IDCases 11 (2018) 22–25

Contents lists available at ScienceDirect

IDCases

journal homepage: www.elsevier.com/locate/idcases

Case report

Two cases of listeria rhombencephalitis

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ARTICLE INFO

Keywords:
Listeria monocytogenes
Rhombencephalitis
Encephalitis
Hindbrain
Meningoencephalitis

ABSTRACT

Listeria rhombencephalitis (LRE) is a rare encephalitis of the hindbrain that can present with a variety of neurological symptoms. It is a diagnostic challenge, but prompt antimicrobial therapy is important to prevent high rates of mortality and morbidity. We report two cases of LRE, with several contrasting clinical features and different disease courses. Despite being rare, it is important to consider listeria in patients with possible meningoencephalitis, even if cultures are negative. Empirical treatment of meningoencephalitis should provide coverage for listeria, especially if the patient is at risk of listeriosis or there is a potential history of listeria exposure.

Introduction

Rhombencephalitis is a rare form of encephalitis of the hindbrain, of which *Listeria monocytogenes* is one of the most common infectious etiologies. It normally presents with a prodromal flu-like illness followed by a phase with neurological manifestations [1], which may include cranial nerve pathology, cerebellar ataxia and long-tract motor and sensory features [2]. Rapid diagnosis and adequate antibacterial treatment are important to reduce mortality and morbidity; however, it can be a diagnostic challenge due to the multitude of possible differential diagnoses and also because the exact etiology can be difficult to determine, despite advances in microbiology and molecular techniques. The presentation, laboratory findings and course of the disease are also highly variable. Here we report two cases with several contrasting features that we managed at a district general hospital in the United Kingdom.

Cases

Case 1

A 79 year old male with a background of localized prostate cancer (on hormonal therapy), ischemic heart disease and hypertension was admitted with a fall and mild confusion. He complained of a mild headache. He was apyrexial and was leaning to the left side but did not have any focal neurological deficits on initial examination. Blood tests revealed lymphopenia (680 cells/microL) and hyponatremia (124 mEq/L). Inflammatory markers were normal. Human immunodeficiency virus antibody and Lyme IgM/G were negative. Unenhanced computerized tomography (CT) of the brain was normal.

Later on the day of admission, he became less responsive (Glasgow Coma Score 12/15) and was started on intravenous ceftriaxone and acyclovir for possible encephalitis. He was transferred to the intensive care unit for observation but his condition continued to deteriorate and, two days later, he required intubation and ventilation for increasing oxygen requirements and a poor cough. Blood cultures then returned as positive for *L. monocytogenes* and his antimicrobial therapy was changed to intravenous amoxicillin 2 g 4-hourly and oral co-trimoxazole 960 mg 6-hourly (administered via nasogastric tube). Lumbar puncture was performed and cerebrospinal fluid (CSF) analysis revealed high protein 115 mg/dL, normal glucose 54 mg/dL and white cell count of 63 cells/microL (90% polymorphs). Culture was negative after 48 h incubation. Magnetic resonance imaging (MRI) of the brain revealed multiple ring-enhancing lesions in the brainstem and cerebellum (Fig. 1), characteristic of listeria rhombencephalitis (LRE).

He failed extubation two days later and required a tracheostomy and underwent a slow respiratory wean. Repeat neurological exam revealed horizontal and vertical nystagmus and bilateral dysmetria. Power was reduced (MRC grade 3/5) in his right upper and lower limbs and there were brisk reflexes on the right side. There were no cranial nerve deficits. He was transferred to a medical ward where he made slow neurological improvement and his hyponatremia gradually

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https://doi.org/10.1016/j.idcr.2017.12.002
Received 16 November 2017; Received in revised form 1 December 2017; Accepted 1 December 2017

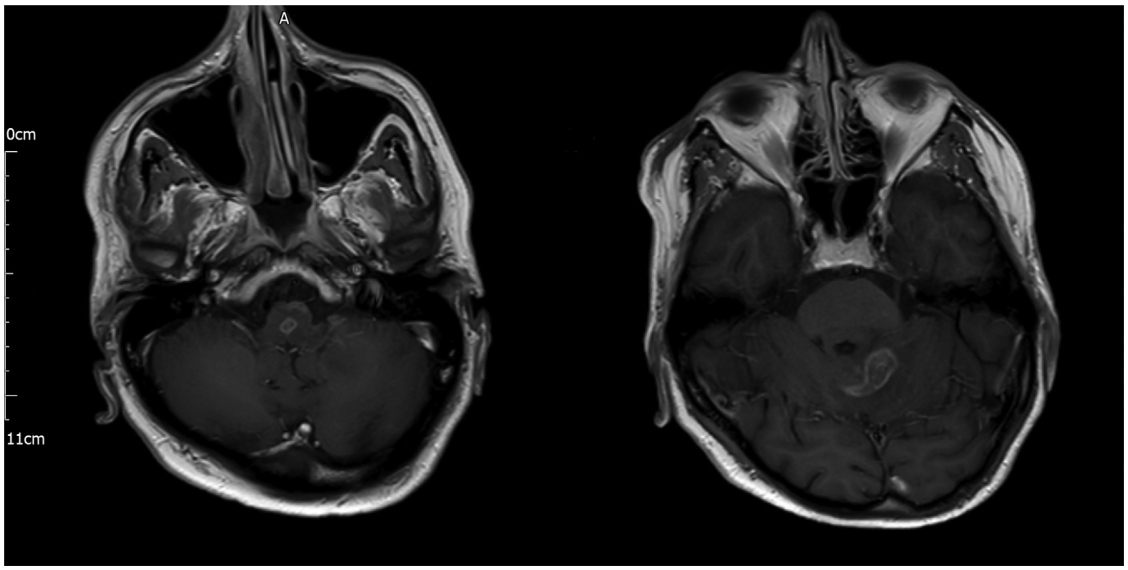

Fig. 1. Cranial magnetic resonance T1-weighted sequence showing ring-enhancing lesions in the brainstem (left) and left cerebellar hemisphere (right).

