Short report

Primary intracerebral Hodgkin's lymphoma

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SUMMARY The case is reported of a 51 year old man with primary intracerebral Hodgkin's lymphoma treated by surgical excision, intrathecal chemotherapy and whole-brain irradiation. One year later the patient had no evidence of Hodgkin's lymphoma intracranially or elsewhere. The possible histogenesis of this rare condition is discussed and a brief review of the literature is presented.

Intracranial Hodgkin's lymphoma is rare, with an incidence of 0.5% or less, and occurs almost exclusively in patients with relapsing disease elsewhere.^{1 2} Haematogenous dissemination is the principal mode of intracranial spread and dural metastases are more common than isolated cerebral involvement.^{1 3} Hodgkin's lymphoma arising primarily within the cranial cavity is exceedingly rare, the optimum treatment and prognosis of which have yet to be determined.⁴⁻⁸ We report the successful treatment of a patient with primary intracerebral Hodgkin's lymphoma who presented with a discrete intracerebellar tumour, and discuss the possible histogenesis of this unusual condition.

Case report

This 51 year old man presented with a 3 month history of increasingly severe and frequent headaches which were associated with nausea and vomiting. On examination bilateral papilloedema was the only abnormal finding. Chest radiographs and laboratory studies including a complete blood count, erythrocyte sedimentation rate and routine biochemistry were normal. Computed tomography (CT) of the brain after contrast administration revealed a uniformly enhancing tumour in the left cerebellar hemisphere with surrounding oedema, distortion of the fourth ventricle and enlargement of the third and lateral ventricles. Vertebral angiography demonstrated an avascular mass.

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A right ventriculoperitoneal shunt was inserted and the patient commenced on corticosteroids. A left suboccipital craniectomy was subsequently performed with the patient in

Fig 1 Representative section of tumour showing a pleocytic infiltrate composed of lymphocytes, plasma cells, histiocytes and Reed-Sternberg cells. (H & E $\times 320$.)

Fig2 Classical binucleate Reed-Sternberg cell. (H & E $\times 800$.)

the sitting position. A firm grey-coloured tumour without dural attachment was found within the left cerebellar hemisphere and completely excised.

The excised tumour consisted of several fragments of grey rubbery tissue with combined measurement of $2 \times 2 \times 1$ cm. Microscopy revealed moderately cellular ill-defined islands set in dense birefringent fibrocollagenous connective tissue. A variety of cell types including lymphocytes, plasma cells, eosinophils, histiocytes, classical binucleate Reed-Sternberg cells and related variants were identified (figs 1 and 2). The cell density varied considerably and in some areas foci of necrosis were noticed. The appearances were interpreted as showing Hodgkin's lymphoma (mixed cellularity type). A nodular pattern was not evident. Towards the periphery abundant astrocytic fibrils (glial fibrillary acidic protein positive) were noted throughout the stroma.

After the operation the patient had vertical ocular misalignment (skew deviation), limb ataxia and a poor gag reflex. Adult respiratory distress syndrome developed due to recurrent aspiration but responded to the appropriate therapy. The neurological deficits slowly improved. In view of the unexpected histological diagnosis the history and examination were reviewed. The patient had no symptoms of fever, night sweats, pruritis or alcohol induced pain and there was no family history of Hodgkin's lymphoma. There was a 4 kg weight loss in the months prior to admission which was attributed to nausea and vomiting. There was no lymphadenopathy or hepato-splenomegaly. Serum protein electrophoresis, immunoglobulin levels, immunoelectrophoresis and lymphocyte subpopulations were normal. Isotope brain scan and CT scans of thorax, abdomen and pelvis were normal. There was no evidence of Hodgkin's

lymphoma on bone marrow aspirate and trephine biopsy examinations or on cytological examination of the cerebrospinal fluid.

Further treatment consisted of weekly intrathecal injections of 12.5 mg methotrexate for 4 weeks, followed by 3000 rads whole brain irradiation with an additional 1500 rads to the posterior fossa in divided doses over a 4 week period. One year following completion of this treatment the patient had made a full recovery and returned to work. There is no evidence of Hodgkin's lymphoma intracranially or elsewhere on clinical, laboratory and radiological examinations.

