Polyneuropathy as Paraneoplastic Syndrome in a Patient with Metastatic Diffuse Large B-Cell Lymphoma

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Abstract

Paraneoplastic syndromes are multisystemic diseases that are seen in association with solid organ tumors and lymphomas. Immune-mediated polyneuropathy, encephalopathy, cerebellar degeneration, and Guillain–Barre syndrome have all been described as paraneoplastic neurologic disorders. Clinical symptoms may appear before the diagnosis of associated malignancy creating diagnostic confusion. Tumor-derived peptides, hormones, and mediators are shown to be associated with paraneoplastic syndromes. Herein, we present an unusual case of stage 4 diffuse large B-cell lymphoma with cutaneous metastatic nodules presenting initially as paraneoplastic polyneuropathy.

Keywords: B-cell lymphoma, paraneoplastic, polyneuropathy

Introduction

Paraneoplastic syndromes are defined as a group of systemic disorders that most commonly develop in association with solid organ tumors and lymphomas.[1] Tumor-related hormones, peptides, mediators as well as immune cross-reaction between normal and tumoral tissues are held responsible for paraneoplastic syndromes.[1,2] Manifestations of systemic involvement may develop during the course of paraneoplastic syndromes.[3] Diffuse large B-cell lymphomas (DLBCL) are known to be associated with paraneoplastic neurologic disorders (PNDs).[4] We present an extraordinary case of stage 4 DLBCL with skin metastases presenting initially as sensory and motor polyneuropathy.

Case Report

A 63-year-old man with a history of hyperlipidemia, benign prostate hyperplasia, and hypertension was referred to us due to enlarging erythematous nodules involving the chest. The patient had pain and numbness sensation radiating from bilateral first, second, third, and fifth fingers to elbows and hypoesthesia between first and second toes 20 days before. Electromyography (EMG) findings results showed prolonged distal motor latencies of bilateral median and right tibial nerve; decreased motor conduction velocities of the right median, tibial and left ulnar nerves; and motor conduction blocks of bilateral median and left ulnar nerve. With EMG findings, he was diagnosed with demyelinating polyneuropathy accompanied by secondary axonal degeneration in both sensory and motor fibers. A provisional diagnosis of multifocal acquired demyelinating sensory and motor polyneuropathy was considered. Diffusion magnetic resonance imaging (MRI) of the brain showed T2 hypointensities, prominent diffusion restriction, and increased signal contrast involving the left parietooccipital, bilateral frontal scalp extending to bilateral temporal subcutaneous tissue [Figure 1B]. However, no pathological enhancement was noted. Cervical MRI showed pathological linear enhancement in the posterior roots of the right T1 nerve, bilateral C7, and C8 nerves; T2 hypointense enhancing soft-tissue lesion was apparent in the right maxillary area. MRI findings

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were compatible with primarily lymphomal involvement. Cerebrospinal fluid analysis showed an increased number of lymphomononuclear cells. The patient reported to have no B symptoms; full blood count and biochemistry were normal. Autoimmune markers and viral markers were all negative. Beta-2 microglobulin and lactate dehydrogenase levels were normal. Seven days after his hospitalization, he developed non-tender violaceus-erythematous nodules involving the anterior chest and right zygomatic area [Figure 1]. He denied any prior history of similar cutaneous nodules. A 4-mm-punch biopsy was performed from the right subcostal area which showed blastic, medium-sized lymphoid aggregates demonstrating diffuse infiltration pattern [Figure 2]. Mitotic activity was high and neoplastic cells were diffusely and strongly positive with CD20 and BCL-2 (B-cell lymphoma 2); BCL-6 (B-cell lymphoma 6) and MUM-1 (multiple-myeloma 1) were found positive in more than 30% of the neoplastic cells [Figure 2]. Ki-67 proliferation index was 70%–80%. EBER (Epstein–Barr virus-encoded small ribonucleic acids) *in situ* hybridization was negative. FISH (fluorescent *in situ* hybridization) analysis revealed MYC (myelocytomatosis) gene translocation but no aberrations in *BCL-2* and *BCL-6* genes [Figure 2]. Bone marrow aspiration biopsy was normal. Thoracoabdominal computed tomography (CT) showed aortocaval and conglomerated right hilar lymph nodes. Radiologic imaging studies suggested the diagnosis of lymphoproliferative disorder. The patient was diagnosed with stage 4 DLBCL, as the presence of pathologic lymph nodes involving thoracoabdominal region was

