## **Conflicts of Interest/Disclosures**

The authors declare that they have no financial or other conflicts of interest in relation to this research and its publication.

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# Listeria monocytogenes brainstem infection (rhombencephalitis) mimicking ischemic stroke



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#### ABSTRACT

The frequency of *Listeria monocytogenes* (*Lm*) infection of the central nervous system is increasing. We report a patient recently treated with chemotherapeutic drugs for pulmonary adenocarcinoma who suddenly developed hemiparesis, was initially diagnosed with stroke, and was then found to be affected by *Lm* rhombencephalitis accompanied by a brain abscess. *Lm* meningoencephalitis mimicking ischemic stroke is rare but must be considered, especially in specific patients.

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## 1. Introduction

Early diagnosis of stroke is becoming indispensable due to the increasing use of thrombolytic therapy. During emergency room evaluation, one must be aware that there are rare conditions that might be falsely interpreted as ischemic stroke. These "stroke mimics" are a heterogeneous group of non-vascular conditions, including seizures, syncope, hypoglycemia, migraine with aura, brain tumors, diverse encephalopathies (hypertensive, toxic, metabolic, and infectious) and acute confusional states [1,2]. The incidence of these conditions is reported to be around 30% [1-3] in cases of focal brain deficits of apparently abrupt onset, but their incidence and nature vary depending on the context. Listeria monocytogenes (Lm) is a gram-positive bacillus that may affect the central nervous system (CNS) causing meningitis, rhombencephalitis or brain abscess [4]. Lm is the third most frequent cause of bacterial meningitis in patients aged >65 years [5] and is an increasingly recognized agent of human infections, concomitant with global changes in eating habits (specifically fast food and ready-to-eat products). This has subsequently increased the population at risk, including the elderly and immunocompromised

## 2. Case report

A 59-year-old woman was admitted to the emergency room for the sudden loss of strength in her left arm and leg. The evening before the hospital admission, she was slightly drowsy and complained of a very mild headache. She had a history of lung adenocarcinoma with vertebral bone metastases and pathological fractures, diagnosed 1 year before and treated with cisplatin and gemcitabine until 2 months previously. At the time of admission, neurological examination showed a left upper motor neuron facial nerve palsy and mild hemiparesis on the left side. The patient was slightly lethargic but able to follow commands and there were no signs of meningism. Her vital signs were within normal limits, body temperature was normal and there were no abnormalities on the blood tests. A cranial CT scan was unremarkable (Fig. 1). She was not treated with thrombolysis because of the presumed high hemorrhagic risk in a patient with multiple metastases. A first work-up for stroke etiology, with blood test for hypercoagulability, electrocardiogram, echocardiogram and carotid artery duplex scan did not reveal significant alterations. During the next day, she became febrile, her hemiparesis worsened, conjugate horizontal eye deviation towards right appeared and the patient's vigilance level further deteriorated. Blood cultures were taken. A chest radiograph demonstrated the known right lung tumor, but no signs of an infective process. Blood test showed mild hyponatremia (127 mEq/L), while the peripheral leukocyte count was within

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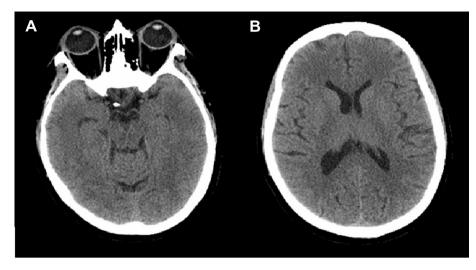


Fig. 1. Unenhanced axial brain CT scan showing no abnormality in the mesencephalon (A) or the internal capsule (B).

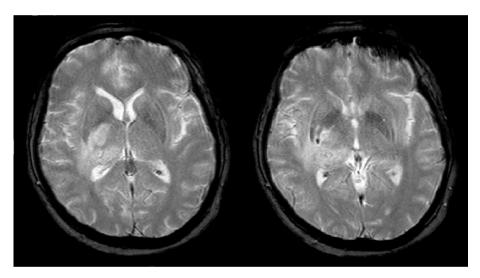


Fig. 2. T2-weighted axial brain MRI showing abnormal signal, mainly due to edema, in the hippocampus, throughout the right thalamus and right internal capsule.

normal limits and other analyses were otherwise unremarkable. A brain MRI on the third day showed patchy regions of abnormal signal in the right uncus and hippocampus, right thalamus and internal capsule characterized by iso-intensity on T1-weighted and hyper-intensity on T2-weighted and fluid attenuated inversion recovery sequences (Fig. 2). After gadolinium injection nodular and ring enhancing lesions of 2-7 mm diameter with abscess-like appearances were detected in the right thalamus and mesencephalon (Fig. 3). Faint right temporo-parietal meningeal enhancement was also detectable. Finally, blood cultures taken on the second day grew Lm and led to a diagnosis of Lm mesenrhombencephalitis. The patient was treated with intravenous ampicillin for 4 weeks and gentamicin for 2 weeks. In a few days, she recovered a normal state of awareness and consciousness and her weakness improved within 2 weeks at which time she could walk, albeit only with a support mainly because of her vertebral disease.

