Discussion

Chairman: PROFESSOR J. M. EVANSON

CHAIRMAN: We have heard mention of raised intracranial pressure. If I remember correctly, in our index case, there was blurring of the disc margins. The fundi are, I gather, in most cases, normal and papilloedema is not a common feature.

PROFESSOR K. MCCARTHY: Could I ask if any of the people describing patients have any information as to whether these people were chronic herpetic, or was there any indication of these being primary infections?

DR F. O. MACCALLUM: Only one of the Oxford cases had a history of herpetic lesions and had any antibodies on admission to hospital.

PROFESSOR K. MCCARTHY: But, with reference to that, where the patient had been known to suffer from recurrent herpes, was there any evidence that the virus isolated during the encephalitis was of the same herpes type as the one from which they had been suffering recurrently?

DR F. O. MACCALLUM: I don't think that there is any evidence on that, Professor McCarthy, it has all been one of history. Certainly, in our cases, all the viruses have been of Type I.

PROFESSOR K. MCCARTHY: It might be possible to sort it out by serology, in fact. If you have serum on admission, you might show that the patient has Type I antibodies and not much Type II, when, in fact, Type II virus is isolated from the brain.

DR F. O. MACCALLUM: Yes, but all our viruses were of Type I.

DR L. A. LIVERSEDGE: I wonder if our colleagues had any success in isolating a virus in the CSF? We haven't. All the people in the literature say it is a waste of time. I wondered if Dr MacCallum might help?

DR F. O. MACCALLUM: We tried it in every case and the only one in which we were successful was from a ventricular puncture, and in this there were fine bits of tissue, probably necrotic brain, but no actual biopsy tissue had been removed. In addition, in another case the virus was isolated from the lumbar CSF by the referring laboratory, and we ourselves isolated it from biopsy material taken on the fifth day of illness; it is almost certain that there was extensive necrosis of brain tissue. I think that one should be able to isolate virus from some of these cases with such necrosis providing that sufficient antibody to neutralize the virus has not developed and leaked into the CSF.

DR M. LONGSON: Could our clinical colleagues tell us whether the radio-isotope scan has any particular part to play in localizing the lesion and showing us where the biopsy ought to be taken?

DR L. A. LIVERSEDGE: Well it is helpful. Obviously in an area where there is isotope uptake, the moment you

decide it is probably herpetic, it is reasonable to stick in a needle, but the great thing is to protect the patient from over-enthusiastic probing of the brain in a wave of diagnostic fervour, thus leaving him disabled. It is perfectly possible to leave a patient with dysphasia, not because of the herpes, but because of the needling.

DR J. OXBURY: We don't have much experience of brain-scanning in this disease, but Dr Sheldon, who is our neuro-radiologist, is very successful at diagnosing the condition on the basis of carotid arteriography. There is a curious sort of vascular change that he sees, that looks to me rather like malignant circulation but which he is capable of differentiating from a tumour with a high degree of accuracy. This is what is usually used in Oxford to decide whether or not and where to biopsy.

DR L. A. LIVERSEDGE: Well that is perfectly true, of course. Cope & Howieson (1967) describe four cases in which there was expansion of the temporal lobes. The critical radiological feature was, of course, space-occupation, but no tumour circulation was seen.

DR B. E. JUEL-JENSEN: One of the patients Dr Oxbury described did have a brain-scan before the carotid angiogram. But you would have to do the carotid angiogram anyway and the scan would only delay matters further.

DR L. A. LIVERSEDGE: At the moment, we are sadly short of information on the real value of the brain-scan as a diagnostic tool in encephalitis, but as Dr Longson implied, it might be very helpful in selecting an area for biopsy. For instance, it might make it possible to choose a silent zone of the brain and avoid Broca's area.

PROFESSOR A. W. DOWNIE: I wonder if those who have been interested in herpes encephalitis have encountered cases of meningitis caused by the herpes simplex virus without any evidence of brain damage? We had a case in Liverpool some years ago where there was herpes simplex virus in the cerebrospinal fluid—the patient was a child, I think. There was no evidence of encephalitis. The patient recovered.

DR M. LONGSON: Does herpes meningitis exist in contrast to herpes encephalitis?

DR L. A. LIVERSEDGE: I have not seen it personally, but the Bergouignan group in Bordeaux talk about it and say there is a meningitic picture which goes on to an encephalitis. Theoretically, there is no reason why it should not develop, and certainly in such cases one should be able to get virus from the CSF, but I have to say that in my reading of the literature, pure meningeal examples have been scarce. I don't know whether Dr MacCallum knows of any.

DR F. O. MACCALLUM: We have not seen this in any of our patients; not one in 10 years, but I think they have

seen such cases in Glasgow where there are a larger number of cases. Perhaps Dr Ross could enlarge?

DR C. ROSS: Yes. Every year we come across one or two cases of meningitis in young children under 5-years-old. Brain biopsies are not usually done in these children and the diagnosis is made by demonstrating a rise in antibody titre to herpes simplex. This may of course be coincidental infection, but such children have had aseptic meningitis with no other positive virological findings.

DR J. OXBURY: I think I should mention that the series of cases we presented this afternoon was restricted to ones in which we have probably had either virus identification or positive histological evidence that our diagnosis was proven. We have had two cases of brain-stem encephalitis with abnormalities entirely restricted to brain-stem signs, and both of them required treatment with tracheostomy; both made full recoveries. Now of course we don't, even in Oxford, biopsy the brain-stem, and so we didn't isolate the virus. Both cases had rising CSF herpes simplex antibody titres. I think brain-stem encephalitis should be considered as another clinical form of the disease.

