American Journal of Medical Case Reports, 2021, Vol. 9, No. 5, 278-280
Available online at http://pubs.sciepub.com/ajmcr/9/5/4
Published by Science and Education Publishing
DOI:10.12691/ajmcr-9-5-4

Varicella Zoster Viral Meningitis in an Immune-competent Young Female without a Rash or a Fever

Abdalla Khalil*, Khalil Hossenbux, Yusuf Ibidapo

Acute Medicine Department, Princess Royal University Hospital, King's College Trust, London, UK
*Corresponding author: abdallak59@gmail.com

Received January 08, 2021; Revised February 09, 2021; Accepted February 23, 2021

Abstract Viral meningitis is the most common identified cause of meningitis in the United Kingdom and represents a challenge to diagnose early and a burden on health care service. A young healthy female was admitted to the hospital with a headache, nausea, vomiting, meningeal irritation, and a strong family history of a cerebral aneurysm. She had no fever or rash and her cerebrospinal fluid CSF showed lymphocytic pleocytosis with high protein and normal glucose. Initially, she was treated empirically with antiviral and antibiotics for acute meningitis and her final workup confirmed the varicella zoster viral meningitis. Rarely, Varicella zoster viral meningitis can affect immune-competent patients. It can also rarely present without a skin lesion or fever. Virology study of the cerebrospinal fluid may reveal the diagnosis of viral meningitis early and reduce the health care burden.

Keywords: *viral meningitis, Varicella zoster virus, immune-competent, skin lesions*

Cite This Article: Abdalla Khalil, Khalil Hossenbux, and Yusuf Ibidapo, "Varicella Zoster Viral Meningitis in an Immune-competent Young Female without a Rash or a Fever." *American Journal of Medical Case Reports*, vol. 9, no. 5 (2021): 278-280. doi: 10.12691/ajmcr-9-5-4.

1. Introduction

In 2017, meningitis occurred in about 10.6 million people worldwide which resulted in 288,000 deaths, down from 464,000 deaths in 1990. [1,2]

Viral meningitis is the most common identified cause of meningitis in the United Kingdom with an estimated annual incidence of 2.73 per 100.000 adults' population and rapid diagnosis of the viral meningitis may reduce the burden on health services. [3]

Enteroviruses account for 20% of all adults patients with meningitis in the UK, while Varicella zoster virus accounts for only 7% of all cases of meningitis. [3]

We are reporting an immune-competent young female patient with varicella zoster viral meningitis without skin lesion who was admitted to our hospital without a febrile illness.

She presented with a severe headache and meningeal irritation and provisional diagnosis was a suspected subarachnoid hemorrhage.

2. Case Presentation

A 23-year-old British Caucasian female presented to the emergency department with a headache for 5 days which was described as the most severe headache she ever had and reached 10/10 intensity within few hours. The headache was located on the right side, pulsatile in nature, accompanied by vomiting, photophobia, and pain in the neck and both shoulders.

She denied any fever, sore throat, earache, or rash. She had no respiratory complaint, no loss of taste, or smell, and no urinary complaint. She had no seizure or weakness.

She had a past history of anxiety and was on quetiapine 25 mg once at night. She had a history of a severe allergy to amoxicillin (anaphylaxis) which had required previous hospital admission.

Her aunt died suddenly after being diagnosed with a cerebral aneurysm.

She lives with her partner, and her daughter and works as a carer in a nursing home.

Her pulse was 82/min regular, her blood pressure was 110/72, her temperature was 36.6C, and oxygen saturation was 97% in room air. Her chest and heart exam were unremarkable.

She had nuchal rigidity on passive flexion with negative Kernig's and Brudzinski's signs.

The rest of the neurological exam was unremarkable and no skin lesion could be detected.

Her full blood count, differential white cell count, renal function tests, liver function tests, and coagulation tests were within the normal range on admission. The CT brain scan and the chest x-ray were unremarkable. She was admitted to the acute medical ward, prescribed IV fluids, antiemetic medications and, pain killers as needed. The provisional diagnosis was a suspected subarachnoid hemorrhage. A lumbar puncture was performed after

admission and initial CSF results are displayed in table [1]. The findings were in favor of acute meningitis with pleocytosis (lymphocytic predominant >50%), a normal CSF glucose ratio compared to simultaneous blood glucose and a high CSF protein.

The CSF Findings and the clinical presentation were discussed with the microbiology consultant and the patient was prescribed IV acyclovir, IV chloramphenicol, and co-trimoxazole empirically to cover both viral and bacterial causative organisms for acute meningitis (both ceftriaxone and ampicillin IV could not be prescribed for our patient because of the previous history of anaphylaxis reaction to amoxicillin. The second line of antibiotic coverage for bacterial meningitis was used with drug level monitoring of IV chloramphenicol).

The serology results (serum and nasal/pharyngeal) were received the next day after admission are displayed in the table (1) .The patient felt better, headache improved, and vomiting resolved. The photophobia and neck stiffness were less.

