Chronic meningitis

Rute Relvas*, Manuel Gonçalves**

Abstract

Chronic meningitis is usually defined as a syndrome of meningeal symptoms and signs lasting for more than four weeks which include infectious and non-infectious aetiology. This syndrome is less common than acute meningitis, yet its frequency has certainly increased in immunosuppressed patients. The authors discuss the clinical picture and the differential diagnoses of the situation.
Keywords: chronic meningitis, CNS infections-

Introduction

The meningeal syndrome corresponds to an inflammatory process of the meninges, characterized clinically by signs and symptoms (fever, headache, lethargy, nuke stiffness, mental confusion, nausea and vomiting) combined in a wide range of ways. Chronic meningitis is an entity in which the above-mentioned signs and symptoms evolve in a slow way, keeping for a period above four weeks.

The causes may be multiple, both infectious as non-infectious, and in a significant percentage of cases the etiologic diagnosis is not established, in spite of resorting to multiple test and supplementary research.

Chronic meningitis frequency in the population is lower than acute meningitis, presenting however a growing incidence and prevalence in immune depressed individuals, whether patients infected by the human deficiency virus (HIV), or in those subject to steroid therapy and other immunosuppressant drugs, in diabetic and in patients with neoplasms.[1]

Etiologic diagnosis

Chronic meningitis usual presentation is in a subacute or chronic forms (days to weeks) with headaches, light fever and nuke stiffness. Cognitive changes are frequent, mainly in advanced stages and marked decrease of the general condition, with a significant weight loss.[2] Symptoms as reduced visual acuity and diplopia are not exceptional.[2,3,4]

For the etiologic diagnosis it is important the data collected in the patients' anamnesis, as trips, occupation, personal and family background and ethnic characteristics. The objective exam is important to value changes suggesting certain pathologies as neoplasms, systemic infections, sarcoidosis, vasculitis, among others.[5]

The cytologic and biochemical exam of the CSF is fundamental to assess such conditions, being important to perform manometry, revealing an increased pressure in a high percentage of cases.[4,5] If pleocytosis is present it indicates meningeal irritation, although not necessarily an infection. The predominant cellular type relates with the nature of the infection and with the stages it is at the moment in time. In the HIV infection is common the existence of lymphocytic pleocytosis in the initial and intermediate stages of the disease. As the immunosuppression progresses, the CSF inflammatory reaction tends to disappear, but may reappear subsequently as a reaction to a pathogenic stimulus (*Table 1*).[5]

Proteins in the CSF increase as a response to inflammatory stimulus (infectious or otherwise) of the brain and meninges, and its increase in general is parallel with those of cells. As important as the dosage of protein levels it is the differentiation of its components, namely the different types of globulin, being the research of the protein intrathecal synthesis crucial to establishing the profile of the change.

Low levels of glucose in the CSF result both from an increase of its use by CNS and leucocytes (especially PMN), whether in changes at the level of the glucose transfer system from the blood to this CSF. Therefore the low level of glucose in the CSF, in the absence of hypoglycaemia indicates a meningeal diffuse lesion.

The bacteriological and mycological tests (both

*Resident to the Neurology Supplementary Internship

**Neurology Interim Assistant

Neurology Service of Santo Antonio Capuchos Hospital, Lisbon

Received for publication on the 8th May 1996

direct as in culture), serology, pathological anatomy, among others are of crucial importance for the etiologic diagnosis of the meningeal syndrome to which we will refer subsequently.

In terms of image techniques, cranial encephalic CT scan shows dural thickening in plate, with increased capture of contrast, dystrophic calcifications, especially in the basis, and sometimes hydrocephalus, infarction and atrophy. In the cranial encephalic nuclear magnetic resonance (CE NMR) it can be seen an exudate, usually after contrast administration, whilst this is isotensive regarding the cerebral parenchyma and increased capture of contrast more accentuated in the basis.[6,7]

Most common causes

Infectious causes

Tuberculous Meningitis: the CNS tuberculosis, being its most common form of presentation Tuberculous Meningitis (TM), is the most lethal manifestation of this infection. MT is fatal if not treated and the risk of mortality and morbidity increases with the delay in the setup of appropriate therapy. Its incidence and prevalence have increased in the last few years namely in the population of HIV-infected patients.

Mycobacterium tuberculosis can affect all structures of the human body, and the CNS is not an exception. Attaining such system is always secondary to another focus, even if this is not clinically apparent.[8,9,10]

The CNS involvement by tuberculosis is made, in most cases, at the time of the primary pulmonary infection, i.e., while the bacterial growth is underway without interference of the immune system (before the onset of cellular hypersensitivity against the agent). In this first stage of bacteremia, tuberculosis lesions will set in the meninges, in the spinal cord and in the cerebral parenchyma. Months or years later, such foci may, due to immune or physical stimuli, increase and behave as a tuberculoma or, after rupture, reaching a subarachnoid space triggering a meningeal process. Neurotuberculosis can also occur in cases of miliary tuberculosis, where the big number of bacilli circulating increases the probability of the agents locating in the meninges and under the form of small tuberculomas.[10, 11]

Clinically, TM presents itself through headache worsening progressively, followed by vomiting, fever (described in some series as an inconstant signal, being absent in 10 to 20% of cases), meningism, mental confusion and cranial pairs paresis (III, IV, VI and VII). These last ones are due to the meningeal primary involvement at the brain basis. Convulsive crisis (usually tonic clonic) can be the starting frame or emerge sometime after.

