

together with isoniazid and pyridoxine. The dose of steroids was gradually reduced and there was little symptomatic or objective change. Four further CSF specimens before July 1980 were abnormal with raised lymphocyte count and low sugar but, again, no organism was grown, cryptococcal antigen and India ink stains were negative as were tests for cryptococcal antigen using latex particles coated with immune globulin. He then had an episode of loss of consciousness and an electroencephalogram at that time showed generalised slowing with a few episodic forms over the temporal areas; he was started on phenytoin when his prednisolone had been tailed down to 4 mg a day. On 22nd July 1980 a repeat CSF grew one colony of a non-encapsulated *Cryptococcus neoformans*. Two subsequent CSF's grew several colonies of the same organism, and cryptococcal antibody against this organism was present in the patient's serum at a titre of 1 in 8 using a fluorescent antibody technique. Cryptococcal antigen tests remained negative because the organism was non-encapsulated. He was then started on a six week course of anti-cryptococcal chemotherapy consisting of amphotericin B 0.3 mg/day as an intravenous infusion and 5-fluorocytosine 150 mg/kg/day orally in divided doses, while continuing on 15 mg prednisolone. Further specimens of CSF showed growth of cryptococci two weeks after starting chemotherapy, but not at four weeks or subsequently, and his CSF glucose levels began to rise. The most recent CSF (in February 1982) showed a pressure of 110 mm of CSF, protein 0.69 gm/l no WBC's and a glucose of 2.9 mmol/l (plasma 5.3 mmol/l). At that time he was off steroids, had no headache and felt that his general health was much improved. He still had mild signs of his old right hemiparesis.

This case illustrates some of the problems involved in diagnosing cryptococcal meningitis. Mr C had an abnormal cerebrospinal fluid for 14 years before a culture diagnosis was made. The response to treatment (in particular the rise in glucose and disappearance of white cells from the cerebrospinal fluid) provides strong evidence that the entire illness was due to chronic cryptococcal meningitis. The prompt response to antifungal chemotherapy, but not to therapy with steroids, make it unlikely that the cryptococcal infection was secondary to some other underlying disease; in particular, sarcoid^{1,2} seems unlikely in view of the negative Kveim test and positive Mantoux.

It is interesting that this man had a

number of CSF examinations over the years which gave not only negative results for cryptococcal antigen and India ink stains (explicable by the absence of capsule from the organism eventually isolated) but also negative cryptococcal culture. Persistent³ and intermittent^{4,5} negative CSF culture in patients with active cryptococcal meningitis has been reported previously. It seems reasonable to assume that here it was the steroids which enabled the organism to grow in culture in view of the temporal relationship between starting the steroids and the first positive culture.

The case is also unusual in the long duration of the untreated disease with only slow deterioration. Reports before any specific treatment was available suggested that up to three quarters of patients died in the first year of their illness,⁶ although there were very occasional cases with intermittent symptoms and persistent meningeal reaction for up to 30 years.^{4,7} It is interesting to speculate that in Mr C's case this may be related to the fact that the organism was non-encapsulated. It is thought that pathogenicity of cryptococci may be related to the capsule; non-encapsulated strains have been shown to be less pathogenic in mice⁸ and studies suggest that a thick capsule impairs killing by neutrophils.⁹ The low level of cryptococcal antibodies may be related either to the lack of capsule or to the chronicity of the disease.

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References

- 1 Nottebart IIC, McGehee RF, Utz JP. Cryptococcosis complicating sarcoidosis. *Am Rev Respir Dis* 1973;107:1060-3.
- 2 Baum GL, Schwartz J, Barlow PB. Sarcoidosis and specific etiologic agents a continuing enigma. *Chest* 1973;63:488-94.
- 3 Snow RM, Dismukes WE. Cryptococcal meningitis diagnostic value of cryptococcal antigen in cerebrospinal fluid. *Arch Intern Med* 1975;135:1155-7.

