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Unexpected infiltration of meninges by generalised diffuse large B-cell lymphoma manifesting as multiple cranial neuropathies in a patient with history of breast carcinoma

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To the Editors

Leptomeningeal spread of malignant tumorous cells occurs more commonly in haematological malignancies (incidence of 10–15%) and less often with solid tumours such as breast cancer, lung cancer, and melanoma (incidence of 1–5%) [1]. Diagnostic methods mainly include clinical assessment, cerebrospinal fluid cytological examinations [2], and magnetic resonance imaging (MRI) to distinguish brain metastases from other brain tumours [3]. We present a case of leptomeningeal malignant infiltration in a patient with known breast carcinoma, that initially presented as multiple cranial neuropathies. Surprisingly, but consistent with previous cerebrospinal fluid (CSF) examinations, the autopsy excluded meningeal carcinomatosis by breast cancer malignant cells, and confirmed generalised B-cell lymphoma, including leptomeningeal infiltration.

An 84-year-old female with a history of diabetes, arterial hypertension, and breast cancer diagnosed three years previously and treated by mastectomy and tamoxifen, presented with multiple cranial nerve palsies. Two months before, she had been hospitalised for acute bleeding into a chronic subdural haematoma, which was treated conservatively (Fig. 1A). Clinical examination revealed an incomplete right oculomotor nerve palsy, peripheral left facial nerve palsy, and left leg instability. Laboratory analysis showed only hyperglycaemia. MRI showed haematoma regression and contrast enhancement of the leptomeninges around the right hemisphere (Fig. 1B).

CSF analysis found elevated cell counts and high total protein levels and increased lactate and glucose levels. Empirical antimicrobial therapy with ceftriaxone was initiated, but discontinued soon after due to CSF cultivation; both it and borreliosis serology were negative. Cytomorphological CSF analysis identified atypical cells and another lumbar puncture was performed for a detailed cytological investigation: the cell count was 240 elements per microlitre with enlarged basophilic cells displaying cytoplasmic and nuclear abnormalities, frequent mitosis, and local cohesive tendencies.

The patient was clinically deteriorating, progressing toward somnolence, with progressive right upper and left lower limb weakness, and renal failure. Chronic neuroinfection, however, was still considered the most probable differential diagnosis; ceftriaxone with ampicillin was started, and a third lumbar puncture was performed.

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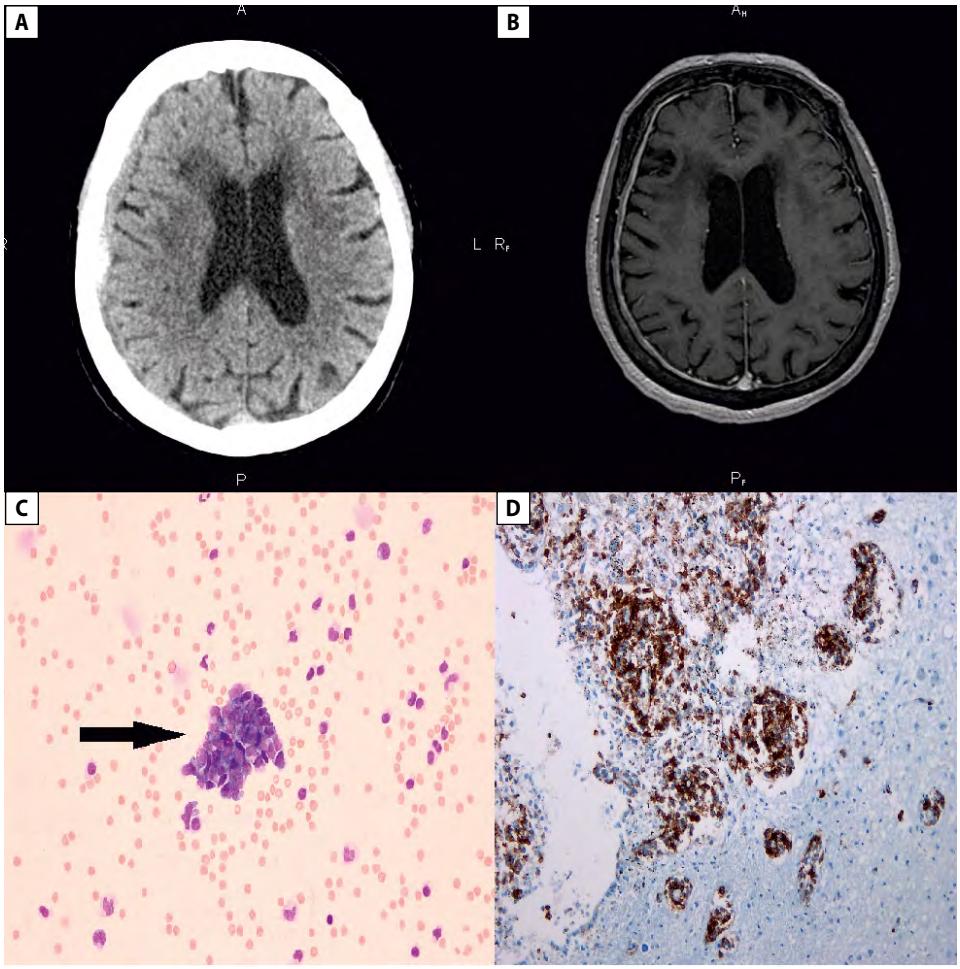

