1 10^9/L , a C-reactive protein level of 27.1 mg/liter, and a hemoglobin concentration of 11.8 g/dl. Based on clinical picture and initial investigations she was managed as viral meningoencephalitis.

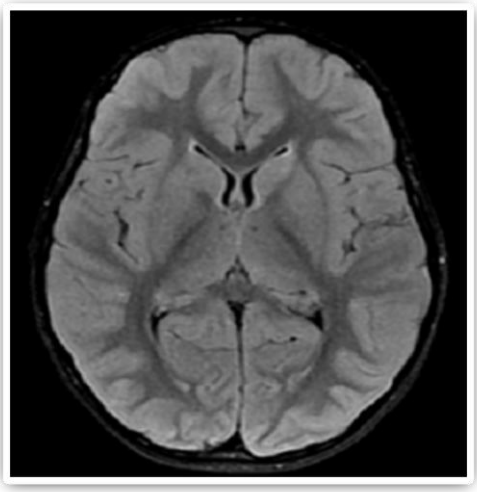
RADIOLOGICAL FINDINGS:

The cranial computed tomography (CT) revealed an ill-defined hypodensity in the left temporal lobe and left cerebellar hemisphere could represent an artifact , although real parenchymal abnormality cannot be excluded. (pic A) MRI brain showed subtle signal change seen in the posterior and to lesser extent of caudate body heads. These are non-specific and could be related to viral meningitis. No evidence of meningitis-related complication was seen. (pic B)

US abdomen: mild increase in parenchymal echogenicity of kidneys.



pic A



pic B

MICROBIOLOGICAL ASSESSMENT :

Patient's BALwas tested for RVP PCR (Polymerase Chain Reaction) using FTD respiratory pathogens 21 Fast Track diagnostic kit .All tested viruses were negative except for HBocV (Human BocaVirus).Tested viruses in the panel included influenza A virus , influenza A (H1N1)virus (swine lineage) , influenza B virus ,parainfluenza viruses 1-4 ,human metapneumoviruses A&B , HBocV , human parechovirus,entrovirus , adenovirus ,RSV A&B ,human rhinovirus , human corona viruses NL63 ;229E;OC43;HKU1 and mycoplasma pneumonia .

As patient presented with suspected meningitis, a CSF sample was obtained and analysis was done showed a high wbc of 30 / ul mainly lymphocytic 80% and 20 % polymorphonuclear cells . Viral CSF PCR panel (FTD Neuro 9 , Fast Track , diagnostic) was done and resulted in negative detection of all tested viruses. This panel included human HSV 1& 2 , VZV , CMV , EBV , adenovirus , enterovirus , human parechovirus , HSV 6 & 7 and human parvovirus B19. When we recognized that the viral CSF PCR panela resulted in negative detection of possible viral cause a repeat CSF sample was sent for a repeat HSV CSF PCR testing in a week time and also was negative. Here we proceed to do bacterial CSF PCR using FTD bacterial meningitis PCR fast track diagnostic. Neisseria meningitides,Hemophilus influenza and streptococcus pneumonia DNA were not detected as well in CSF sample making the diagnosis of bacterial meningitis further unlikely. A plan was made to test the CSF sample for TB PCR but unfortunately, there was no sample left after all testing done. A human bocavirus testing in CSF and whole blood samples were not feasible as the test is not validated for that purpose and results would not help if turn to be negative.

A confirmation of HBocV associated meningitis should follow identification of genomic matched HBocV genes in CSF, serum or Bal samples mainly using molecular techniques like PCR or WGS (Whole Genome Sequencing) (7).A more specific testing mentionedin some studies is the use of sequencing for both viral structural and nonstructuralproteins(8). Nucleotide Sequence of amplicons in PCR positive samples is another sequencing method and Phylogenetic Analysis can be done to confirm the diagnosis(7).Another method is to use ELISA(Enzyme Link ImmunoSorbant Assay) for HBocV IgG and IgM in both serum and CSF(7). Ideally to confirm HBocV meningitis presence of bothHBocV DNA and antibodies will very much support the diagnosis ,however the absence of antibodies cannot rule out the diagnosis and the presence of them can represents a past infection sometimes.

The gold standard of HBocV meningitis diagnosis is by detection of the virus in cell culture followed by electron microscopy examination of clinical sample looking for CPE(CytoPathic Effects) ,but due to its difficulty and non-feasibility , a switch toward molecular is most common nowadays(7). All PCR runs(CSF ,BAL) were done in a clean area and an internal control was used with each PCR to out rule contamination.Around 60 % - 85% of encephalitis case worldwide have no known confirmed etiological cause despite a varying range of new molecular testing modalities (8) probably due to hematogenous spread, viremia , bacteremia and a difficulty isolating fastidious pathogens .

PROGRESS DURING ADMISSTION:

Initially she didn't show good improvement with antimicrobials in the first week of admission. But in the second week of admission, the patient showed clinical improvement. She remained afebrile, less irritable and she was back to her normal personality. She stayed in the hospital for total twenty days where she received twenty days of acyclovir and fourteen days of ceftriaxone. She was discharged home in general condition with no neurological sequalae. After discharge, hearing assessment was normal. Patient was seen in the infectious disease team outpatient clinic as follow up and she was totally fine.

DISCUSSION:

Our patient is highly suspected to have viral meningitis and we could not find any explanation apart from HBoV which was detected in RVP. There are limited studies of HboV related CNS infection either meningitis or encephalitis. But It is known that hematogenous spread is the most common route that viruses take to enter the central nervous system and cause encephalitis/meningitis, we focused our attention on theHBoV, which is able to cause viremia (6) and, therefore, has the potential to disseminate to other parts of the body to initiate infection. It was documented that HboV has been implicated in causing life-threatening encephalitis in Bangladeshi children(7).

So, we conclude that several rare but possible etiologies are difficult to confirm using gold standard methods as in the case of meningitis due to HboV and human metapneumovirus in CSF, although these pathogens were previously shown to be associated with a distinct clinical entity. Thus, this case is an alarm signal and reminder to test for HboV in case of unclear neurological symptoms. We need to keep in mind that there are some viral agents apart from the one tested in CSF viral PCR panel that can cause meningitis . A validation to test such agent in different clinical samples should be done by the referral central virology laboratory.

CONCLUSION:

A 5 years old girl who presented with symptoms and signs suggestive of meningoencephalitis along with non-specific abdominal pain and acute myositis. Her presentation was highly suggestive of viral meningitis therefore Bocavirus meningitis was diagnosed by exclusion of other possible viral meningitic causes. The case requires further demonstration that HboV can cause variable range of symptoms like abdominal symptoms, myositis and in the same time may induce neurological symptoms as meningitis picture. The yield of including bocavirus in CSF PCR could prevent prolong hospital stay and unnecessary use of antimicrobials.

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