Case report

An unusual presentation of *Listeria monocytogenes* rhombencephalitis

Albert Acewicz a,*, Grzegorz Witkowski a, Rafał Rola a, b, Danuta Ryglewicz a, Halina Sienkiewicz-Jarosz a

a First Department of Neurology, Institute of Psychiatry and Neurology, Warsaw, Poland
b Department of Neurology, Military Institute of Aviation Medicine, Warsaw, Poland

**A R T I C L E   I N F O**

Article history:
Received 16 July 2016
Accepted 22 December 2016
Available online 10 January 2017

Keywords:
Listeria monocytogenes
Rhombencephalitis
Stroke mimics
Brain infection

**A B S T R A C T**

We describe a case of 52-year-old woman with a medical history of Crohn’s disease presented abrupt fever, asymmetrical multiple cranial nerve palsies and focal neurological symptoms localized to the brainstem. The patient was initially diagnosed with ischaemic stroke, because of acute clinical course and results of neuroimaging. Cerebrospinal fluid analysis revealed mild infection with negative Gram staining and culture. Final diagnosis of *Listeria monocytogenes* brainstem infection (rhombencephalitis) was set up on the basis of further clinical course and positive blood cultures. Listerial rhombencephalitis should be kept in mind in immunocompromised adult patients who develop fever, asymmetrical multiple cranial nerve palsies and focal neurological symptoms localized to the brainstem even without typical neuroimaging, cerebrospinal fluid findings and negative cultures. Early diagnosis and adequate antibiotic treatment is of crucial importance.

© 2017 Polish Neurological Society. Published by Elsevier Sp. z o.o. All rights reserved.

1. **Introduction**

*Listeria monocytogenes* is a Gram positive bacillus, foodborne pathogen, commonly found in soil, water, decaying vegetation, and mammalian faeces [1–3]. Infection usually originates with the ingestion of contaminated food and can cause gastroenteritis and cutaneous listeriosis (non-invasive forms of listeriosis), bacteraemia, perinatal and central nervous system infection (invasive forms of listeriosis), particularly life-threatening in newborn babies, pregnant women, elderly people, and people with impaired immunity [1–3]. There is a significant increasing trend of listeriosis in Europe in recent years with notification rate 0.52 cases per 100,000 population in European Union in 2014 [4]. Central nervous system involvement by *L. monocytogenes* occurs in 30–55% of patients with listeriosis [2].

Rhombencephalitis corresponds to inflammatory diseases affecting the hindbrain (brainstem and cerebellum) and has a wide variety of aetiologies including infections, autoimmune diseases, and paraneoplastic syndromes [5]. Listerial rhombencephalitis is a rare infection with high mortality and serious consequences for survivors [1,6,7]. Early diagnosis and adequate antibiotic treatment is of crucial importance to survival.

* Corresponding author at: First Department of Neurology, Institute of Psychiatry and Neurology, 9 Sobieskiego St., PL-02957 Warsaw, Poland. Tel.: +48 22 4582888; fax: +48 22 45 82 566.
E-mail address: acewicz@ipin.edu.pl (A. Acewicz).
http://dx.doi.org/10.1016/j.pjnn.2016.12.004
0028-3843/© 2017 Polish Neurological Society. Published by Elsevier Sp. z o.o. All rights reserved.
and reduction of neurological sequelae [7,8]. However, listerial rhombencephalitis can be easily misdiagnosed, especially at an early stage of the disease.