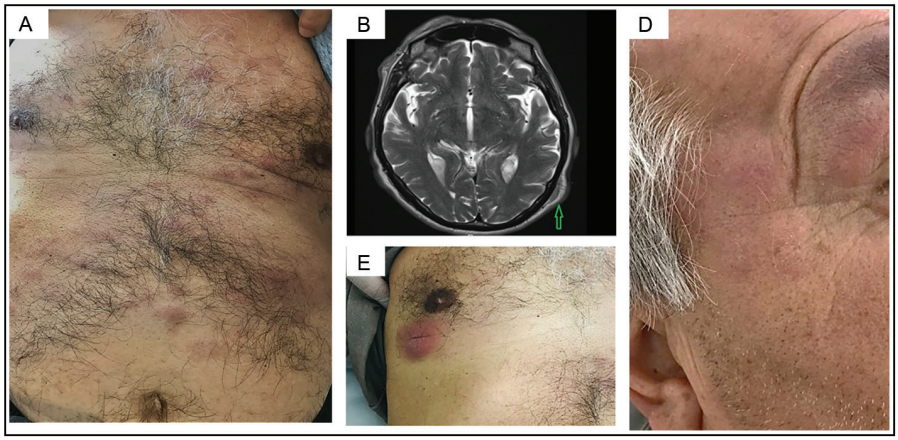

Figure 1: Dermatologic examination revealing widespread erythematous nodules involving the anterior chest (A), most prominent on the right inframammarian area (C) and the right face (D). T2-weighted magnetic resonance imaging showed iso-hyperintense lesions in the left temporoparietal area (arrow, B)

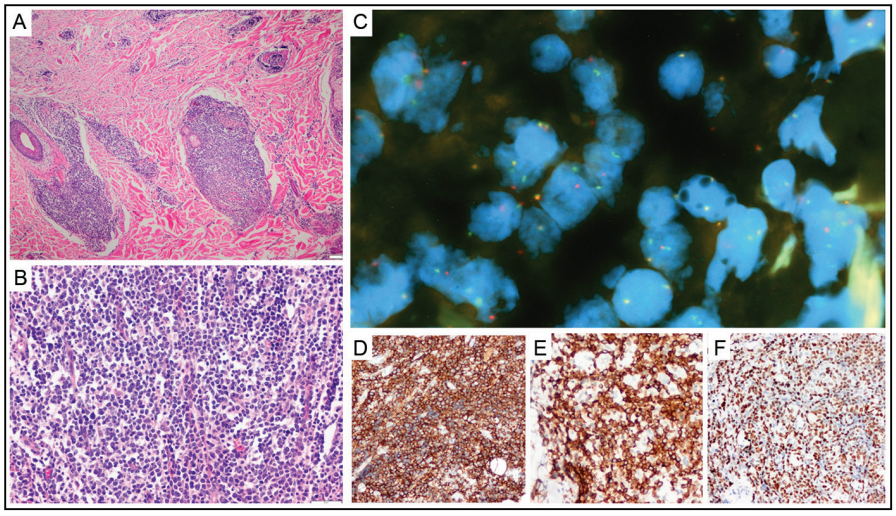

Figure 2: On low-power lymphoid neoplasm centered around skin adnexae in dermis with concomitant subcutaneous fat involvement was seen (A) (HandE, 40X). Neoplastic population was composed of medium-sized atypical lymphoid cells with blastic chromatin, irregular nuclear contours and small nucleoli (B) (HandE, 200X). Immunohistochemically these cells were diffusely and strongly positive with CD20 (D, 400X), Bcl-2 (E, 400X). Ki-67 proliferation index was relatively (%80) high (F, 400X). Findings supported a high-grade B cell lymphoma, for further subclassification FISH was performed. On FISH examination neoplastic cells showed a pattern consistent with MYC gene translocation (C, 1000X). Together with the immunophenotypic and morphological findings the patient was finally diagnosed as *MYC-positive diffuse large B cell lymphoma*