# 3. Discussion

We finally diagnosed meningoencephalitis with cerebral abscesses caused by *Lm* in our patient presenting with an acute onset motor deficit. Neurolisteriosis may manifest in humans as

meningitis and meningoencephalitis, which are the most common presentations, followed by brain abscesses and brainstem infection (rhombencephalitis) [4]. Lm brain abscesses present with different features compared to those caused by other pathogens, particularly due to the location in unusual subcortical areas (such as thalamus, pons or medulla) and concomitant meningitis [7]. One large review of CNS listeriosis reported that predisposing factors were immunosuppression, age >50 years and underlying conditions such as malignancy or diabetes [8]. Blood cultures are positive in 85% of cases, a frequency much higher than abscesses caused by other agents [7] and, of note, Lm is more commonly isolated in blood culture than in cerebrospinal fluid [8]. Rhombencephalitis is caused by the extension of the infection and inflammatory process to the brainstem with predominant infiltration of the nuclei, tracts and intraparenchymal parts of the corresponding cranial nerves [9]. Clinical signs classically appear in two phases: the first is characterized by nonspecific symptoms such as headache, malaise, nausea and vomiting; and the second by asymmetrical cranial nerve deficits, cerebellar signs and hemiparesis or hemisensory defects which can be concomitant to meningeal signs [4,10].

Regarding the available literature, our patient presented with most of the typical characteristics of *Lm* brain abscess and rhombencephalitis, including the lack of fever or meningism [4]. The

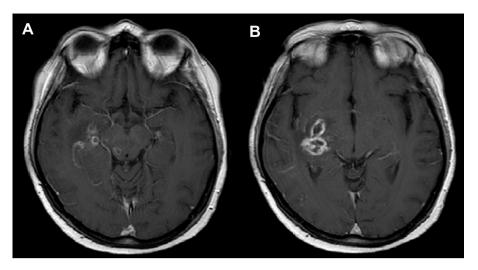


Fig. 3. T1-weighted axial gadolinium enhanced brain MRI showing ring enhancement in the sub-insular regions (A) and in the right thalamus, posterior mesencephalon and mesial temporal lobe (B), with a meningeal enhancement at right temporo-parietal lobes.

patient also had an impaired immune system due to malignancy and chemotherapy. Finally, her neuroimaging was quite typical for Lm encephalitis [11].

Among stroke mimics, infectious diseases of the CNS represent a minority but compared to other mimics that may be easier to diagnose (such as hypoglycemia and seizures), may be more difficult to suspect and exclude, especially in the acute context. Otherwise, the presence of clinical hints obliges the physician to consider these hypotheses in the diagnostic workflow. In an observational study of 790 consecutively admitted patients presenting with an ischemic attack in a stroke unit, the clues to search for an alternative diagnosis were younger age and absence of stroke risk factors, transient pure or predominant hemisensory symptoms and longer duration of symptoms [12]. Additional signs and symptoms to watch for are the presence of minor meningeal symptoms and signs such as mild headache, confusional state, nausea or vomiting and fever which may appear during the first days of hospitalization.

Our patient had few unusual presenting features which may have induced a suspicion of other diseases in the emergency room. Her headache had started hours before the onset of the motor deficit and the slight consciousness impairment may have pointed to a meningoencephalitis. Additionally, a tumor may have a stroke-like presentation; in this instance, malignant cerebral tumors are more frequently the cause [1]. The immunocompromised condition of our patient due to malignancy and chemotherapy was an additional suspicious element. In the presence of these factors it is advisable to perform additional investigations such as enhanced CT scan or MRI.

Differential diagnosis between meningoencephalitis and stroke is commonly not difficult when meningism, elevated temperature and altered routine laboratory parameters are present. But it can be very challenging, especially in the case of sudden onset and normal CT scan. To our knowledge, this is the first case of listerial CNS infection in which a clear and prodromal phase could not be identified and the patient suffered an entirely acute onset of symptoms [13].

Our report emphasises the fact that CNS listeriosis should be considered as part of the differential diagnosis in parenchymal brain involvement in immunosuppressed patients, and in those with simultaneously affected meninges and brain parenchyma subcortical brain abscesses.

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