Discussion

Intracranial neurological complications of Hodgkin's lymphoma are rare, with a reported incidence of 0.6%.¹ The majority of these are due to direct tumour involvement, but occasionally remote tumour effects in the form of paraneoplastic syndromes such as progressive multifocal leucoencephalopathy, subacute cerebellar degeneration, granulomatous angiitis and encephalitis are responsible.^{1,3} Intracranial deposits of Hodgkin's lymphoma are very rare with an incidence of 0.25 to 0.5%, and are usually due to haematogenous dissemination in patients with relapsing disease elsewhere.^{1,2,9} Metastasis to the dura mater is the most common form of intracranial involvement.³ Cranial nerve palsies, motor deficits, headaches and seizures are the most frequent symptoms of these lesions.¹

Primary intracranial Hodgkin's lymphoma is exceedingly rare. This tumour was not observed in the series of 8000 intracranial neoplasms reported by Jellinger *et al*,¹⁰ but occurred in 14 of the 7000 patients (0.2%) with central nervous system (CNS) tumours reported by Zimmerman.⁸ A majority of these patients presented with symptoms and signs of a space occupying lesion and were found to have a circumscribed tumour, as occurred in our patient. Others developed diffuse cerebral signs and clinical manifestations suggestive of encephalitis and were found to have a diffusely infiltrating tumour process. Predilection for the septum pellucidum has been suggested, but involvement of the cerebral lobes, basal ganglia, hypothalamus, tuber cinereum, optic chiasm, brain stem, cerebellum and dura mater have also been described.⁴⁻⁸ Mixed cellularity and lymphocyte depleted variants are most common.

Primary CNS lymphomas occur with increased frequency in a variety of congenital and acquired immunodeficiency states, and more recently the importance of the acquired immunodeficiency syndrome (AIDS) in their development has been emphasised.¹¹⁻¹⁴ However, a clear relationship between immunodeficiency states and primary intracranial Hodgkin's lymphoma has not been established, and there are no definite predisposing factors for the

development of this tumour. There was no evidence of immunosuppression in our patient.

The pathological diagnosis of Hodgkin's lymphoma depends on the observation of characteristic Reed-Sternberg cells (RSC) in an appropriate histological setting.⁹ While the malignant characteristics of this cell and its mononuclear variants are widely accepted, there is much controversy concerning the histogenesis which is as yet undetermined.⁹ Putative progenitor cells include lymphocytes, macrophages, and more recently the interdigitating and/or dendritic reticulum cells.¹⁵⁻¹⁸ Of these only macrophages are considered as constituents of normal brain and it has been shown that the normal intact CNS contains approximately 280,000 macrophages.¹⁹ If the present case is truly an example of primary intracerebral Hodgkin's lymphoma as we believe, then the observation lends further support, albeit indirect, to a macrophage origin for the RSC.

The preferred therapy for primary CNS lymphomas has been surgery followed by whole brain irradiation.¹¹ Few patients have received chemotherapy and then usually as a last resort.¹¹ More recently however combination chemotherapy has been recommended as part of the initial treatment of these tumours.¹² Much less information is available on the treatment of intracranial Hodgkin's lymphoma either primary or metastatic. Excision of intracranial Hodgkin's masses appears to improve survival.³ Whole brain irradiation of 2000 to 3000 rads supplemented by a local boost field to bring the dose to known sites of intracranial involvement to between 4000 and 5000 rads has been recommended for patients presenting with intracranial metastases.¹ Our patient was treated along similar lines with complete excision of the tumour, a short course of intrathecal methotrexate and whole brain irradiation with a total dose of 4500 rads to the site of tumour involvement. While our patient is free of disease one year following completion of this treatment, there are no guidelines in the literature to allow accurate survival prediction following treatment of primary intracerebral Hodgkin's lymphoma.

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