Short report

Brain biopsy in the diagnosis of cerebral mycosis fungoides

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SUMMARY A case of cerebral mycosis fungoides co-existing with progressive multifocal leucoencephalopathy presented with dementia. Brain biopsy established the diagnosis of mycosis fungoides after cerebrospinal fluid examinations and computerised tomographic scanning of the brain produced non-specific abnormalities.

Mycosis fungoides is a cutaneous lymphoma with characteristic histological and cytological features. Visceral infiltration is a common necropsy finding and although the nervous system usually is spared, metastatic involvement of many parts of the nervous system and various non-metastatic neurological complications have been described (table). Cytological examination of the CSF has been helpful in establishing the diagnosis of meningeal mycosis fungoides in a few patients, but in others the CSF has been normal although meningeal and parenchymal infiltration was found at subsequent necropsy. As mycosis fungoides is potentially treatable with radiotherapy or chemotherapy or both, other techniques are needed to establish the diagnosis. This case report describes the use of CT scan and brain biopsy, neither of which have previously been reported, and the unexpected occurrence of both progressive multifocal leucoencephalopathy (PML) and cerebral infiltration with mycosis fungoides.

Table Neurological complications of mycosis fungoides*

<table>
<thead>
<tr>
<th>Metastatic</th>
<th>References</th>
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<tbody>
<tr>
<td>Eye</td>
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<tr>
<td>Cranial nerve</td>
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<td>Peripheral nerve</td>
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<td>Spinal ganglia, roots</td>
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<td>Cerebral parenchyma</td>
<td>1, 4, 6, 10, 14, 18, 19</td>
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<tr>
<td>Meninges</td>
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<td>Ventricles, choroid plexus</td>
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<td>Pituitary</td>
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<tr>
<td>Non-Metastatic</td>
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<tr>
<td>Infection</td>
<td></td>
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<tr>
<td>Viral (progressive multifocal leucoencephalopathy)</td>
<td>20</td>
</tr>
<tr>
<td>Fungal (cryptococcus)</td>
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<tr>
<td>Bacterial (Listeria m)</td>
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<tr>
<td>Protozoal (Toxoplasma)</td>
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<td>Nutritional, metabolic (central pontine myelinolysis)</td>
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<td>Iatrogenic (radiotherapy, chemotherapy, diagnostic or surgical procedures)</td>
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<td>Idiopathic (demyelination)</td>
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<td>Dermatomyositis</td>
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<td>Myelopathy, neuromyopathy</td>
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*Complications without references are known complications of lymphomas not yet described in mycosis fungoides.
Case report

A 62-year-old engine driver was admitted to a dermatology department in March 1980 with a 4 year history of discoid and annular lesions of parapsoriasis on the back, the flank and the legs, and with an itchy raised, scaly fissured lesion on the dorsum of the right hand for 6 months. Biopsy showed features consistent with mycosis fungoides and treatment was started with superficial radiotherapy and cyclophosphamide 50 mg twice daily. Four months previously he had developed a right anterior uveitis, treated with topical atropine and betamethasone. Two weeks before admission he developed slight confusion and disorientation, expressive dysphasia, and a mild left hemiparesis. An isotope scan showed increased activity superficially in the left frontal region, and the right posterior parietal region. The illness was attributed to a stroke, and he was discharged home. He became increasingly confused over the next 3 weeks and was admitted to the Department of Neurology in April 1980. On examination he was obese, with cutaneous features of mycosis fungoides and parapsoriasis. He was disoriented in time and place, could not give a history, read, calculate, dress or recall short or long-term items. His speech was incomprehensible except for profanities, and he responded to simple commands only. The optic fundi were normal, and the pupils dilated and unreactive (owing to atropine). The cranial nerves were intact. Power was minimally less on the left than the right. Muscle tone was normal, tendon reflexes brisk and symmetrical, and the plantar responses extensor bilaterally. Bilateral grasp reflexes were present. The gait was broad-based and shuffling. Movements of the hands were clumsy. He perceived pin-prick but other modalities of sensation could not be reliably assessed.

After admission he developed a right facial palsy, dysphagia, and the confusion increased. Full blood count, ESR, serum electrolytes, liver function tests, chest and skull radiographs, and an ECG were normal. TPHA and FTA-ABS were negative. An EEG showed diffuse slow-wave activity, more marked over the left hemisphere. A CT scan showed, after contrast injection, enhancement in the left periventricular region (fig 1). At lumbar puncture the opening pressure was 10 cm H2O. The CSF protein concentration was 453 (normal less than 400) mg/l, IgG 83 mg/l, and the glucose was 4-1 mM/l. There were 57 erythrocytes and 8 white cells/mm3 of CSF (70% lymphocytes, 30% polymorphs). Centrifuged deposits showed several large and small lymphoid cells but no pleomorphic histiocytic cells. Bacteriological examination and culture was negative. At a repeat examination a week later the CSF protein concentration was 329 mg/l, the IgG 157 mg/l, and cytological examination again showed lymphoid cells only.

