can not only show "some abnormality that encourages angiographic examination" but can also diagnose dissections involving the pretransverse, C6-C7 and C5-C4 intertransverse segments of the VA. "The diagnosis is based on the association of a localised increase in arterial diameter with haemodynamic signs of stenosis or occlusion and/or decreased pulsatility and intraluminal echoes at the same level. Furthermore, ultrasonic examination is an excellent tool for the follow up of dissection.


Hinse and Thie reply.

We thank Dr. M. and colleagues for their interest in our recent paper,1 and we appreciate the opportunity to comment on a few of the issues raised by them.

Our paper did not deal with the incidence of vertebral artery (VA) dissection which remains unknown. Better diagnosis and systematic study will hopefully shed more light on incidence of this condition in the future. In our analysis, we have included only case reports providing sufficient detail of the individual patient, but not summarised series, thus the results of Mokri et al2 were not considered. We apologise for not including the well documented patients by Mas et al3.

The question of internal carotid artery (ICA) dissection was not the subject of our paper. We argue that angiographic visualisation of all four brain-supplying vessels should be attempted in acute VA dissection in order not to miss concomitant asymptomatic ICA dissection. This point is of particular importance in spontaneous VA dissection: in 5 of 29 reviewed cases ICA dissection was documented, but not in 28 patients with traumatic VA dissection. Mas et al4 correctly state that dissection as a cause of arterial occlusion may be hard to diagnose. However, the angiographic appearance of tapering occlusion is highly suggestive of dissection.5 In our patients, complete recanalisation of a formerly occluded VA (cases 2 and 3) and visualisation of a small pseudoaneurysm (case 2) made the diagnosis of VA dissection highly probable.

The value of ultrasound method in the diagnosis of VA dissection remains to be determined. Our own experience6 and the work of Touboul et al7 on three patients examined by duplex scan are too preliminary to allow any firm conclusions. As we have pointed out in our paper, ultrasound methods may be suitable for diagnosis of recanalisation, possibly obviating the need for repeated angiography in some patients. The same holds true for modern neuroimaging methods. Contrast-enhanced CT scan and MRI may corroborate the diagnosis of VA dissection, and are also increasingly recommended for follow up studies. However, both methods do not allow examination of the affected vessels in their entire length. These neuroimaging techniques will have to prove their value in a systematic study against the present "gold standard" (angiography).

The role of many other supposedly predisposing conditions, in particular migraine, use of oral contraceptives or hypertension, remains totally obscure. It is speculative whether some of these factors might act by merely facilitating the occurrence of stroke after dissection, but not dissection itself. It is also unknown why minor trauma may induce cervical dissections in some patients at any particular time, but why recurrences in these patients are rare.

First, the authors suggest that their patient's late onset (at age 14) distinguishes his disease from globoid cell leukodystrophy (GLD) distinct from the infantile and late infantile subtypes. This may be true for the first type, but the latter can occur within one family together with a later onset type.

Second, it would be interesting to know whether the white matter hyperintensities on the MRI were diffuse or rather restricted to the occipito-parietal white matter, as described in other late onset GLD.8 If so, this posterior white matter involvement on MRI would seem to be very useful to distinguish GLD from other cerebral white matter diseases.

Aseptic meningitis associated with high dose intravenous immunoglobulin therapy

We read with great interest the report by Watson et al9 and we would like to draw the authors attention to a similar case we published last year.10

Our patient was a seven year old boy with idiopathic thrombocytopenic purpura who was readmitted after two episodes of acute aseptic meningitis on two occasions following the second intravenous dose of immune globulin. On these two occasions, the patient developed aseptic meningitis on day three; quite identically to the previous experience reported by Watson, whereas Kato's patient developed the aseptic meningitis two days after a five day course of intravenous immune globulin therapy.

In our patient the immune globulin preparation used was Sandoglobulin IV (Sandoz), which is a formulation prepared by cold ethanol fractionation. It was given at a dose of 0.4 mg/kg of body weight infused over a 1 hour period.

Late onset globoid cell leukodystrophy

I read with great interest the paper by Grewal et al.1 We would like to add a few comments.

First, the authors suggest that their patient's late onset (at age 14) distinguishes his disease from globoid cell leukodystrophy (GLD) distinct from the infantile and late infantile subtypes. This may be true for the first type, but the latter can occur within one family together with a later onset type.

