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CASE REPORT

Lyme neuroborreliosis: An unusual case with extensive (peri) vasculitis of the middle cerebral artery

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Abstract

Lyme disease is a tick-borne infection caused by *Borrelia burgdorferi* sensu latu. Neuroborreliosis is reported in approximately 10% of patients with Lyme disease. We report a patient with central nervous system (CNS) large vessel vasculitis, ischemic stroke, and tumefactive contrast-enhancing brain lesions, an unusual complication of neuroborreliosis. A 56-year-old man presented with headache and disorientation for 1 month. Magnetic resonance imaging revealed basal meningitis with rapidly progressing frontotemporoinsular edema and (peri)vasculitis. Transcranial ultrasound confirmed stenosed medial cerebral arteries. [^{18}F]GE-180 microglia positron emission tomography (PET) showed frontotemporoinsular signal more pronounced on the right. [^{18}F]FET amino acid PET demonstrated low tracer uptake, suggesting an inflammatory process. Cerebrospinal fluid (CSF) showed lymphomonocytosis (243/µl), intrathecal anti-*Borrelia* IgM (CSF/serum index = 15.65, normal < 1.5) and anti-*Borrelia* IgG (CSF/serum index = 6.5, normal < 1.5), and elevated CXCL13 (29.2 pg/ml, normal < 10 pg/ml). Main differential diagnoses of neurotuberculosis and perivascular CNS lymphoma were ruled out by biopsy and Quantiferon enzyme-linked immunosorbent assay. Ceftriaxone (28 days), cortisone, and nimodipine (3 months) led to full recovery. Neuroborreliosis is an important differential diagnosis in patients with CNS large vessel vasculitis and tumefactive contrast-enhancing brain lesions, mimicking perivascular CNS lymphoma or neurotuberculosis as main neuroradiological differential diagnoses. Vasculopathy and cerebrovascular events are rare in neuroborreliosis but should be considered, especially in endemic areas.

KEYWORDS
CNS vasculitis, Lyme disease, neuroborreliosis

INTRODUCTION

Lyme disease is a tick-borne infection caused by gram-negative spirochetes, *Borrelia burgdorferi* sensu latu. Lyme neuroborreliosis (LNB) is reported in approximately 10% of patients with Lyme disease [1]. In rare cases, LNB might yield cerebrovascular complications [2–4]. Here, we report a patient with extensive cerebral large vessel (peri)vasculitis as neurological manifestation of LNB without typical symptoms of Lyme disease.

CASE REPORT

A 56-year-old man from upper Bavaria was admitted with a 4-week history of persistent right-sided stabbing headache, progressive spatial and temporal disorientation, and impaired concentration. Medical history included arterial hypertension and active nicotine abuse. Besides analgesics against the headache, he did not take any medication. He did not recall a tick bite or erythema. He showed deficits in short-term memory, temporal orientation, and spatial

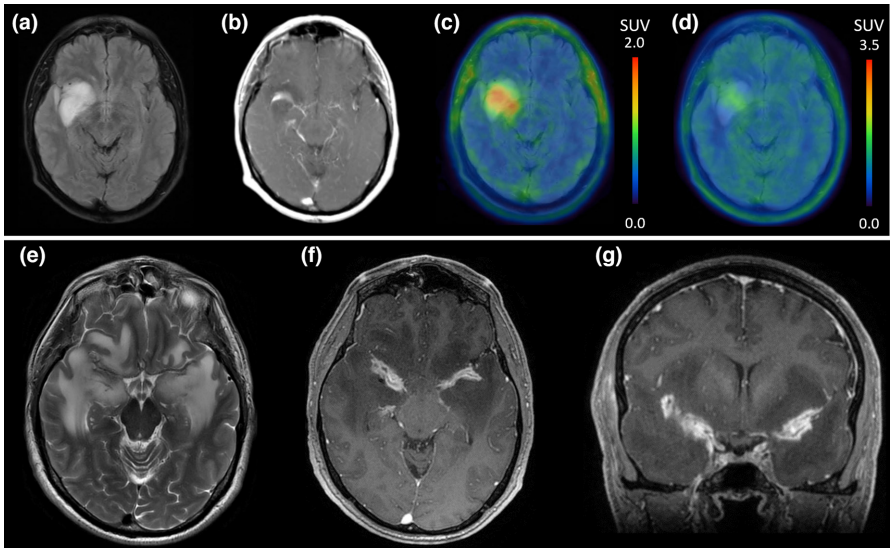

FIGURE 1 Brain magnetic resonance imaging (MRI), [^{18}F]GE-180 positron emission tomography (PET), and [^{18}F]FET PET. Brain MRI 4 weeks after symptom onset showed right-sided frontotemporoinsular edema (axial T2-weighted turbo spin-echo sequence [a]) and basal meningitis with perivascular contrast enhancement (axial T1-weighted fast spoiled gradient-echo sequence [b]). Axial microglia PET with [^{18}F]GE-180 showed intense frontotemporoinsular signal on the right (c), whereas axial amino acid PET with [^{18}F]FET demonstrated low tracer uptake (d). Brain MRI 5 weeks after symptom onset showed extensive bilateral frontotemporoinsular edema (axial T2-weighted turbo spin-echo sequence [e]) and basal meningitis with bilateral perivascular contrast enhancement (axial [f] and coronal [g], T1-weighted fast spoiled gradient-echo sequences). SUV, standardized uptake value