- 4 Campbell GD, Currier RD, Busey JF. Survival in untreated cryptococcal meningitis. *Neurology (NY)* 1981;31:1154-6.
- 5 Diamond RD, Bennett JE. Prognostic factors in cryptococcal meningitis. *Ann Intern Med* 1974;80:176-81.
- 6 Butler WT, Alling DW, Spickard A, Utz JP. Diagnostic and prognostic value of clinical and laboratory findings in cryptococcal meningitis. *N Engl J Med* 1964;270:59-67.
- 7 Beeson PB. Cryptococcal meningitis of nearly sixteen years' duration. *Arch Intern Med* 1952;89:797-801.
- 8 Bulmer GS, Sans MD, Gunn CM. Cryptococcus neoformans. I. Nonencapsulated mutants. *J Bacteriol* 1967;94:1475-9.
- 9 Diamond RD, Root RK, Bennett JE. Factors influencing killing of cryptococcus neoformans by human leukocytes in vitro. *J Infect Dis* 1972;125:367-76.

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The reliability of clinical assessment of Parkinson's disease

Sir: The subjective assessment of disability of patients with Parkinson's disease has generally been based on a variety of rating scales of symptoms and signs, or of functional disability.¹⁻³ These clinical rating scales have often formed the basis of both single centre and multicentre clinical trials of new drugs for this disease. They permit the conversion of clinical features to numerical scores for mathematical purposes. Since the statistical evaluation of any such trial depends on the reliability of the scorers it is important that there should be inter- and intra-observer consistency.

We recently had the opportunity to evaluate this point using the commonly performed Webster rating scale.¹ The performance of seven patients with idiopathic Parkinson's disease on seven of the ten listed items (bradykinesia of hands; posture; upper extremity swing; gait; tremor; facies; speech) was prerecorded on video tape. Nineteen practising consultant neurologists, all of whom had some experience using the Webster rating scale, participated. Each neurologist had available a full description of the scale. For each patient a video recording illustrating the seven items was presented and then scored in the order described above. The first session took place in the morning (Session 1) and the same procedure was repeated some eight hours later (Session 2). The Parkinsonian patients were mildly or moderately affected, the mean total score ranging from 2.4-11.1 out of a possible maximum of 21. There was considerable observer variability, three

neurologists tending to give higher scores in Session 1 than Session 2 and two neurologists the converse. There was also inter-observer variability, two neurologists tending to be high scorers while two other neurologists were low scorers. The standard deviation of the scores of individual patients was quite high ranging between 1.3 and 2.2 for any single set of scores.

The Kendall coefficient of concordance among the observers was 0.633 in Session 1 and 0.624 in Session 2. An analysis of variance of the data from neurologists was performed and the total variance of the scores was 2.75 corresponding to a standard deviation of ± 1.7 . The inter-observer variance of the neurologist's score at the same session was 1.38 corresponding to a standard deviation of ± 1.2 . The inter-observer variance of the average of the scores by one neurologist at the two sessions was 1.71 corresponding to a standard deviation of ± 1.3 .

Although only seven of the 10 items in the Webster scale were scored, seborrhea, rigidity and self care being omitted, we think that they were representative of clinical scales in general.

The number of patients scored was small and more severely affected patients were not included. However, we do not think this invalidates our observations since in our experience one of the major difficulties in using such a clinical rating scale in which each major sign or symptom is rated between 0-3 is determining the value for the milder abnormalities. The small number of patients did not permit a conclusive analysis of variance on individual items of the scale. With a bigger patient group it would be possible to identify individual items of the scale in which ambiguities of description make an excessive contribution to the overall variance.

The group of neurologists ranged in their familiarity with rating Parkinsonian patients using the Webster scale from those who performed it frequently to those performing it only occasionally. Some neurologists complained that some of the procedures described by Webster used in the video recording were not their standard technique for assessment. For example Webster rates bradykinesia by assessment of pronation-supination movements of the hand placed on the thigh whereas a common clinical test used by some of the neurologists was rapid sequential opposition of thumb to fingers. Even those most used to the scale were not entirely consistent over the two sessions.

