Fluorine-18–labeled fluorodeoxyglucose–positron emission tomography studies of acute brainstem Lyme neutoborreliosis

Case report

MICHAEL PLOTKIN, M.D., HUBERTUS HAUTZEL, M.D., BERND JOACHIM KRAUSE, M.D., STEPHAN MOHR, M.D., KARL JOSEF LANGEN, M.D., AND HANS-WILHELM MÜLLER, M.D.

Department of Radiology, Nuclear Medicine and Radiooncology, Campus Virchow-Klinikum, University Hospital Charité, Berlin; Department of Nuclear Medicine, Research Centre Jülich, Heinrich-Heine-University Hospital Düsseldorf; Department of Nuclear Medicine, University Hospital Ulm; Department of Neurology, Johanna-Etienne-Hospital, Neuss; and Institute of Medicine, Research Centre Jülich, Germany

The authors report on a patient suffering from acute Lyme borreliosis who underwent two consecutive [¹⁸F]fluorodeoxyglucose–positron emission tomography (FDG-PET) studies demonstrating the course of the disease. The first FDG-PET study revealed markedly increased glucose metabolism in the brainstem, matching exactly the signal abnormalities exhibited on magnetic resonance images and indicating a brainstem tumor. A second PET scan demonstrated no abnormality in this region, thus reflecting clinical remission following antibiotic therapy. Data in the present case indicate that hypermetabolic findings on FDG-PET studies in the brainstem region should be regarded with caution and that neutoborreliosis must be considered as a possible differential diagnosis.

KEY WORDS • neuroborreliosis • [¹⁸F]fluorodeoxyglucose–positron emission tomography • Lyme disease

Lyme borreliosis is a multisystem infectious disease caused by Borrelia burgdorferi. Involvement of the central nervous system is frequent in Lyme disease and may include encephalopathy or, less often, encephalomyelitis. The diagnosis of neuroborreliosis is based on immunological tests. In the event of white matter involvement, however, differentiation of an infectious lesion from a brain tumor or demyelination remains difficult. This report represents an FDG-PET study of acute brainstem Lyme encephalomyelitis and a follow-up study after remission.

Case Report

History and Examination. This 58-year-old woman was referred to our department for evaluation of an unclear brainstem process. Two weeks earlier she had experienced unilateral cervical dysesthesia, which progressively expanded over portions of her face within a few days and was accompanied by earache. One week after the onset of symptoms she was admitted to the hospital because of progressive left-sided hemidysesthesia, ataxia, and abasia as well as nausea and vomiting. A neurological examination revealed weakness in the left hand and spasticity in the left leg, although her reflexes were normal. A few days after hospitalization she exhibited thermodysesthesia and spastic paresis of the right leg and Brown–Séquard syndrome with tactile hemidysesthesia in the left arm and impaired fine motor function in both hands. Results of electroencephalography, extracranial and transcranial duplex ultrasonography, electrooculography, thoracic CT scanning, skeletal scintigraphy, transthoracic echocardiography, and abdominal ultrasonography revealed no abnormalities. Note, however, that white blood cell count and C-reactive protein were elevated (13.3 × 10⁹/L and 1.4 mg/dl, respectively). Cerebral MR imaging with contrast depicted a T₂-hyperintense, T₁-isointense, nonenhancing lesion in the brainstem, which expanded caudally to the cervical spinal cord and caused slight aqueductal stenosis of the foramen of Magendie (Fig. 1 upper left). The lesion was diagnosed as a brainstem glioma. An FDG-PET study was performed 2 weeks after the onset of symptoms to evaluate glucose metabolism in the brainstem to differentiate the suspected glioma from a possible infectious lesion. The PET scan revealed markedly increased FDG uptake (SUVₘₖₜ₆.2) in the brainstem/spinal cord, which matched exactly the signal abnormalities on

Abbreviations used in this paper: CT = computerized tomography; FDG-PET = [¹⁸F]fluorodeoxyglucose–positron emission tomography; Ig = immunoglobulin; MR = magnetic resonance; SUVₘₖ₆ = maximal standard uptake value.
MR images (Fig. 1 upper right and lower left). An additional MR image of the neck (data not shown) demonstrated edema of the medulla oblongata extending into the proximal cervical spinal cord up to C2–3. Furthermore, results of this investigation revealed a contrast-enhancing diffuse lesion in the ventrocentral and dorsolateral left cervical spinal marrow. Subsequent serological tests, including those for herpes simplex, varicella-zoster virus, Treponema pallidum, and Listeria, were nondiagnostic. Antibodies against B. burgdorferi were elevated (IgM 1.1, IgG 2.7 [normal range < 0.8]) and the Lyme IgG titers measured using Western blot were slightly increased, thus indicating the inflammatory nature of the lesion.

Treatment. The patient was treated with Rocephin (2 g/day) for 2 weeks. One week after initiating therapy the patient’s state improved markedly and she experienced a striking recovery in motor function. When she was discharged, only a slight sensible spinal ataxia remained. Consequently, the serum Lyme IgM titer became negative whereas the IgG elevation persisted (2.2).

