Letters

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Immuno-gold silver staining in the diagnosis of herpes encephalitis

Sir: The practical difficulties of obtaining a definitive diagnosis of herpes encephalitis are well documented,¹ and the diagnostic method based on the detection of a central nervous system immune response to Herpes virus simplex (HSV), previously reported from this laboratory,² is not wholly reliable in the early stages of the disease (that is, less than 10 days after onset). Until more reliable non-invasive diagnostic tests become available, brain biopsy (albeit an increasingly unpopular procedure³) will remain the most reliable means of achieving an early diagnosis.

Brain material may be examined in a variety of ways⁴ including electron microscopy, immunofluorescence, immunoperoxidase and peroxidase anti-peroxidase staining. We have recently applied a new histochemical method, immuno-gold silver staining (IGSS)⁵ to the detection of virus antigen in such specimens. In this procedure the specimen is overlaid with a rabbit anti-HSV serum (antiserum prepared in this laboratory to HSV strain Syn 17+), followed by anti-rabbit colloidal gold conjugate (Janssen Life Sciences Products, Belgium). The presence of virus antigen is then revealed as

distinct black staining deposits by silver development.

The procedure although slightly more time consuming (about 3½ hours) than staining by immunofluorescence or immunoperoxidase is straightforward and appears to offer considerable advantages in terms of ease of reading and sensitivity of detection.

In the evaluation of brain material examined post-mortem and for studies related to pathogenesis, this procedure provides advantages over methods used to date. The sensitivity of the method will allow improved investigation of viral spread within the brain. In addition, in comparison with other histochemical methods, the IGSS method is able⁶ to detect antigen in tissue where there has been a significant reduction of antigenicity during fixation or paraffin processing.

The figure shows an area of virus infection within the temporal lobe, of a patient with herpes encephalitis, stained using the IGSS method. Controls in which specimens were "stained" with the primary antiserum replaced by normal rabbit serum showed no reactivity. Also there was no background interference which might have hindered

interpretation. Specific staining, predominantly of the nuclear and cytoplasmic membranes of both neurons and glial cells, is observed with IGSS. The distribution of "stain" correlates well with areas of viral activity detected by peroxidase-anti-peroxidase or immunofluorescence.

Current use in this laboratory leads us to believe that IGSS will be the method of choice as long as biopsy material is to be used in the diagnosis of herpes encephalitis. The full potential of this method will be realised when IGSS is more widely applied.

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IGSS staining of a 5 µm section of paraffin embedded brain (× 350). The patient died from herpes encephalitis, brain biopsy proven (culture (HSV type 1) and immunofluorescence positive). Grey matter of left temporal cortex with particulate staining of four neurons, this is present in the cytoplasm but in the neuron in the lower right (arrow head) there is also nuclear staining. Neuron in upper field (arrowed) not stained.

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Carcinoma of the bronchus presenting with hemichorea

Sir: We report the case of metastatic adenocarcinoma of the bronchus causing hemichorea.

An 86-year-old man presented one month after suddenly developing uncontrollable jerking movements of his left arm and leg. He had lost 13 kg in weight over the previous year and for 4 months had had pain in his left wrist and ankle. He had given up his lifelong habit of smoking five years before. Examination revealing clubbing of fingers and toes and a swollen tender left wrist confirmed on radiographs to be due to hypertrophic osteoarthropathy. There was bilateral gynecomastia, testicular atrophy and a left hemichorea. Left arm and leg movements were almost hemiballismic with abduction/adduction of the shoulder and flexion/extension of elbows and hands. Power tone and reflexes were normal, both plantars were flexor; there were no cerebellar signs. A chest radiograph showed possible right hilar enlargement but bronchoscopy was normal apart from slight narrowing of the right upper lobe bronchus consistent with extrinsic compression. Cytology and biopsies were however normal. Alkaline phosphatase was moderately raised at 127 IU/l (normal <100) consistent with hypertrophic osteoarthropathy but all other biochemical and haematological values were normal. A CT scan of the brain with contrast (fig 1) showed an enhancing lesion in the region of the right thalamus and zona incerta

Fig 1 CT Scan with contrast showing enhancing lesion in right Thalamus and zona incerta.

with surrounding oedema suggestive of a neoplasm.

Before the results of the CT scan became available, the clinical diagnosis was of carcinoma of the lung with a coincidental vascular lesion involving the right caudate and subthalamic nuclei and he was given a trial of therapy with codeine mesylate (Hydargine). Within 48 hours the movements had completely resolved and did not recur after stopping the drug one week later.

He was discharged after one month with no abnormal neurological signs. However, within 3 weeks of discharge he returned with urinary incontinence and had developed an extensor left plantar response but no other convincing pyramidal signs. Tomograms of his right upper lobe of lung confirmed the presence of a mass around the bronchus. Over the next four weeks he developed increasing weakness of his left side and a throbbing headache but no papilloedema. Dexamethasone improved his symptoms and signs but four weeks later he died at home.

At necropsy a bronchial carcinoma, 40 mm in diameter was found occluding the right upper lobe bronchus. Histologically this was a primary moderately well differentiated adenocarcinoma. Metastases were present in the right adrenal gland, liver, cerebrum and dura of the right posterior cra-

nial fossa. The cerebral metastasis (fig 2) was a well circumscribed necrotic tumour, 30 mm in diameter, in the right inferior part of the thalamus at the level of the mamillary bodies. It extended for 15 mm anteroposteriorly. The tumour was infiltrating the internal capsule into the globus pallidus destroying the subthalamic nucleus and compressing and displacing the third ventricle to the left.

Hemichorea and hemiballismus classically develop with lesions of the caudate nucleus and the subthalamic nucleus of Luys. The pathological process most frequently described is localised encephalomalacia,¹ however lacunar infarction,^{2,3} small circumscribed haemorrhages and emboli,⁴ trauma,⁵ venous angiomas⁶ and arteriovenous angiomas^{7,8} have also been reported. There have been two previous reports of metastatic cancer and hemiballismus associated with widely disseminated breast carcinoma,⁹ and disseminated carcinoma of unknown primary.¹⁰ Legre *et al*¹¹ reported 57 cases of tumours of the central nuclei of the brain confirmed at operation or necropsy of which two were metastatic tumour. No details of clinical presentation are given.

The rapid resolution of the movement disorder following the administration of codeine mesylate is difficult to explain. It