improved. Repeat MRI was performed one month post-admission and revealed improvement in edema around the posterior fossa and brainstem lesions but some hemosiderin deposition suggestive of some hemorrhagic transformation. He completed six weeks of intravenous amoxicillin and oral co-trimoxazole (only given intravenously when there were problems with the patient's nasogastric tube or concerns about safe swallow) and was then discharged with a further six week course of oral co-trimoxazole monotherapy. He was reviewed in clinic two months post-admission and had residual horizontal nystagmus and left-sided dysmetria.

Case 2

A 66 year old female with a history of mild chronic obstructive pulmonary disease (on inhaled therapy only) and hypertension presented with a two day history of gradually worsening diplopia and unsteadiness. She had been feeling generally unwell for the preceding 10 days, with a mild frontal headache and lethargy. She was apyrexial with a normal mental state and no signs of meningism. She had an ataxic gait, right-sided gaze-evoked nystagmus and dysmetria. Cranial nerve examination was unremarkable. Peripheral nervous system examination revealed brisk right lower limb reflexes with an upgoing Babinski reflex.

Bloods tests revealed neutrophilia (14,400 cells/microL). All bloods cultures were negative. Human immunodeficiency virus antibody, Lyme IgM/G, anti-nuclear and anti-neuronal antibodies were negative. Unenhanced CT of the brain was normal. Cerebrospinal fluid analysis revealed high protein 167 mg/dL, normal glucose 64.8 mg/dL and high white cell count 195 cells/microL (95% polymorphs). Culture was negative after 48 h incubation. Cerebrospinal fluid polymerase chain reaction (PCR) was negative for Herpes simplex, Epstein-Barr and varicella zoster viruses, *L. monocytogenes*, *Streptococcus pneumoniae*, *Escherichia coli*, bacterial 16 s rRNA and fungal 18 s rRNA. She was initially treated with intravenous ceftriaxone and acyclovir for a possible diagnosis of meningoencephalitis. Magnetic resonance imaging was performed on day two post-admission and T2-weighted and fluid-attenuated inversion recovery (FLAIR) sequences revealed hyperintensity in the cerebellum, with extension into the brainstem and internal capsule bilaterally (Fig. 2). Hemosiderin deposition was seen in the right cerebellum suggesting previous hemorrhage. She was diagnosed with rhombencephalitis.

Despite a negative CSF PCR, CSF culture and blood cultures, a trial-of-treatment was undertaken for a presumptive diagnosis of *L. monocytogenes* rhombencephalitis, the cause most consistent with the clinical, hematological, radiological and CSF findings. After six weeks of intravenous amoxicillin 2 g 4-hourly and intravenous co-trimoxazole 960 mg 6-hourly, repeat MRI showed almost complete resolution, in keeping with the complete resolution of her neurological deficits. She was discharged with six weeks oral co-trimoxazole.

Discussion

Rhombencephalitis is a form of encephalitis that affects the hindbrain. Diagnosis is difficult because it may present with a variety of neurological features [2]. This was observed in the described cases, with the second patient presenting with both cerebellar and long tract motor features and the first patient having no focal neurological findings at presentation but rapidly developing respiratory failure – a complication that occurs in 41% of patients [3]. Various etiologies may be implicated in the pathogenesis of rhombencephalitis. Non-infectious causes are most common and include multiple sclerosis, Behçet's disease and paraneoplastic syndromes. Frequently reported infectious causes include *L. monocytogenes*, Epstein-Barr virus, tuberculosis and *Streptococcus pneumoniae* [3,4].

L. monocytogenes is one of the most common infectious causes of rhombencephalitis. In a Spanish case series of 97 patients with rhombencephalitis, *L. monocytogenes* accounted for nine cases (47% of the 19 cases with an identified infectious etiology) [4]. *L. monocytogenes* is a gram-positive facultative intracellular bacterium, for which soil appears to be the chief environmental reservoir and flowing bodies of water are thought to facilitate spread [5]. Ready-to-eat foods, soft cheeses, undercooked or inadequately reheated meats and delicatessen meats are among the most common modes of transmission to humans [6]. On retrospective questioning, the first described patient had not been exposed to any risk foods; however, the second patient did remember eating a large quantity of brie two weeks prior to admission. After exposure, extremes of age, pregnancy, immunosuppression, and comorbidities such as malignancy or diabetes are major risk factors for developing listeriosis [7]. These groups are at risk due to the critical role of T-cell mediated immunity, particularly $CD8^+$ T-cells, in the protection against *L. monocytogenes* [8–10]. A depression in cell-mediated immunity (CMI) occurs in pregnancy to allow fetal retention [11] and the CMI of newborns is immature. Aging also causes a depression in CMI, due to a reduction in bone marrow progenitor cells, thymic involution and a reduction in the function of mature lymphocytes [12]. Both of the described patients were older than 65 years of age but were