2. Case report

A 52-year-old woman with a medical history of Crohn’s disease and schizophrenia was admitted because of fever, diplopia and left-sided weakness that had begun 3 h earlier. There were no history of loss of consciousness, seizures, headache, rash, sore throat, coughing, jaundice, nausea, vomiting, diarrhoea or weight loss. Although, one episode of mild, lower gastrointestinal bleeding appeared last month, probably due to Crohn’s disease or haemorrhoids. She was receiving treatment with methylprednisolone (16 mg daily), mesalazine, olanzapine and aripiprazole. On admission the patient was alert and oriented to person, place and time. Physical examination revealed a temperature of 38.0°C; cardiovascular, pulmonary, and abdominal exams were unremarkable. Neurological examination revealed mild dysarthria, central left facial nerve palsy, right abducens nerve palsy, mild left-sided hemiparesis with no signs of meningeal irritation. A computed tomography (CT) scan of the brain was normal. Diffusion-weighted MRI (DWI) demonstrated restricted diffusion corresponding with decreased signal in ADC and increased signal on fluid-attenuated inversion recovery imaging (FLAIR) in the right midbrain, upper part of dorsal pons and right internal capsule (Fig. 1). Carotid artery duplex ultrasonography and brain angio-CT scans did not reveal significant alterations. Chest radiograph was normal and an electrocardiograph revealed sinus rhythm. An initial laboratory work-up showed a white blood cell count 13.49 mg/L (78.3% neutrophils, 12.2% lymphocytes, 8.7% monocytes) and a C-reactive protein level (CRP) of 15 mg/L (normal range: <5 mg/L). Because physical examination revealed no focus of infection, urine and blood cultures were taken. Patient’s medical history (Crohn’s disease) together with episode of gastrointestinal bleeding with no other visible cause of infection suggested intra-abdominal infection and patient

Fig. 1 – Diffusion-weighted axial brain MRI (DWI) at admission. Restricted diffusion (A) corresponding with decreased signal in ADC (B) together with an increased signal on fluid-attenuated inversion recovery imaging (FLAIR) (C) in the right midbrain are shown.

Fig. 2 – Fluid-attenuated inversion recovery imaging (FLAIR) axial brain MRI few days after admission demonstrated increased signal in the midbrain, right internal capsule and left globus pallidus.
received empirical antibiotic therapy with ceftriaxone and metronidazole. Because of gastrointestinal bleeding thrombotic treatment was not introduced.

In the next days of hospitalization the patient’s physical and neurological condition worsened with subsequent deterioration of consciousness level. She was still febrile (up to 39.5 °C), obtunded but able to follow simple commands and response to simple questions. Left oculomotor nerve palsy and right-sided hemiparesis appeared. Control DWI showed enlargement of the midbrain lesion and new lesions close to right lateral ventricle and in the left globus pallidus (Fig. 2). Control laboratory tests showed a further increase in CRP level (165 mg/L). Previously collected blood and urine cultures were negative, although another blood cultures were taken. Cerebrospinal fluid (CSF) analysis revealed pleocytosis (68 white blood cells/mm³ with 55% neutrophils and 23% lymphocytes), increase red blood cells count (72/mm³), elevated protein (68 mg/dL) and glucose (120 mg/dL). A Gram stain showed no pathogens. Because of the suspicion of L. monocytogenes infection treatment with intravenous ampicillin was introduced (3 g four times daily).

Next day the patient was still obtunded, responding only to painful stimuli, febrile up to 41 °C, developed tachyarrhythmia, hypotension and hypoventilation requiring mechanical ventilation and vasopressors. Control CT revealed multiple hypodense lesions involving both cerebral peduncle, both thalami, both internal capsule and left globus pallidus. After couple of hours sudden cardiac arrest occurred and patient died despite resuscitation. Permission for autopsy was not granted by family. Few days later blood cultures grew L. monocytogenes and cerebrospinal fluid culture was negative.

3. Discussion

Brainstem encephalitis accounted for 9% of listerial central nervous system infections but it is likely unrecognized and underreported [1]. The disease has a characteristic biphasic course. A nonspecific prodrome of fever, headache, nausea and vomiting is followed by abrupt, progressive neurologic syndrome, consisting of single or multiple asymmetrical cranial nerve palsies, cerebellar signs, hemiparesis or hypoesthesia, and impairment of consciousness [6,7]. In MRI hyperintense, patchy lesions within the brainstem and/or multiple microabscesses are observed [6,7,9]. CSF findings are benign with respect to the clinical picture and CSF often remains sterile with only mild, uninformative abnormalities with lymphocyte predominance [7,10].

