Neurolymphomatosis caused by diffuse large B-cell lymphoma presenting as isolated brachial plexopathy

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To the Editor: A 66-year-old female complained of muscle weakness, numbness, and pain in her left shoulder and arm for 16 months, after which muscle atrophy and forearm swelling gradually developed. Before admission, she had been diagnosed with brachial plexus neuritis and received intravenous methylprednisolone with 500 mg for 3 days, followed by a tapering of oral prednisolone. However, she did not benefit much from the treatment. Her personal medical history and family history were not remarkable. The previous chest computed tomography (CT) scan and magnetic resonance imaging (MRI) scans of her brain, cervical spinal cord, and brachial plexus [Figure 1A] were not remarkable. Needle electromyography examination revealed the weakened motor unit recruitment with abnormal spontaneous activities, including positive sharp waves and fibrillations in the part of muscles innervated by left brachial plexus. The nerve conduction studies showed that compound muscle action potential and sensory nerve action potential amplitudes decreased greatly with prolonged distal latency in the muscles innervated by branches of left brachial plexus. This presentation was more readily visible in the inferior-trunk-innervated regions, such as ulnar-nerve-innervated muscles. Otherwise, the reduction of nerve conduction velocities was negligible.

After admission, neurological examination revealed reduced muscle strength (medical research council [MRC] 2/5) in the proximal and distal parts of the left arm. An apparent atrophy in deltoid and interosseous muscles was detectable. The left biceps, triceps, and radial periosteal reflexes were completely absent. The perception of light touch, pinprick, and temperature was severely impaired in the entire left forearm. MRI revealed extensively enlarged brachial plexus trunk [Figure 1B], and partial segments and several swollen supraclavicular lymph nodes showed enhancement [Figure 1C]. Positron emission tomography (PET) scan showed increased uptake of 2-deoxy-2-[fluorine-18] fluoro-D-glucose in the upper area with MRI abnormality (Figure 1D). Subsequently, a lymph node biopsy was performed in the left supraclavicular region for pathological investigation. The hematoxylin and eosin staining showed that the normal structure was destroyed and substituted by cancerous cells [Figure 1F and 1G]. Diffuse large B-cell lymphoma (DLBCL) was finally confirmed by immunohistochemical staining (Figure 1H–M). Thereafter, she underwent therapy with rituximab and doxorubicin hydrochloride liposome after returning to the local hospital. After eight courses of aggressive therapies for 10 months, repeated MRI and PET scan [Figure 1E] revealed remarkable elimination of lesions, but there was no apparent improvement of clinical manifestations.

Brachial plexopathy has many non-injury etiologies, such as hereditary neuropathy, autoimmune neuropathy, neoplasms, and other inexplicit etiology (eg, thoracic outlet syndrome). Generally, a slowly progressing unilateral brachial plexopathy without remission strongly suggests a possibility of neoplasm including primary nerve tumors and secondary (local or metastatic) tumors. Primary tumors including neurinomas, schwannomas, and neurofibromas are more common than the secondary tumors.[1] Most secondary tumors involving unilateral brachial plexus arise from local tumors. These include Pancoast tumor and breast cancer. It is unusual that brachial plexus is involved by neurolymphomatosis (NL). NL is a clinical disorder that presents with peripheral neuropathy due to lymphomatous infiltration of the nerves. It occurs in three per 100 cases of intermediate or high-grade non-Hodgkin lymphoma patients and occasionally invades brachial plexus.[2] In a literature review of case reports, the prevalence of brachial plexus involvement is 18% (8/44) in NL.[2]

Symptoms of NL differ greatly according to the sites involved. Painful neuropathy, however, developed in 76% of NL patients and suggests that pain may be an important