Figure 1. A. Axial non-contrast CT image (two months before disease onset) shows heterogenous subdural effusion above right cerebral convexity, indicating acute bleeding into chronic subdural haematoma; **B.** Axial T1 contrast-enhanced image shows regression of subdural haematoma with asymmetric enhancement of right-sided dura; **C.** CSF cytology — a cluster of lymphoma cells (marked by arrow). May-Grunwald Giemsa stain, 40×; **D.** Neuropathology — diffuse infiltration of meninges at base of mesencephalon by CD20 positive malignant B-cell lymphoma cells. Immunohistochemical staining using an anti-CD20 antibody, 40×

PCR investigation excluded the most likely pathogens. Immunocytochemical typing of cytologically suspected cells (Fig. 1C) surprisingly identified CD45 and PAX5, both hallmarks of B-cell lymphoma.

The patient's condition continued to deteriorate, and she died 11 days after admission. Autopsy confirmed a massive pulmonary embolism as the cause of death. The major finding concerning the aetiology of meningeal involvement (including the spread to cranial nerves at brain stem level) (Fig. 1D) was a generalised tumour affecting several organs (the lungs, stomach, and lymphatic nodes). A detailed histopathological investigation definitively excluded breast cancer extension, and finally confirmed generalisation of high-grade diffuse large B-cell lymphoma as the source of the leptomeninges infiltration.

Establishing the final diagnosis was a difficult task given the concurrence of the unrelated subdural haematoma and a past history of breast cancer. MRI leptomeningeal enhancement was ascribed initially to the subdural haematoma rather than meningeal infiltration. Moreover, the immunocytochemical investigations of potentially malignant cells in CSF were primarily focused on breast carcinoma.

There have been several published cases with a history of malignancy presenting as a spontaneous nontraumatic subdural haematoma that ultimately turned out to be leptomeningeal tumour infiltration [4–7]. However, in our case the regression of the haematoma (Fig. 1B) confirmed the coincidence of a subdural haematoma and tumour, and not subdural haematoma mimicking [8].

This case report offers guidance regarding patients with a known medical history of malignancy. It is always necessary to consider tumour duplicity and be open to a disorder caused by an entirely new type of tumour (in this case, breast cancer and B–cell lymphoma) [9]. This case clearly demonstrates the

importance of close cooperation between clinicians, radiologists, and laboratory specialists in establishing the proper diagnosis.

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