Merkel cell carcinoma (MCC) is a rare aggressive skin cancer, the incidence of which is increasing rapidly (1). Various paraneoplastic syndromes have been associated with MCC, due to its neuroendocrine nature, and these could be the first manifestations of cancer (2–7). We report here a case of a patient whose diagnosis of MCC with unknown primary was made following the identification of 2 uncommon neurological disorders. This case report highlights the complexity of paraneoplastic syndrome associated with MCC and the importance of a multidisciplinary approach.

CASE REPORT

An otherwise healthy 59-year-old man was admitted to the neurology clinic at the emergency department due to rapidly worsening difficulties in walking, and limb weakness associated with ataxia, diplopy and nystagmus in the previous 2 weeks. Radiological imaging, including high-resolution computed tomography (CT) and magnetic resonance imaging (MRI), did not disclose any significant abnormalities. Viral and bacterial serological tests were negative. Motor-nerve conduction studies showed post-exercise facilitation, and a qualitative assay for the presence of P/Q-type voltage-gated calcium channel antibodies was positive. These results led to a diagnosis of Lambert-Eaton myasthenic syndrome (LEMS) associated with manifestations of cerebellar degeneration. Symptomatic treatment with fampridine, a potassium channel blocker, was tried with partial improvement. Positron emission tomography (PET; Fig. 1) revealed hyper-metabolic lesions in left inguinal lymph nodes. An excisional biopsy showed positive immunohistochemical reactions with anti-synaptophysin antibodies (Fig. 2A), cytokeratins AE1/AE3, cytokeratin 20 (Fig. 2B), and chromogranin A. MIB-1 proliferative activity was 70%; the presence of numerous mitoses (15/10 high-power field) and areas of necrosis was reported (Fig. 2C). These findings were consistent with a diagnosis of lymph node deposit of metastatic cells of Merkel cell carcinoma (MCC).

The clinical history was unremarkable regarding previous excisions or spontaneous regressions of skin lesions. A careful clinical and dermoscopic examination did not find any cutaneous lesions suggestive of MCC, and PET scan did not show any other hyper-metabolic lesions. The multidisciplinary oncological committee opted for moderate hypofractionated radiotherapy with a total dose of 50 Gy, as the patient’s performance status did not allow a radical surgical treatment. A computed tomography (CT) scan performed 2 months later demonstrated remission of the disease.

After 6 months’ follow-up, the patient showed a partial improvement in walking, but persistence of ataxia, diplopy and nystagmus due to referable to a paraneoplastic cerebellar degeneration (PCD).
in association with LEMS consequent to MCC with unknown primary.

**DISCUSSION**

MCC is a rare malignant neuroendocrine skin carcinoma associated with a high rate of local and distant metastases and poor prognosis. Typically, MCC is a primary carcinoma of the skin, but it can be detected in different sites without an apparent primary localization (1). Few cases of lymph node involvement by MCC with an unknown primary tumour have been reported in the medical literature. It remains unclear whether the nodal MCC is a primary tumour of the lymph node or a metastasis from an occult or regressed extranodal lesion (8).

The current case is of interest due to the association of 2 paraneoplastic disorders in a patient with unknown primary MCC. LEMS is an antibody-mediated disorder of the neuromuscular junction, while PCD is a consequence of autoimmune destruction of cerebellar Purkinje cells.

Paraneoplastic syndromes can be associated with MCC, although this is rarely reported (only 27 cases have been published to date in the English literature) (2–7). Of these, 8 patients presented with LEMS and 5 were affected by PCD associated with MCC. It should be noted that almost the half of the 27 cases described were secondary to MCC with unknown primitive. To our knowledge, the association of both LEMS and PCD with MCC has been described only in a patient with MCC metastasis in the axilla and unknown primary (7).

In the current, the first-line treatment considered would have been complete lymphadenectomy; however, after multidisciplinary discussion, this was not performed, due to patient’s general conditions (9). We therefore opted for radiotherapy, discarding the possibility of anti-PD-L1 therapy due to the immune manifestations already present in the patient. Regarding the only slight improvement in the neurological symptoms, a possible explanation could be the current persistence of occult MCC neoplastic cells, or non-resolution of the paraneoplastic picture, following treatment of the underlying oncological disease.

This case report highlights the importance of multidisciplinary management; dermatologists should be aware of the possible paraneoplastic syndromes associated with MCC.

*The authors have no conflicts of interest to declare.*

**REFERENCES**

1. Bichakjian CK, Olenczi T, Aasi SZ, Alam M, Andersen JS, Blitzblau R, et al. Merkel cell carcinoma, version 1.2018, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw 2018; 16: 742–774.

2. Iyer JG, Parvathaneni K, Bhatia S, Tarabadkar ES, Blom A, Doumani R, et al. Paraneoplastic syndromes (PNS) associated with Merkel cell carcinoma (MCC): a case series of 8 patients highlighting different clinical manifestations. J Am Acad Dermatol 2016; 75: 541–547.

3. Simmons DB, Duginski TM, McClean JC, Amato AA, Sladky JH. Lambert-Eaton myasthenic syndrome and Merkel cell carcinoma. Muscle Nerve 2016; 53: 325–326.

4. Nguyen ND, Simmons DB, Bursabe AR, Duginski TM, Sladky JH, Walton D, et al. Lambert-Eaton myasthenic syndrome and Merkel cell carcinoma. Cutis 2019; 103: E19–E23.

5. Sharobeam A, Ray J, Dong J, Chong V. Subacute cerebellar degeneration due to a paraneoplastic phenomenon associated with metastatic Merkel cell carcinoma: a case report. Case Rep Oncol 2017; 10: 764–768.

6. Queen D, Gu Y, Lopez A, Chen D, Geskin LJ. Paraneoplastic cerebellar ataxia in Merkel cell carcinoma of unknown primary. JAAD Case Rep 2019; 5: 398–400.

7. Pavolucci I, Giannini G, Giannoccaro MP, Foschini MP, Lang B, Avoni P, et al. Paraneoplastic cerebellar degeneration and Lambert-Eaton myasthenia in a patient with Merkel cell carcinoma and voltage-gated calcium channel antibodies. Muscle Nerve 2017; 56: 998–1000.

8. Lawrence LEB, Saleem A, Sahoo MK, Tan SK, Pinsky BA, Natkunam Y, et al. Is Merkel cell carcinoma of lymph node actually metastatic cutaneous Merkel cell carcinoma? Am J Clin Pathol 2020; 154: 369–380.

9. Naseri S, Steiniche T, Ladekarl M, Bønnelykke-Behrndtz ML, Hölmich LR, Langer SW, et al. Management recommendations for Merkel cell carcinoma – a Danish perspective. Cancers (Basel) 2020; 12: 554.