Two weeks after admission, a wedge biopsy was taken

Fig 1 CT scan with contrast enhancement showing abnormality in the left periventricular region.

Fig 2 Brain biopsy. An infiltrate consisting mainly of polymorphic mycosis cells occupies a Virchow-Robin space in deep cerebral white matter. H and E × 250.
from the left frontal cortex and underlying white matter and needle biopsies were taken in deeper tissue. The
cortex was normal, but the deeper cores contained white
matter and some fragments of caudate nucleus with
striking perivascular and intravascular infiltration by a
polymorphous collection of mitotically-active histiocytes,
lymphocytes and smaller numbers of other inflammatory
cells (fig 2). There was oedema and astrocystosis but no
demyelination. These appearances were considered to be
in keeping with cerebral mycosis fungoides. Two days
after the biopsy a repeat CT scan showed an area of
enhancement in the left thalamus and hypothalamus, and
air at the biopsy site. Intravenous infusion of carmustine
(BCNU), 200 mg/m² (400 mg) over 2 hours was given
and radiotherapy was planned. He continued to deterio-
rate into deep coma and developed Cheyne-Stokes
respiration and bilateral basal crepitations. Despite
antibiotic therapy and intensive care he died on the
day after the biopsy.

At necropsy there were changes of broncopneumonia,
the skin changes of mycosis fungoides, but no visceral
involvement apart from the central nervous system.
Macroscopic examination of the fixed brain revealed foci
of opaque yellow necrosis 5-12 mm in diameter in the left
anterior hypothalamus, right mid-parietal cortex, right
middle frontal gyrus, both hippocampal gyri and white
matter, and the right posterior parietal white matter.
The cerebellum showed multiple small (2-3 mm) grey punctate
areas of white matter, but the spinal cord was macro-
scopically normal. Histologically, these changes were seen
to be those of progressive multifocal leukoencephalopa-
graphy. Foci of coagulative necrosis were surrounded by
variable demyelination and other smaller areas of
demyelination without necrosis were also present. The
white matter was oedematos and showed striking
astrocytic hyperplasia with many giant and bizarre
binucleate and multinucleate forms. Occasional eosino-
philic inclusions were seen in glial nuclei. In addition,
there was infiltration of many of the Virchow-Robin
spaces and parts of the subarachnoid space by mycosis
fungoides cells similar to those found in the brain biopsy.

Discussion

The neurological complications of mycosis fungoides
are summarised in the table based on the reports of
14 cases.5-10 The average duration of preceding skin
involvement was 7-5 years with a range of 8-5 months
to 30 years. Neurological features indicate a poor
prognosis for the time from the onset of neuro-
ological symptoms to death ranged from six weeks to
eight months. In our case the time interval was nine
weeks. As in our case, the mycosis infiltrate typically
involves the Virchow-Robin perivascular spaces.7-12 15-19
Occasionally, the infiltrates spread to the cerebral parenchyma diffusely.6-14 19 form
nodules10 18 19 or infiltrate nerves.8 11 13 18 19

The dominant disorder revealed by histology was
progressive multifocal leukoencephalopathy. This
has been previously described in a patient with
generalised mycosis fungoides60 without cerebral
infiltration with mycosis fungoides. Our case also
differs in having limited skin infiltration and no
evidence of diffuse reticuloendothelial involvement.
Progressive multifocal leukoencephalopathy is
usually associated with impaired immunological
mechanisms such as occurs with reticulos or cyto-
toxic therapy. In our case, neurological features
preceeded treatment with a modest dose of cyclo-
phosphamide at 25 mg twice daily for one month
before his death. The precise relationship of the
cutaneous lymphoma, impaired immunity, cerebral
infiltration and progressive multifocal leuko-
encephalopathy is unclear. We speculate that the
altered immune mechanisms associated with mycosis
fungoides may have allowed an opportunistic viral
infection associated with progressive multifocal
leukoencephalopathy to develop. There was no
evidence of polyoma virus. The encephalopathy may
have facilitated the infiltration of perivascular tissues
with neoplastic cells of mycosis fungoides. It is
likely that the spread of mycosis fungoides was
haematogenous, although direct spread from over-
lying scalp to the brain has been reported.10 Thus the
mechanism of spread appear to be similar to those
postulated for other lymphomas,21 albeit less
commonly.

Although abnormal, the CT scan was not diag-
nostic of either leukoencephalopathy or cerebral
mycosis fungoides but was helpful as a guide to the
site of the biopsy. We suggest that a brain biopsy
should be done in patients with mycosis fungoides
who develop unexplained neurological abnormalities
with localising CT scan abnormalities and CSF
changes which are not diagnostic. Some improve-
ment with radiotherapy and chemotherapy in
patients with meningeal mycosis fungoides has been
reported,7 but the survival was less than 8 months
after the onset of neurological symptoms. A brain
biopsy may allow earlier diagnosis and therapy and
so improve the prognosis.

We gratefully acknowledge the assistance in the
management of the patient of Mr J Block, Dr Rogers,
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References

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