Second, it would be interesting to know whether the white matter hyperintensities on the MRI were diffuse or rather restricted to the occipito-parietal white matter, as described in other late onset GLD. If so, this posterior white matter involvement on MRI would seem to be very useful to distinguish GLD from other cerebral white matter diseases.
From these three reports, we conclude: 1 Intravenous immune globulin can induce aseptic meningitis in children as well as adults: the strong temporal association (on day three in our patient and in Watson’s patients) and the repetitive occurrence in the same patient (on two occasions in Kato’s patient and in our patient) are both strong arguments in favour of this. It should no longer be a hypothesis. 2 Several preparations of intravenous immune globulin can induce aseptic meningitis. Up till now it has been reported with four different preparations: with immunoglobulin prepared with polyethylene glycol and with a sulphohated preparation,1 with a formulation prepared by cold ethanol fractionation (Sangoglobulin)2 and with a low PH formulation prepared with ethylene glycol (Intragam).1 3 As with any other intragenic diseases, the aseptic meningitis in itself is rather benign and resolves rapidly with cessation of the therapy. But not recognising this complication as such might result in potentially dangerous and/or unnecessary extractions (lumbar puncture in a thrombocytopenic patient; CT scan). The possible occurrence of aseptic meningitis following immune globulin infusion should thus be known by all physicians and should be mentioned by the pharmaceutical firms.

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The brain in schizophrenia

The excellent editorial by Ron and Harvey notes that “to have forgotten that schizophrenia is a brain disease will go down as one of the great aberrations of twentieth century medicine”.4 However, it is only to question as to whether schizophrenia can be considered as a brain disease in the same way as established brain diseases such as viral or atrophic disorders of the CNS. There may be more general reservations with the validity of the concept of schizophrenia itself, but I have four specific reservations with calling schizophrenia a brain disease: 1) Unlike neuropsychiatric conditions, there is as yet no diagnostic pre- or post-mortem biological or other physical marker for schizophrenia. 2) Compared to most brain diseases, there is no predictable pattern of deficit in sensory or motor functions or in “primitive” reflexes. 3) Unlike most brain diseases, psychological or psychosocial variables play a significant part in the aetiology and stability of outcome of many patients with schizophrenia. 4) The relationship between neurobiological features of patients with schizophrenia and the pattern or severity of psychiatric disturbance is much more equivocal than in the case of analogous relationships in brain diseases.

At present I would therefore feel comfortable in calling schizophrenia a brain dysfunction, but I do not think there is yet sufficient evidence to call it a brain disease. It is possible that the term disease, if commonly applied to schizophrenia, may in the perception of some clinicians limit the range of viable therapeutic options.

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(‘(To)-HM-PAO SPECT and dementia in Parkinson’s disease

With great interest we read the article from Spampinato et al and we would like to comment on some aspects of the article.

We performed single photon emission computed tomography (SPECT) using (‘(To)-HM-PAO as a tracer in 5 clinically demented and 6 non-demented patients with Parkinson’s disease (PD). HM-PAO uptake was measured in the frontal, parietal and temporal-parietal cortex and was expressed as cortical/cerebral cortex. None of our patients had a reduction of HM-PAO uptake of more than 20%, which seems to be in concordance with Spampinato et al. In contrast to Spampinato et al, however, we found no difference between the demented and non-demented PD patients. We investigated whether there was a relation between SPECT-scan data and neuropsychological tests in our group as a whole (n = 11). Using the Spearman rank correlation test, we found no significant correlations between neuro-psychological performance and SPECT data on any tests.

One of the main problems in our research was the estimation of dementia in PD. Of the 5 patients who fulfilled the criteria for dementia as described in the DSM-III-R, all lacked typical cortical features. All of our patients were able to undergo the neuro-psychological tests. In the study by Spampinato et al, diagnosis of dementia was based on neuropsychological assessment, according to which the PD patients were divided into two groups of 15 patients. However, five of their patients could not be tested, probably due to severe dementia. It was not stated by the investigators whether their demented PD patients were free from cortical features.

In our opinion, one of the possible explanations for the differences in results is that patients had no cortical dysfunction and therefore no Alzheimer-like pathology. Further elucidation of dementia as seen in PD seems mandatory.

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