Progressive hemiparesis and asymmetrical cranial nerve palsies, multiple, progressive lesions in the brainstem and brain hemispheres, together with fever and signs of inflammation in CSF allowed us to suspect listerial rhombencephalitis. The diagnosis was confirmed by positive L. monocytogenes blood cultures. However, atypical clinical picture made the differential diagnosis more difficult. First, clinical picture was unusual for listerial rhombencephalitis with lack of prodromal phase, i.e. confusion state, nausea, headache, malaise, vomiting. To the best our knowledge, only few papers described similar, atypical clinical course. For example, Marini et al. [11] present a patient who suffered only mild headache before acute abrupt of neurological signs.

Second, sudden onset of neurological symptoms together with normal CT scans indicated ischaemic stroke. Due to that suspicion short MRI protocol composed of DWI, ADC and FLAIR but without T1, T2 and contrast-enhanced sequences was done. The results of neuroimaging seemed to support the initial diagnosis. However, progression of MRI lesions with involvement of cerebral peduncles, thalami and basal ganglia was suggestive of inflammatory process. Clinical course with corresponding evolution of patchy lesions in the brainstem and hemispheres surrounded by oedema followed by ring, contrast-enhancing abscess-like appearances usually are enough to set up the diagnosis of rhombencephalitis [11,12]. Less frequently neuroimaging reveal an isolated brainstem lesion as in cases described by Reynaud et al. [8] and Mrowka et al. [9].

Third, there were interesting findings in CSF examination. Contrary to typical CSF findings in L. monocytogenes central nervous system infections, in this case CSF analysis revealed pleocytosis with neutrophilic predominance, increase red blood cells count, elevated protein and glucose with negative Gram staining and culture. Thus, neutrophilic predominance might suggest other bacterial infection. On the other hand, an increased number of red blood cells without a presence of intracerebral haemorrhage or traumatic spinal tap can be found in Herpes simplex encephalitis [6,13].

Several phenotypic and genotypic typing methodologies have been used for phylogenic studies and to categorize L. monocytogenes isolates into higher-level groups, such as evolutionary lineages, clonal complexes (CCs), epidemic clones. L. monocytogenes can be divided into 4 genetic lineages (I–IV) that have different pathogenic properties; isolates from human cases most frequently belong to lineages I and II [14]. More recently, Jensen et al. [15] analyzed correlation between molecular type and clinical course of L. monocytogenes strains isolated from patients with listeriosis in Denmark during 2002–2012 and showed that CC1, CC2, and CC6 isolates within lineage I are associated with higher proportion of CNS infections. Thus, more studies are needed to find out which L. monocytogenes CCs are associated with listerial rhombencephalitis.

This illustrative case provides several interesting clinical and teaching points. Diagnostic problem faced with this patient was to differentiate between progressive, multiple strokes, which was supported partially by the clinical course and the results of applied neuroimaging and the CNS infection. In the suspicion of L. monocytogenes rhombencephalitis, contrast enhancement MRI should be performed as soon as possible to reveal possible brain parenchyma lesions, oedema or brain abscess. The clinicians should be aware of atypical CSF findings which may mimic both bacterial or HSV-infection and lead to delayed or missed diagnosis. In listerial rhombencephalitis cultures of CSF are positive in 41% of cases and the rate of blood culture positivity (61%) is higher than CSF culture [7]. Therefore, when the patient presents symptoms of unclear infection and clinical signs of brainstem involvement, especially with multiple, asymmetrical cranial nerve palsies, need to be evaluated for Listeria by repeated blood cultures. Overall mortality is up to 50% for listerial brainstem encephalitis and early empirical therapy is still crucial for attaining favourable
outcome [7,8,10]. Ampicillin is considered the treatment of choice for listeriosis [16]. Moreover, several authors suggest concomitant therapy with gentamicin, particularly in patients with severely impaired T-cell function and central nervous system infection [16].

Conflict of interest

None declared.

Acknowledgment and financial support

Institute of Psychiatry and Neurology provided financial support for this study.

Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; Uniform Requirements for manuscripts submitted to Biomedical journals.

REFERENCES