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LETTER TO THE EDITOR

A case of neurolymphomatosis involving cranial nerves: MRI and fusion PET-CT findings

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Dear Editor

Neurolymphomatosis (NL), or lymphomatous infiltration of peripheral nerves, is a rare neurologic manifestation that usually develops in patients with widespread systemic non-Hodgkin's lymphoma (NHL) but may be the sole relapse site of NHL [1]. Cranial neuropathy is an unusual syndrome of NL that is sometimes difficult to diagnose using conventional imaging modalities. We report a patient with NL of cranial neuropathy in whom fusion ^{18}F-fluoro-2-deoxy-D-glucose (FDG) PET-CT aided in establishing the diagnosis of NL.

A previously healthy, 66-year-old man presented with gastric lymphoma of CD20-positive, diffuse large B-cell phenotype. A thorough systemic evaluation revealed Ann Arbor stage IV NHL with multiple metastases in the neck and lung lymph nodes. Eight cycles of R-CHOP chemotherapy lead to complete remission. Three months later, he acutely developed left facial numbness, followed by right-sided peripheral facial palsy and diplopia. Over the next 2 weeks, he continued to deteriorate to the point of complete bilateral ptosis, bilateral facial hypesthesia, and severe dysarthria. On admission, he was alert and fully oriented. Neurologic examination was significant for 5-mm pupils unreactive to light, bilateral complete ptosis, remarkable extraocular movement limitations, bilateral facial anesthesia, and facial diplegia, consistent with bilateral third, fifth, and seventh nerve palsies. Brain MRI showed enlargement and enhancement of the cisternal segments of bilateral trigeminal nerves that was extending to the Meckel's caves and cavernous sinuses, more pronounced in the left (Fig. 1a). Whole body fusion PET-CT was performed to assess the extent of relapse, showing increased FDG uptake along the bilateral trigeminal nerves and Meckel's caves, stronger in the left (Fig. 1b). CSF analysis revealed 8 white cells/mm^3, markedly increased protein (340 mg/dl), and positive cytology for malignant lymphocytes. CSF tests for tuberculosis, virus, parasite, syphilis, and fungus were all negative. Finally, a diagnosis of NL involving multiple cranial nerves was made. Intense chemotherapy was scheduled but delayed due to bouts of serious infections. He could not recover from septicemia and multiple organ failure despite aggressive treatments, and finally he died two weeks later.

Our patient's MRI revealed enlargement and enhancement of trigeminal nerves, suggesting direct lymphomatous infiltration. However, these MRI findings are not specific for perineural spread of neoplastic diseases but can also be seen in various infectious and inflammatory processes. PET revealed increased FDG uptake in the trigeminal nerves and Meckel's caves, probably representing lymphomatous infiltration of cranial nerves, subsequently confirmed with positive CSF cytology.

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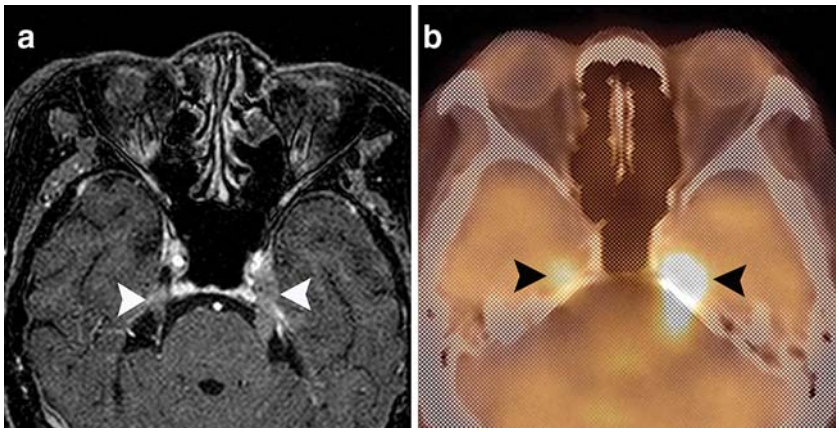

Fig. 1 (**a**) Axial gadolinium-enhanced T1-weighted MRI showing enlargement and enhancement of the bilateral trigeminal nerves that was incorporating into the Meckel's caves, more prominent in the left side (white arrowheads). Note lack of diffuse leptomeningeal or brain parenchymal enhancement. (**b**) Fusion PET-CT showing increased FDG uptake along the bilateral trigeminal nerves and Meckel's caves, stronger in the left side (black arrowheads), probably representing lymphomatous involvement of trigeminal nerves

Diagnosis of NL is often difficult and depends on histopathologic identification of infiltrating malignant lymphocytes in the affected nerves. Nerve biopsy, however, may show false negative results despite the widespread lymphomatous infiltration of peripheral nerves [2]. More limited is the role of CSF cytologic examination. Only minority of NL cases were reported to have positive CSF cytology at initial diagnosis, which may lead to false diagnosis [1]. Alternatively, imaging studies are of great utility in diagnosing NL before histopathologic confirmation and the most commonly used is enhanced MRI. While MRI typically shows enlargement and enhancement of affected nerves, it does not always provide optimal visualization of lymphomatous involvement of peripheral nerves [1]. Recently, FDG-PET has emerged as a powerful imaging modality for diagnosis, staging, and therapeutic monitoring of NHL. The advanced technique of fusion PET-CT provides better anatomical details of less commonly involved peripheral nerves, especially in cases with NL. Recent reports have demonstrated the clinical utility of the fusion PET-CT in diagnosis of NL [3–5]. Likewise, we demonstrated the diagnostic utility of fusion PET-CT in our patient allowing visualization of involved cranial nerves that was comparable to enhanced MRI, and this is, to our knowledge, the first case of NL showing FDG uptake in multiple cranial nerves. However, FDG-PET also has diagnostic limitations similar to MRI. FDG uptake is highly sensitive for tumor but is not specific and may also be seen in any process where the rate of glycolysis is increased, such as infection or inflammation [6]. Taken together, the diagnosis of NL of cranial neuropathy should require integration of clinical information and imaging findings as well as CSF cytologic examination.

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