DR F. O. MACCALLUM: These two patients have now completely recovered.

DR L. A. LIVERSEDGE: May I ask an academic question here? Was it your impression that this mesencephalic presentation was a disorder of white matter function, or was it one of nerve cell function? I think this distinction is of considerable importance.

DR J. OXBURY: Well, I think it was one of nerve cell function, not one of long-tracts.

DR J. O. TOBIN: Back in 1951, Afzelius-Alm described aseptic meningitis due to herpes in soldiers. I am just wondering if the features of herpes meningo-encephalitis have in fact changed over the intervening 20 years. The focal form may be more common now, and the aseptic form of meningitis may be becoming very much less common today.

DR A. H. TOMLINSON: Dr Liversedge, you described the grouping of various types of herpetic brain infection. I presume this classification was done on a retrospective view of each case? Do you see any possibility of classifying cases at onset? If any trials of therapy are to be done, it will be important to compare results in similar types of case.

DR L. A. LIVERSEDGE: I think that this would be a very good part of a prospective study, but just how valuable it would be remains to be seen. It would, of course, be very helpful in the study of the prognosis if we did know something about the initial presentation of cases that did well on treatment.

DR I. M. S. WILKINSON: Can I ask Dr Oxbury if he did any sort of an EEG study, and if so, did he find the Upton & Gumpert (1970) complexes a frequent finding, and also, if anyone in whom it was found subsequently had a post-mortem, so that we might know the pathological correlation for the EEG complexes?

DR J. OXBURY: I am sorry to say that very few patients in our series had EEGs done, and they were mostly done after the acute phase.

DR B. E. JUEL-JENSEN: One of the practical snags about this was that these people were acutely ill and we haven't an available portable EEG in Oxford.

DR J. OXBURY: This is, of course, one of the problems in deciding whether or not to do a brain biopsy. If you are not careful, you can make a large number of remarkable diagnoses by brain biopsy which could be diagnosed by what Dr Tomlinson would probably call cheaper methods.

MR G. P. DUFFY: Could I make a suggestion? From a surgical point of view, there is a criterion which is of value in diagnosis, and that is the appearance of the brain at biopsy. In the cases we have had, all of which have been proved as herpes encephalitis, the brain presents a typical picture to the point where, in the cases which I have operated upon, I thought I could make the diagnosis in the theatre and start treatment straight away. The brain is very very vascular; there is a capillary vascularity and the brain is very very soft and gelatinous. In all the positive cases, this was so, and in those cases where the diagnosis was not established, the brain would not appear like this. I would also like to make the point that decompression is, I think, a very important aspect of treatment and I don't think this has been stressed, but I think it could well be of substantial importance and equal to the use of cytotoxic drugs.

CHAIRMAN: Macroscopically, can you tell the difference between temporal lobe swelling caused by abscess and an acute necrotizing encephalitis?

MR G. P. DUFFY: Oh yes, it is totally different from an abscess and it appears to be totally different from any other form of encephalitis.

DR M. RAPPEL: In our department, we have precisely the same impression; we can diagnose the disease just by looking at the brain during operation. But, I must add that, thanks to the experience we gained, acute necrotizing encephalitis is now becoming a bedside diagnosis.

DR L. A. LIVERSEDGE: About this decompression business—it is a fascinating concept, but it is theoretically absolute rot! But, I was interested in your suggestion that increased pressure within the brain was responsible for the symptoms. That can't be right. We know that there is no serious increase in overall intracranial pressure and the disease-process is within the nerve cell because of a virus which is attacking it. I know that many decompressions have been done because of the space-occupying appearances in the temporal lobe, but if one reads the literature carefully, the people who have had temporal lobe decompression have done just as badly as all the rest.

MR G. P. DUFFY: We obviously see selected cases from the surgical point of view, and we mostly get the ones which have been referred as abscesses. I think that before we actually take them into theatre, we are all pretty sure that it isn't, in fact, an abscess, and that it is probably a herpes encephalitis. When I operate, I don't, in fact, do a burr-hole. I do a craniotomy. I find that these brains are extremely tight and I am glad to say that we have three survivors; one was a computer engineer who is now back at work at the computer. I am also quite certain that the decompression in the other two cases was of vital importance—they used their decompression. In all three cases, as I have said, the brain was very tight and was very swollen.

DR L. A. LIVEREDGE: Mr Duffy—how many decompressions have you performed which have not done as well?

MR G. P. DUFFY: Four, but these were patients that died within an hour of starting treatment.

DR. K. TUTTON: If decompression works, what about dexamethasone? Has anybody tried?

DR M. RAPPEL: In our department, we would always decompress. The literature is very scanty but I think there are just about twenty cases of decompression, and about half of these patients are, or were, living at about the time of the description. This figure is just slightly better than in the cases receiving no treatment.

DR D. SUMNER: I would merely like to say that dexamethasone does work. I was going to talk about this tomorrow.

References

- AFZELIUS-ALM, L. (1951) Aseptic encephalomeningitides in Gothenburg, 1932–1950. *Acta medica Scandinavica*, **263**, Suppl. 1.
- COPE, V. & HOWIESON, J. (1967) Radiological findings in acute necrotizing encephalitis due to herpes simplex virus. *Clinical Radiology*, **18**, 109.
- UPTON, A. & GUMPERT, J. (1970) Electroencephalography in diagnosis of herpes simplex encephalitis. *Lancet*, **i**, 650.