navigation. Vital signs, body temperature, and blood examination including systemic inflammatory markers were normal. Initial cerebrospinal fluid (CSF) analysis revealed lymphomonocytosis (cell count = 243/µl, normal < 5/µl) and elevated protein (127 mg/dl, normal < 45 mg/dl) with normal glucose. Brain magnetic resonance imaging (MRI) at admission showed T2/fluid-attenuated inversion recovery (FLAIR) hyperintensities, in the sense of vasogenic edema, within the right temporal and insular lobes (Figure 1a) and distinct (peri)vascular contrast enhancement of the proximal middle cerebral artery, more pronounced on the right (Figure 1b). Microglia imaging with [^{18}F]GE-180 positron emission tomography (PET) revealed intense right-sided frontotemporoinsular tracer uptake (Figure 1c), whereas amino acid PET with [^{18}F]FET demonstrated low tracer signal (Figure 1d), suggesting an inflammatory process. A 1-week follow-up MRI showed a rapidly progressing bilateral frontotemporoinsular edema, basal meningitis with bilateral (peri)vascular contrast enhancement (Figure 1e–g), and tiny ischemic lesions in the right putamen. Transcranial ultrasound confirmed segmental arterial stenosis with increased peak systolic velocity (PSV) most pronounced in the right anterior and medial cerebral arteries.

Main neuroradiological differential diagnoses were neurotuberculosis and perivascular central nervous system (CNS) lymphoma, ruled out by stereotactic biopsy of the lesion in the right temporal lobe 8 days after admission. Neuropathological examination revealed unspecific inflammatory infiltrates of mostly CD3-positive T cells and only few CD20-positive B cells without evidence of atypical cells.

Computed tomographic imaging of neck, chest, and abdomen, and extensive laboratory tests were negative, except for positive intrathecal anti-*Borrelia* antibody indices (AIs; anti-*Borrelia* IgM AI = 15.65, anti-*Borrelia* IgG AI = 6.5; normal < 1.5). CXCL13 was elevated to 29.2 pg/ml (normal < 10 pg/ml).

Treatment with ceftriaxone 4 g daily for 28 days and 5-day cortisone pulse therapy with 1 g methylprednisolone/day and oral tapering thereafter was started as soon as intraoperative frozen section analysis of the brain biopsy confirmed an inflammatory process. Additionally, nimodipine 3 × 60 mg and ASS 100 mg were initiated.

Thus, definite diagnosis was cerebral large vessel (peri)vasculitis due to LNB. Clinically, treatment led to a rapid and full recovery. Follow-up MRIs with magnetic resonance angiography revealed stepwise remission of edema and (peri)vascular contrast enhancement. Values of CSF cell count, protein, and anti-CXCL13 dropped during treatment. Three months after discharge, PSV values had normalized under gradual tapering of nimodipine. The patient was able to return to work without any cognitive deficits or other sequelae. Lifelong secondary stroke prevention was recommended. In >20 months of regular follow-up, clinical examination and MRI revealed no signs of CNS lymphoma or other pathology. Written informed consent was obtained from the patient for research purposes.

DISCUSSION

Lyme disease has only rarely been identified as a cause of ischemic or hemorrhagic stroke due to vasculitis in adults [2–4]. Typically, patients with LNB-associated vasculitis live in an endemic area and have a medical history of tick bite, erythema migrans, headache, radiculitis, and/or cranial neuritis [2]. Our patient suffered from headache,

short-term memory impairment, and spatial disorientation, but had no other symptoms. MRI findings in the form of extensive space-occupying and contrast-enhancing tumefactive lesions as in our case are extremely rare in LNB. Classical clinical presentations of LNB reveal either unremarkable cerebral MRI or contrast enhancement of the meninges and/or of clinically affected cranial nerves (i.e., particularly facial nerve) [1]. Rarely, LNB is associated with parenchymal lesions in the basal ganglia and posterior circulation as predilection sites for cerebrovascular events [2, 4]. The unique imaging findings in our patient with tumefactive (peri)vasculitic T2/FLAIR hyperintensities and contrast enhancement, large vessel stenosis, and basal meningitis necessitated a stereotactic biopsy to rule out the main neuroradiological differential diagnoses neurotuberculosis [5] and primary CNS lymphoma [6]. Interestingly, microglia PET showed signs of microglia activation, fitting anatomically to the MRI findings in the right temporal and insular cortices. Elevated glial activation has been shown in patients with persistent cognitive symptoms after LNB treatment [7], but not during acute infection. Our case demonstrates that [^{18}F]GE-180 PET may also be a marker of neuroimmune activation in LNB.

To conclude, LNB is an important differential diagnosis in patients presenting with CNS large vessel (peri)vasculitis and tumefactive contrast-enhancing brain lesions. Vasculopathy and cerebrovascular events are rare in LNB but should be considered, especially in endemic areas [2, 3]. In line with preexisting case series and single case reports [2, 3], prognosis of our patient was excellent after antibiotic treatment and additional immunosuppression.

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CONFLICT OF INTEREST

None of the authors has any conflict of interest to disclose.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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