The CSF virology results received on the third day after admission and both blood culture and CSF cultures were negative. Virology results of CSF are displayed in the Table 1.

Table 1. Significant investigations of the patient

Investigation and result	Normal range
Serum CRP < 1 mg/L	(0-5 mg/l)
CSF Protein 1.33 g/L	(0.25-0.45 g/L)
CSF microscopy White blood cells 316^6/L Neutrophils 11 x 10^6/L Lymphocytes 306 x ^6/L Red blood cells 8x 10^/6/L Gram film no organism India ink stain negative	 (0-5^6/L) (0-2^6/L) (0-3^6/L)
CSF Glucose 2.5 mmol/L blood glucose 4.4 mmol/L	Normal >50% of simultaneous blood glucose
CSF Lactate 2.63 mmol/L	(1.00- 2.00 mmol/L)
CSF Xanthochromia negative	
Serum 6-D-Glucan test (fungal screen) negative pg/ml	
Serum meningococcal screen PCR negative	
Serum pneumococcal screen PCR negative	
Combined nose throat swab Influenza A negative Influenza B negative Respiratory Syncytial virus PCR negative	
Serum HIV 1 & 2 Antibody/Antigen negative	
CSF Culture No growth >72 hours Blood Culture No growth >72 hours	
CSF virology *(received 3rd day after admission))* CMV DNA PCR negative IU/ml Adenovirus DNA negative copies/ml EBV DNA negative copies /ml Varicella Zoster virus DNA Positive Enterovirus RNA negative Herpes Simplex virus DNA negative	
Serum Quantiferon TB Gold Negative	

The patient was discharged on the fifth day after admission and acyclovir was prescribed orally for another 5 days.

3. Discussion

Viral meningitis is a notifiable disease in England and Wales, but many cases go unreported.

In 2005-2006, 2898 people were admitted to hospital with a diagnosis of viral meningitis, 10 times the number of cases notified to the Health Protection Agency for England and Wales during the same period. [4]

In the study in the British Medical Journal BMJ, 42 % of all patients with meningitis had unidentified cause for meningitis, 36% had viral meningitis, and 16% had bacterial meningitis. The length of stay for viral meningitis patients was 4 days, and 9 days for those who received antivirals. [3]

These findings represent the challenge to reach the causative organism in patients with suspected meningitis and the health care burden.

In a multicenter European study, fever was reported in 73%-97% in patients with bacterial meningitis BM, and the classical triad of fever neck stiffness and altered mental status was noted only in 41%-51% of patients. [5]

In French study patients with acute viral meningitis AVM, had similar, and even higher mean temperature and nuchal rigidity than bacterial cases (mean temperatures were 39.1 vs. 38.9 C and nuchal rigidity 55% vs.46%, respectively). Headache is noted more commonly in AVM than bacterial infections (72% vs. 40%). In contrast, confusion is more prevalent in bacterial meningitis than AVM. [6]

VZV varicella zoster viral infection of the central nervous system such as encephalitis, meningitis, or myelitis occur less frequently than VZV reactivation with dermatomal neuralgia and carry serious outcomes. Usually, CNS infection with VZV presents with skin lesion but can rarely develop without rash [7].

Acute infection or VZV reactivation affects predominantly elderly patients and immunocompromised patients, but rarely reported in immune-competent patient [8].

Our young female immune-competent patient did not have a fever on the presentation or after admission and not did have any skin lesion. She had a positive family history of cerebral aneurysm and the provisional diagnosis on admission was a suspected subarachnoid hemorrhage.

In a study using serum CRP C reactive protein to distinguish between bacterial and viral meningitis in children (325 consecutive patient) with negative stain CSF, CRP had a sensitivity, specificity and negative predictive value of 96%, 93% and 99% respectively. [9]

A met-analysis of nine studies revealed that serum procalcitonin PCT is a highly accurate diagnostic test that can be used by clinicians for rapid differentiation between bacterial and viral causes of meningitis in adults. PCT was superior to CRP which had a pooled diagnostic odds ratio DOR of only 22.1 (95% CI 12.7-38.3). [10]

In the previous French study (254 adults patients with meningitis with a negative direct CSF examination, 35 had BM and 181, VM), the most highly discriminative parameters for the differential diagnosis of bacterial meningitis BM proved to be CSF lactate, with a sensitivity of 94%, a specificity of 92%, a negative predictive value of 99%, a positive predictive value of 82% at a diagnostic cut-off level of 3.8 mmol/L. [6]

Our patient's serum CRP was low on admission, and no serum procalcitonin was requested.

Her CSF lactate was slightly raised 2.63 mmol/L, but this CSF lactate was less than the cut-off 3.80 mmol/L of bacterial meningitis in the French study.

In the previous British Medical Journal's meningitis study, most of the viral meningitis were lymphocytic meningitis i.e. more than 50% of WBC in the CSF were lymphocytes (203 out of 231 patients with viral meningitis).

In the lymphocytic meningitis group of patients within same study, there were 8 patients with Streptococcus pneumoniae infection, 4 patients with Neisseria Meningitides, 8 patients with Mycobacterium tuberculosis and one patient with Cryptococcus neoformans.