supported by CT and disseminated erythematous nodules were accepted as cutaneous metastases given that they appeared simultaneously 7 days ago. He was started on rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone chemotherapy regimen and a total dose of 30 mg intravenous immunoglobulin was administered over 5 days which resulted in diminution of neurologic symptoms.

Discussion

PNDs developing in association with solid organ malignancies or lymphoid malignancies may present themselves in a wide spectrum of syndromes.[5] Frequently reported neurological syndromes are encephalomyelitis, cerebellar degeneration, autonomic neuropathies, subacute sensory neuronopathies, and optic neuritis.[5] PNDs are shown to be associated with antineuronal autoantibodies such as anti-Hu, anti-Ri, anti-Ma, and anti-mGluR1 produced in the setting of underlying neoplasm.[6] Primary cutaneous B-cell lymphomas and systemic lymphomas presenting with cutaneous metastases are reported to be associated with various PNDs.[7] Ho *et al*.[7] reported a rare case of mononeuritis multiplex observed in a patient diagnosed with primary cutaneous large B-cell lymphoma of the leg and breast. In addition, Jiang *et al*.[8] described another case of DLBCL which presented as a painful lump on the cheek and was associated with sensorimotor demyelinating polyneuropathy, which is very similar to our case. These cases show that primary cutaneous lymphomas or skin involvement of the systemic lymphomas may also present with neurologic symptoms before the diagnosis. In conclusion, we present an extraordinary case of stage 4 DLBCL with widespread metastases to skin, developing demyelinating sensory and motor polyneuropathy involving upper, lower limbs. Before the appearance of metastatic skin lesions, the relationship between DLBCL and neurologic symptoms was not able to be established. Therefore, skin biopsy was the fundamental diagnostic approach for the underlying lymphoid neoplasm. An associated malignancy should always be considered in patients presenting with progressive sensory or motor polyneuropathy of unknown origin. Full-body dermatologic examination should always be completed to detect any visible cutaneous metastases which could provide physicians a hint for the right diagnosis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

References

1. Pelosof LC, Gerber DE. Paraneoplastic syndromes: An approach to diagnosis and treatment. Mayo Clin Proc 2010;85:838-54.
2. de Beukelaar JW, Sillevis Smitt PA. Managing paraneoplastic neurological disorders. Oncologist 2006;11:292-305.
3. Ma GM, Chow JS, Taylor GA. Review of paraneoplastic syndromes in children. Pediatr Radiol 2019;49:534-50.
4. Nevison S, Rizek P. Anti-CV2-associated paraneoplastic hemichorea secondary to diffuse large B-cell lymphoma. Can J Neurol Sci 2019;46:480-1.
5. Rosenfeld MR, Dalmau J. Update on paraneoplastic neurologic disorders. Oncologist 2010;15:603-17.
6. Graus F, Dalmau J. Paraneoplastic neurological syndromes. Curr Opin Neurol 2012;25:795-801.
7. Ho SL, Tang BY, Chai J, Tan SH. Cutaneous large B-cell lymphoma of the leg: Presenting initially as mononeuritis multiplex. Singapore Med J 2009;50:e158-60.
8. Jiang Z, Ju W, Luo S, Yang Y. Diffuse large B-cell lymphoma involving peripheral nervous system with IgM antibodies against GM1 and GD1B: A case report. Medicine (Baltimore) 2019;98:e15049.