Posttreatment Course. The FDG-PET and MR imaging studies were repeated when the patient was in clinical remission 4 weeks after ending the antibiotic therapy. Visual analysis of the second PET study demonstrated no abnormalities in this region. In fact, the SUV\textsubscript{max} decreased to 4.5, whereas the MR image revealed a persisting signal hypodensity in the brainstem (Fig. 1 lower center). To illustrate the pre- and posttreatment effect further, subtraction of the normalized FDG-PET scans was performed. Results of this analysis revealed a marked increase in the glucose metabolism in the pretreatment study (Fig. 1 lower right).

**Positron Emission Tomography and MR Imaging**

At the initial PET study the patient presented in a fasting state with a glucose level of 75 mg/dl. A PET scan of the cranium was obtained during the first 60 minutes after the intravenous administration of 137 MBq FDG. The PET data were acquired on a unit (CTI ECAT EXACT HR+ scanner, Siemens, Knoxville, TN) with a transaxial field of view of 10 cm and an in-plane resolution of 4.5 mm full width at half maximum in the center of the field of view. For further analysis, frames were summed from 30 to 60 minutes postinjection. For attenuation correction, transmission scans were acquired using a \(^{68}\)Ge\(^{68}\)Ga rod source. Transverse slices were reconstructed iteratively by using a Gauss–expectation maximization algorithm. A 256 × 256 matrix was used for reconstruction. The reconstructed in-plane image resolution was 6.2 mm full width at half maximum. Data acquisition at the second FDG-PET session following successful treatment was performed in the same manner as in the first study. At this second session, the glucose level was 110 mg/dl while 133 MBq FDG was administered.

The high-resolution MR image was obtained on a 1.5-tesla MR imaging system (Siemens Magnetom Vision, Erlangen, Germany), using a T\textsubscript{2}-weighted three-dimensional magnetization-prepared rapid-acquisition gradient-echo...
Positron emission tomography in neuroborreliosis

sequence with TR 11.4 msec, TE 4.4 msec, TI 300 msec, field of view 217 mm, and matrix 200 × 256 and a T2-weighted turbo–spin echo sequence with TR 5400 msec, TE 99 msec, flip angle 180°, and matrix 198 × 512. The PET scans were automatically coregistered with individual MR imaging data, normalized, and subtracted from each other by using commercially available software (MPI Tool; ATV, Inc., Kerpen, Germany).

Discussion

Acute myelitis caused by B. burgdorferi is rare. The clinical course of the disease can mimic a brain tumor, stroke, or demyelination process. Apparently, morphological imaging is not helpful in differentiating these diagnoses. In those few published cases of Lyme myelitis, which have included MR imaging studies, the images demonstrated varied patterns of signal abnormality that did not contribute to the correct diagnosis. No PET data were available in these cases. Recently, an FDG-PET study revealed cerebral hypometabolism in patients suffering from neuroborreliosis, which was most pronounced in the temporal lobes. Nevertheless, the authors found no pathognomonic pattern that would allow the diagnosis of neuroborreliosis.

Given the acute onset of the neurological symptoms in the patient in the present case, a malignant brainstem tumor was suspected initially. Results of an MR imaging study were inconclusive because the findings were compatible with both a brainstem tumor and a localized inflammatory process. On the first FDG-PET scan, malignancy was indicated based on increased glucose uptake in the brainstem lesion. Note, however, that the diagnosis of Lyme borreliosis was finally established by a positive index of specific IgM and IgG antibodies against B. burgdorferi and corroborated by a dramatic improvement in the patient’s neurological symptoms and a decreasing IgM titer following antibiotic therapy. Confirmation of the diagnosis by CSF immunology was not prompted by the responsible physicians because the combination of the aforementioned criteria appeared reliable to establish the diagnosis of a neuroborreliosis. In addition, the decrease in FDG uptake on the second PET scan during clinical remission confirmed retrospectively the inflammatory nature of the lesion.

Thus MR imaging and FDG-PET were not helpful in the differentiation of a malignant and an inflammatory process in the brainstem at the onset of clinical symptoms. The limitation of FDG-PET in differentiating these processes is well known. An increased FDG uptake can often be demonstrated by inflammatory lesions, leading to false–positive interpretations of PET scans. In the case presented here, a pathological brainstem accumulation of FDG corresponded to a circumscribed Lyme borreliosis. In the absence of additional lesions, which would prompt the diagnosis of an inflammatory/infectious disease, the PET finding appeared to be a tumor and was therefore misleading for the primary diagnosis. During clinical follow up, however, FDG-PET studies appeared to be more useful than MR imaging. Although FDG uptake in the lesion reflected the clinical course (pre- and posttreatment period) of the infectious disease, the morphological changes as revealed on MR imaging persisted.

Conclusions

To the best of our knowledge, no other case of localized positive FDG-PET studies of neuroborreliosis has been reported so far. Our findings indicated that hypermetabolic findings on FDG-PET studies in the brainstem region should be regarded with caution, and neuroborreliosis must be considered as a possible differential diagnosis.

References


Manuscript received May 25, 2004.
Accepted in final form November 22, 2004.
Address reprint requests to: Michail Plotkin, M.D., Klinik für Strahlenheilkunde, Universitätsklinik Charité, Campus Virchow-Klinikum, Augustenburger Platz 1, 13353 Berlin, Germany. email: michail.plotkin@charite.de.