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LETTERS TO THE EDITOR

Sudden Death Secondary to Mycosis Fungoides of the Midbrain

Sir,

Mycosis fungoides (MF) is typically an indolent T-cell cutaneous lymphoma that progresses over many years, but in some instances it may be an aggressive neoplasm with systemic involvement. Extra-cutaneous MF is commonly found at autopsy, but it is less apparent clinically. Up to 75% of autopsies show lymph node involvement, 50% show visceral organ involvement and 14% show central nervous system (CNS) involvement (1). Patients with symptomatic CNS involvement present with advanced stage MF, often when receiving chemotherapy or electron beam therapy to control the cutaneous manifestations (2). They may present with neurological complications or an altered mental state (1) and prognosis is poor when neurological symptoms occur. We present a case of MF with tumour stage disease clinically confined to the skin in whom there was no focal neurology and the presenting symptom of CNS involvement was sudden death.

CASE REPORT

A 56-year-old man presented with a 6-month history of a rapidly growing ulcerated lesion on the left temple. He was an anxious man, but otherwise well. He smoked 20 cigarettes a day, was a moderate drinker, took no medication, and had no past medical history of note. Examination was unremarkable, except for the temporal lesion. Investigations showed a normal full blood count, blood film, plasma viscosity, blood biochemistry, liver function tests and chest X-ray. A biopsy of the lesion showed malignant T-lymphocytes, which expressed CD45Ro, CD3 and CD30 on immunostaining. There were dermal abscesses, with eosinophils and plasma cells present in the infiltrate. The affected skin was excised and grafted. Eight months later he presented with a red scaly eruption on his right thigh. Biopsy was consistent with MF with pleomorphic CD45Ro, CD3, CD4 immunoreactive mononuclear cells that had cerebriform lobulated nuclei and showed epidermotropism. A further full blood count and blood film was normal, as was a CT scan of the chest, abdomen and pelvis.

Plaques and ulcerated lesions typical of MF developed intermittently over the following 18 months. These were managed with a combination of PUVA and orthovoltage radiotherapy. As the disease progressed, he declined further treatment and often failed to attend clinic appointments. Close family members noted a more withdrawn affect and increased alcohol consumption. No evidence of focal neurology or clinical depression was detected by his family doctor, relatives or hospital clinicians.

He was found dead at home one morning 2 years after initial presentation. Post-mortem examination disclosed no lymph node or organ involvement by MF. Macroscopic examination of the body did not reveal the cause of death and a toxicology screen (including alcohol) was negative. No macroscopic abnormalities were evident in the fixed brain. Blocks taken for histological examination of the brain showed an extensive perivascular and interstitial infiltrate of tumour cells in the frontal cortex, internal capsule, midbrain, pontine tegmentum and cerebellar peduncles. The tumour cells had hyperchromatic, irregularly convoluted cerebriform nuclei and scanty cytoplasm. Macrophages and eosinophils were also present. Immunohistochemistry for CD45Ro confirmed that the tumour cells were of T-lymphocyte origin. Death was presumed to be due to their extensive infiltration of the brainstem reticular formation, including vital structures involved in cardiovascular and respiratory control, probably leading to a cardiac arrhythmia.

Symptomatic involvement of the CNS by MF is rare. A retrospective study of 316 cases of MF from the Mayo Clinic, USA, found 19 cases with CNS involvement, all of whom had preceding neurological complications (3). Meningeal infiltration is the most common form (1). There are often Sezary cells in the peripheral blood and visceral involvement, and these cases may mimic viral meningitis or encephalitis (4). Local infiltrates in the brain or spinal cord have been described that mimic space-occupying lesions, such as neoplasms or abscesses (1). Multifocal demyelination and neoplasia in MF have been reported as mimicking multiple sclerosis or progressive multifocal leukoencephalopathy. Several case series have shown that brain imaging and CSF analysis will allow diagnosis of the majority of cases that present with focal neurological signs or an altered mental state (1, 2). MF in the CNS, often becomes apparent during chemotherapy for advanced disease, and the CNS may act as a sanctuary for MF tumour cells in a similar fashion to that described for leukaemic cells (1). There is a variable response to chemotherapy that includes intrathecal methotrexate, although in some patients this has resulted in a resolution of the CNS symptoms and a loss of the Sezary cells from the CSF (1–4).

The case described here illustrates that a change in mental state due to MF infiltration of the brain may be subtle, and that focal neurology may not be apparent. There is one case report of a 68-year-old man with MF without visceral involvement who complained of fatigue and lightheadedness. Six months later, neurological examination revealed bilateral frontal lobe signs with a space-occupying lesion confirmed on an MRI scan and cerebriform lymphoid cells in the CSF (5). To our knowledge, our case report is the first example of MF infiltration of the brain leading to sudden death. Without histological examination of the brain, similar cases may be missed. If further cases are reported, it may be worth including brain imaging and CSF examination as part of the routine staging procedure, especially if intratheccal methotrexate can alter the course of the disease within the CNS.

REFERENCES

1. Filipe PL, Coutinho VS, Canhao P, Gouveia R, Cabecadas J, Osorio A, et al. Mycosis fungoides with early central nervous system involvement. Acta Derm Venereol 1994; 74: 63–64.
2. Hallahan D, Griem M, Griem S, Duda E, Baron J. Mycosis fungoides involving the central nervous system. Clin Oncol 1986; 4: 1638–1644.
3. Sentis HJ, Padberg G, Buruma OJS, Bots GTAM, Willemze R, van Vloten WA. Neurological complications in patients with cutaneous T-cell lymphoma. Br J Dermatol 1986; 114: 359–366.
4. Kaufman DK, Habermann TM, Kurtin PJ, O'Neill BP. Neurological complications of peripheral and cutaneous T-cell lymphomas. Ann Neurol 1994; 36: 625–629.
5. Zonenshayn M, Sharma S, Hymes K, Knopp EA, Golfinos JG, Zagzag D. Mycosis fungoides metastasizing to the brain parenchyma: case report. Neurosurgery 1999; 42: 933–937.

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