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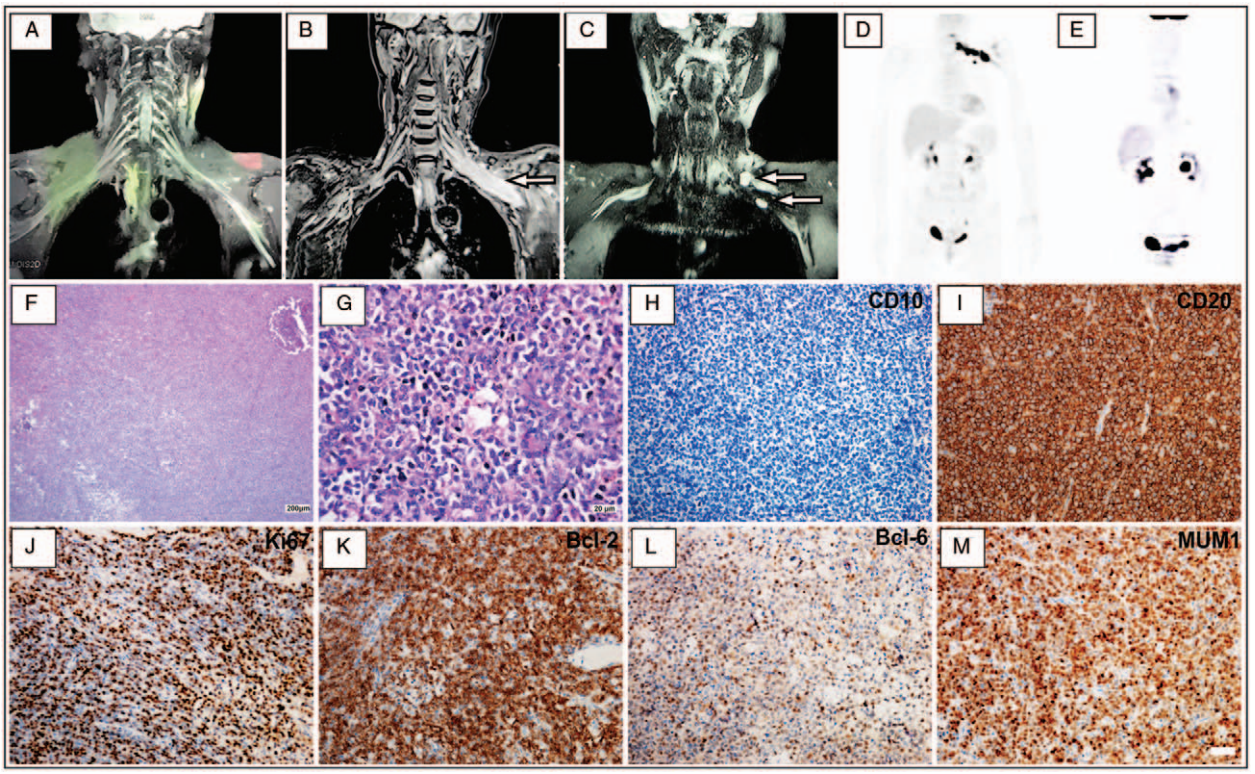

Figure 1: Representative images of the patient. (A) In the 12-month course of the disease, STIR MRI of brachial plexus showed nothing remarkable. (B) In the 16-month course of the disease, STIR MRI revealed the thickening trunk of left brachial plexus (arrow). (C) Swollen lymph nodes in the supraclavicular position were enhanced (arrows). (D) FDG-PET CT scan showed an increased uptake of 18F-FDG in the thickening trunk and supraclavicular lymph nodes. (E) In the 26-month course of the disease, FDG-PET CT scan indicated the previous uptake of 18F-FDG was vanished. (F–G) The lymphatic normal structure was deconstructed (F, HE staining, original magnification ×40) and substituted by cancerous cells (G, HE staining, ×400). (H–M) The immunohistochemical stain: the expression of CD10 (–) (H, ×400), CD20 (+) (I, ×400), Ki67 (80% +) (J, ×400), Bcl-2 (+) (K, ×400), Bcl-6 (60%+) (L, ×400), and MUM1 (+) (M, ×400) in the supraclavicular lymph nodes. Bcl-2: B-cell lymphoma-2; CD: Cluster of differentiation; FDG-PET CT: Fluoro-D-glucose positron emission tomography computed tomography; HE: Hematoxylin and eosin; MRI: Magnetic resonance imaging; MUM1: Multiple myeloma oncogene 1; STIR: Short TI inversion recovery.

symptom and is associated with the infiltration of lymphoma to nerves.[2] For this patient, after 1 year of brachial plexopathy onset, the routine MRI scan was still not remarkable, which led doctors to make an incorrect early diagnosis. The MRI indicated that the thickening presentation of nerve fibers maybe not obvious in the early stage of NL, so enhanced MRI or PET-CT scan may be particularly valuable to patients with unexplained courses of progression of unilateral brachial plexopathy. According to the previous report, the sensitivity of the MRI was 77% for diagnosis and the PET-CT was more effective, reaching 88% sensitivity to identify NL.[3] Although biopsy is the diagnostic gold standard, half of NL patients did not undergo a biopsy because of the possibility of permanent nerve damage. For this patient, lymph node biopsy helped to establish the pathological diagnosis of DLBCL.

Once the diagnosis of primary NL is established, the median survival of patients is 20 months.[2] Currently, there is no standard treatment for NL. For systemic chemotherapy of non-Hodgkin's lymphoma, rituximab plus CHOP (including cyclophosphamide, hydroxydaunorubicin, oncovin, prednisone) is used as the first-line regimen (R-CHOP). As reported in previous studies, a high dose of intravenous methotrexate can penetrate the blood-nerve barrier. It is considered effective in patients with NL.[2] For this patient, the relatively low ki-67 expression (80%) might indicate the tumor was not so aggressive.[4] Accordingly, no tumor metastasis occurred in the long course. Finally, the patient benefited from the systemic therapies, while her irreversible neurological dysfunction could be attributed to a long-time injury to the brachial plexus.

In conclusion, DLBCL, the most common type of NL, can present as unilateral isolated brachial plexopathy. When approaching a patient with progressive painful unilateral brachial plexopathy, NL should be considered. Completing the contrast-enhanced MRI and PET-CT and performing biopsy to extra-nerve involved tissues can help establish clear diagnostic and therapeutic protocols for this rare condition.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the work, the patient gave her consent for her images, and other clinical information to be reported in the article. The patient understands that neither

her name nor initials will be published, and due effort will be made to conceal her identity, although total anonymity cannot be guaranteed.

Conflicts of interest

None.

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