Our patient s CSF revealed pleocytosis (high white blood cells 316 x ^6/L) with predominant lymphocytes count >50%, high protein, and normal CSF glucose compared to simultaneous blood glucose (was >50%). She was started empirically on both IV antiviral and antibacterial coverage for acute meningitis. First-line treatment for bacterial meningitis could not be prescribed (history of anaphylaxis with amoxicillin). The second line of treatment for bacterial meningitis (chloramphenicol and cotrimoxazole IV) were empirically prescribed.

In a recent case series in a university hospital in China, 4 patients with headache and fever were found to have VZ viral meningitis. Two of the patients had signs of meningeal irritation, one patient developed a skin rash after symptoms of meningitis, and all four patients had normal MRI brain and EEG electroencephalogram. The white blood cell counts and protein levels were significantly elevated in CSF samples (median 317 × 10^6/L, range 147-478 × 10^6/L; median 1.41 g/L, range 0.57-1.79 g/L). The cytology of CSF demonstrated a lymphocytic pleocytosis and most multinuclear cells. Two cases were started on anti-tuberculosis treatment for suspicious tuberculous meningitis. The next-generation sequencing NGS of CSF (the Vision Medical Research Institute) detected specific sequences of VZV in the 4 cases within 72 h after admission. [11]

Oral valacyclovir has been prescribed to treat VZV meningitis in immune-competent patient. [12]

Our patients received IV acyclovir for 5 days then another 5 days orally after the resolution of symptoms.

4. Conclusion

Viral meningitis is the commonest known cause of meningitis in the United Kingdom which is still a challenge to diagnose early and represents a burden on the health care service.

Varicella Zoster meningitis can rarely affect immune-competent young patients.

It rarely occurs with neither a skin lesion nor a fever.

The viral study of the cerebrospinal fluid of patients with suspected meningitis may clarify viral meningitis early and decrease the health care burden.

References

[1] GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018 Nov 10; 392(10159): 1789-1858.

[2] GBD 2013 Mortality and Causes of Death Collaborators. Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2015 Jan 10; 385(9963): 117-71.

[3] McGill F, Griffiths MJ, Bonnett LJ, Geretti AM, Michael BD, Beeching NJ, et al; UK Meningitis Study Investigators. Incidence, aetiology, and sequelae of viral meningitis in UK adults: a multicentre prospective observational cohort study. Lancet Infect Dis. 2018 Sep; 18(9): 992-1003.

[4] Logan SA, MacMahon E. Viral meningitis. BMJ. 2008 Jan 5; 336(7634): 36-40.

[5] van de Beek D, Cabellos C, Dzupova O, Esposito S, Klein M, Kloek AT, et al. ESCMID Study Group for Infections of the Brain (ESGIB). ESCMID guideline: diagnosis and treatment of acute bacterial meningitis. Clin Microbiol Infect. 2016 May; 22 Suppl 3: S37-62.

[6] Viallon A, Desseigne N, Marjollet O, Birynczyk A, Belin M, Guyomarch S, Borg J, Pozetto B, Bertrand JC, Zeni F. Meningitis in adult patients with a negative direct cerebrospinal fluid examination: value of cytochemical markers for differential diagnosis. Crit Care. 2011; 15(3): R136.

[7] Gilden DH, Kleinschmidt-DeMasters BK, LaGuardia JJ, Mahalingam R, Cohrs RJ. Neurologic complications of the reactivation of varicella-zoster virus. N Engl J Med. 2000 Mar 2; 342(9): 635-45.

[8] Douglas A, Harris P, Francis F, Norton R. Herpes zoster meningoencephalitis: not only a disease of the immunocompromised? Infection. 2010 Feb; 38(1): 73-5.

[9] Sormunen P, Kallio MJ, Kilpi T, Peltola H. C-reactive protein is useful in distinguishing Gram stain-negative bacterial meningitis from viral meningitis in children. J Pediatr. 1999 Jun; 134(6): 725-9.

[10] Vikse J, Henry BM, Roy J, Ramakrishnan PK, Tomaszewski KA, Walocha JA. The role of serum procalcitonin in the diagnosis of bacterial meningitis in adults: a systematic review and meta-analysis. Int J Infect Dis. 2015 Sep; 38: 68-76.

[11] Chen L, Xu Y, Liu C, Huang H, Zhong X, Ma C, Zhao H, Chen Y. Clinical features of aseptic meningitis with varicella zoster virus infection diagnosed by next-generation sequencing: case reports. BMC Infect Dis. 2020 Jun 22; 20(1): 435.

[12] Gnoni M, Zaheer K, Vasser MM, Singh M, Ajmeri A, Harter SR, Mughees Rana A, Aguilar R. Varicella Zoster aseptic meningitis: Report of an atypical case in an immunocompetent patient treated with oral valacyclovir. IDCases. 2018 Aug 25; 13: e00446.

© The Author(s) 2021. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (http://creativecommons.org/licenses/by/4.0/).