We conclude, therefore, that there is a considerable variance in the Webster rating

scores performed by a number of different neurologists on the same group of patients. We suggest that doctors taking part in clinical trials of drugs for Parkinson's disease using such clinical rating scales spend some time familiarising themselves with the scale preferably practising the ratings on patients prior to the commencement of the trial. This should ensure a higher degree of internal consistency. In addition, in multi-centre trials the trialists should be brought together prior to commencement to reach agreement on the various ratings and we would recommend the use of video recordings of patients for this purpose.

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References

- Webster DD. Clinical analysis of the disability in Parkinson's disease. *Mod Treat* 1968;5: 257-82.
- Canter CJ, de la Torea R, Mier M. A method of evaluating disability in patients with Parkinson's disease. *J Nerv Mental Dis* 1961; 133:143-7.
- Hoehn MM, Yahr MD. Parkinsonism; onset, progression and mortality. *Neurology (Minneapolis)* 1967;17:427-42.

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Painful ophthalmoplegia in systemic lupus erythematosus

Sir: Painful ophthalmoplegia is a combination of ocular pain, ipsilateral ocular palsies, and sensory loss in the ophthalmic and sometimes maxillary distributions of the fifth nerve. Vision can be impaired. The syndrome may be caused by lesions in the cavernous sinus or superior orbital fissure, including idiopathic inflammation, neoplasms, infections, endocrinopathies, thrombosis of the orbital veins or cavernous sinus, and vascular malformations. We report here a patient with a painful ophthalmoplegia as an initial manifestation of systemic lupus erythematosus.

In May 1978, a 38-year-old woman was admitted with severe pain behind the right eye, blurred vision, diplopia and nausea. Physical examination revealed a right third nerve palsy with a dilated and fixed pupil, a right fourth nerve palsy, and sensory loss in the right ophthalmic and maxillary distributions of the right fifth nerve with diminished corneal reflex. The ocular fundi were normal. Routine laboratory studies showed an erythrocyte sedimentation rate (ESR) of 25 and 52 mm, and serologic tests for syphilis were negative. Roentgenograms of the skull and chest, orbital tomograms, bilateral carotid and vertebral angiograms, and electromyographic studies were normal. Visual evoked potentials showed amplitude and latency abnormalities in the response from the right eye, consistent with a prechiasmatic lesion in the right side. Steroid therapy was initiated. Eye pain and the muscle ocular palsies disappeared over the following week, and ten days later, visual evoked potentials became normal. In December 1979 and October 1980 she suffered generalised tonic-clonic seizures. In May 1981 she returned after the sudden development of a left hemiplegia. Physical examination showed Raynaud's phenomenon and facial erythema. Laboratory investigations revealed an ESR of 106 mm, thrombocytopenia, a positive antinuclear factor native DNA antibodies and antibody-type circulating anticoagulant. Cranial CT scan showed a right temporoparietal infarct. The diagnosis of systemic lupus erythematosus was established and the patient was started on steroid therapy. Ten months later she developed right hemiplegia and aphasia. The patient subsequently died but no authorization for necropsy was obtained.

We report a patient with painful ophthalmoplegia believed to be an initial manifestation of systemic lupus erythematosus. The sensory disturbance was confined to the ophthalmic and maxillary divisions, and the sixth cranial nerve was unimpaired. This supports the diagnosis of a lesion involving the lateral wall of the cavernous sinus, and distinguishes it from lesions confined to the superior orbital fissure.¹ Mathew and Chandy² suggested that the syndrome of painful ophthalmoplegia may be a manifestation of a more generalised autoimmune disease, since half of their patients had positive test for LE cells and raised ESR. Only one patient affected by systemic lupus erythematosus with painful ophthalmoplegia has been reported, but not as a primarily manifestation.³ Painful