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NEUROLYMPHOMATOSIS OF THE THORACIC SYMPATHETIC CHAIN

Neurolymphomatosis (NL) is defined as lymphomatous invasion of cranial or peripheral nerves by non-Hodgkin lymphoma (NHL). While most cases of NL are due to secondary dissemination from systemic or CNS sites, in rare cases it can be the primary manifestation of the malignancy.^{1–3} Early recognition of the disease and its precise neuroanatomic localization is critical for successful treatment.

We present an unusual account of secondary NL infiltrating the sympathetic chain diagnosed antemortem.

Case report. A 62-year-old woman presented to our institution with longstanding pain in the left lateral wall of her lower trunk and increased sweating. Her medical history included hypertension, irritable bowel disease, papillary thyroid cancer with subsequent thyroidectomy, and follicular center cell lymphoma with areas of diffuse large B-cell lymphoma. At the time of diagnosis, this NHL localized to axillary, mediastinal, and inguinal lymph nodes as well as the left orbit. It was in complete remission for 10 years after systemic R-EPOCH (rituximab, etoposide, prednisolone, vincristine, cyclophosphamide, doxorubicin) and prophylactic intrathecal liposomal cytarabine treatment. Family history was unremarkable. Neurologic examination was normal and physical examination only revealed an intensifying pain upon applying direct pressure to the lower left trunk. ¹⁸F-fluorodeoxyglucose (FDG) PET revealed avid tracer uptake within a longitudinal paravertebral mass lesion in the thoracolumbar retropleural and retroperitoneal space (SUV_m 8.6) and less avid uptake in the right S2 nerve root (SUV_m 4.3) (figure, A). Corresponding to the region of FDG avidity on the PET scan, MRI of the lumbar spine demonstrated right S2 nerve root enlargement and enhancement. Bone marrow biopsy, MRI of the brain, and CSF analysis failed to reveal any abnormalities. Biopsy of the left paraspinal mass performed at an outside institution revealed a B-cell lymphoproliferative process infiltrating an autonomic ganglion (figure, B–D). Flow cytometry showed a subset of B-cells with dim CD19 expression and dim kappa light chain restriction. A diagnosis of NL involving the sympathetic

chain was established. Treatment with high-dose methotrexate and rituximab was initiated. The patient achieved complete remission after 4 cycles as documented by FDG-PET. The patient underwent successful collection of autologous stem cells (course of high-dose cytarabine and etoposide followed by filgrastim, subsequent leukapheresis). She is now scheduled for myeloablative chemotherapy followed by stem cell transplantation.

Discussion. NL is an uncommon complication of NHL. While one autopsy study found NL in 37% of deceased patients with lymphoma,⁴ clinical experience suggests a relative frequency of less than 1%. Most frequently, NL infiltrates peripheral nerves (60%), followed by spinal nerve roots (48%), cranial nerves (46%), and plexus (40%).² Our case represents an unusual account of secondary NL infiltrating the sympathetic chain diagnosed antemortem. A comprehensive literature review using the PubMed database only revealed a single report of infiltration of sympathetic ganglia by NHL diagnosed at postmortem examination.⁵

The clinical presentation of NL naturally depends on localization and extent of dissemination of NHL within the peripheral nervous system. Polyneuropathy with or without pain is most commonly encountered. Mononeuropathies affecting a single cranial or peripheral nerve occur less frequently.³ In our case, however, symptoms were nonspecific. Pain was either nociceptive or neuropathic from nerve compression by the paravertebral mass. Surprisingly, right S2 nerve root infiltration caused no sensory or motor deficits. Also, despite extensive infiltration of the sympathetic chain, there was no clinical evidence of autonomic dysfunction.

Diagnosis of NL is especially challenging in the context of a nonspecific clinical presentation. Nevertheless, not only histopathologic but also neurologic topical diagnosis are of utmost importance, since patients with nervous system infiltration, central or peripheral, appear to benefit from the addition of high-dose methotrexate to the systemic treatment regimen in order to achieve therapeutic concentrations beyond the blood–brain and blood–nerve barriers.^{1–3} Of all diagnostic tools, imaging studies are of greatest utility, with MRI and FDG-PET providing the highest topical diagnostic yield.^{2,3,6} Biopsy remains

(A) FDG-PET/CT images in axial and coronal planes demonstrate avid uptake in left thoracic retropleural and retroperitoneal space (SUVm 8.6). (B) Hematoxylin & eosin stains demonstrate a dense atypical lymphoid population diffusely infiltrating and surrounding ganglion cells, which leads to an effacement and distortion of the sympathetic ganglion cytoarchitecture. (C) Immunohistochemical staining for synaptophysin highlights ganglion cells, which are characterized by large heterochromatic nuclei and a prominent nucleolus. (D) CD20 immunohistochemistry reveals the B-lymphocyte predominance of the atypical lymphoid infiltrate. (B-D) Original magnification $\times 40$.

the gold standard for securing the diagnosis, but is not always feasible.³

Systemic polychemotherapy including high-dose methotrexate is the treatment of choice for NL, with retrospective studies describing response rates exceeding 50%.^{1,2} As in the case of our patient, individuals with excellent performance status achieving complete remission benefit from consolidation with myeloablative chemotherapy followed by autologous stem cell transplantation.³

Our case adds to the diverse clinical spectrum of NL. Diagnosis and appropriate treatment require not only knowledge about this rare condition but also the integration of clinical examination, imaging data, and results of neural tissue biopsies.

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