The clinical staging, based on the neurologic evolution, can be correlated with the prognosis. [10]

Stage I – individual aware, with meningeal signs, without any other neurological signs.

Stage II – confused patient or with focal signs

Stage III – patient in coma with paraparesis or hemiparesis of advanced grade.

TABLE I

Diferential diagnosis of pleocytosis

Meningitis with PMN Pleocytosis
Bacterial Nocardia; Actinomyces; Arachnia; Brucella
Fungal Blastomyces; Coccidioides; Candida; Aspergillus; Zygomycetes; Cladosporium; Pseudoallescheria
Chemical Endogen: epidermoid tumors or craniopharyngioma Exogen: drugs or contrast agents
Systemic Lupus Erithematous (SLE)
Meningites with lymphocytic meningitis
Bacterial Treponema pallidum; Leptospira; Actinomyces israelii; Arachnia propionica; Nocardia; Brucella (+ 90%); Borrelia burgdorferi; Mycobacterium tuberculosis; Listeria monocytogenes
Fungal Cryptococcus neoformans; Candida; Coccidioides immitis; Histoplasma capsulatum; Blastomyces dermatitides; Sporothrix schenckii; Pseudoallescheria boydii
Parasitic (Meningoencephalitis) Toxoplasmosis; Cysticercosis; Angiostrongylus cantonensis
Viral HIV; Enterovirus –> Coxsackie B, ECHO; Lymphocytic choriomeningitis; Herpes simplex; Arbovirus
Parameningeal Foci Cerebral Abscess
Non-Infectious Neoplasms (meningeal carcinomatosis), sarcoidosis, vasculitis, SLE, CNS lymphoma, multiple sclerosis
Unknown

Almost all patients in the stage I recover totally, with the appropriate therapy. Mortality is high in stage III, showing in most studies to be above 45%. [10]

The initial CSF investigation can reveal mixed pleocytosis or PMN predominance, but sometime afterwards it is defined almost always as lymphocytic pleocytosis. In immune depressed patients, cell count can be normal. Proteins are increased and glucose in the CSF is reduced. The CSF opening pressure is usually high. Pleocytosis can also remain for some months after beginning the therapy, even after the fever and the patient complaints are gone. [10]

BAAR identification at direct test is described in around 37% of cases in some series, and this number can rise if serial punctures are carried out (4 LP - 87% of the identification). [12] The CSF direct exam can be made through three staining methods – Ziehl – Nielsen, Kinyion and fluorescence. The first one is the most commonly used, but at present it is preferably fluorescence due to higher sensitivity. [12]

The culture test is traditionally made in means based in egg (Lowstein-Jensen) and agar (Middlebrook), needing an average period of 6 to 8 weeks of incubation. At present, it can be used a radiometric detection system, BACTEC (Becton Dickinson Diagnostic Systems: Sparks, MD), with the advantage of detecting positive cultures between the 8th and the 14th day.[12]

There are also some specific tests for diagnosing such pathology carried out in the CSF and may be direct and indirect.

Indirect tests are the dosage of the adenosine deaminase (ADA) activity determining antibody titers for *Mycobacterium* through ELISA.

A high-level of ADA (>6 – 8 U/L) is observed in 63 – 100% of patients with TM and in around 16% of other forms of meningitis.[13]

Direct specific tests are biochemical identification of *Mycobacterium* products and the detection of the antigen for CSF bacillus. The latter, made by Eliza techniques or latex agglutination particles, seems to be extremely specific, with sensitivity depending on different groups ranging from the 50 – 100%.

Polymerase chain reaction (PCR) in the CSF, an amplification test preceding the identification of the genetic code of MPB64 protein, is considered as a rather sensitive and specific index, and can be carried out relatively quickly (in agarose gel electrophoresis).[14]

A β-2 microglobulin is a score of immunologic activation, being an unspecific marker of infection and CNS neoplasm. Its serial dosage can be a good monitoring of the therapy effect.

Image tests, as cranial encephalic CT scan and NMR, are very useful in the study of these patients, not only as a means of diagnosis but also due to the correlation of image with the prognosis. There is an increased uptake of contrast, related with a process of exudative arachnoiditis, as an image translation for both methods. Other detected changes for this test are the intracranial tuberculomas, hydrocephalus (more often found in children) and in deep cerebral infarction. In a variable percentage of cases (depending on the studies) and rather higher for CT, there are not image changes.[6,7]

Meningeal syphilis: In the last 10 years syphilis has lost the status of a disease with a primarily historical interest, to become a priority situation in terms of public health. During such period, its incidence and prevalence have been increasing, being epidemiologically related with the HIV infection. [15]

Meningeal syphilis occurs usually during the first year of infection and it is featured by headache, meningeal signs, nausea and vomiting. The involvement of the cranial pairs is common, being translated clinically by deafness, facial paresis of peripheral type, and visual alterations. The CNS is involved in around 20 – 40% of (such percentages vary depending on the studies)[15,16] primary syphilis cases, and the initial condition is usually of an acute or chronic meningitis (according to some authors, meningitis occurs in around 25% of all syphilis cases).[15, 16, 17]

The diagnosis is based in an evaluation of the CSF in an individual presenting positive serology for *Treponema Pallidum*. The cytobiochemical exam shows usually a lymphocytic pleocytosis, increase of proteins and normal glucose values in the CSF.

A reactive CSF for VDRL test is highly suggestive of a diagnosis, but a negative result does not exclude the diagnosis. Conversely, a negative FTA – ABS test eliminates the possibility of CNS involvement through infection.[15, 17, 18]

Meningeal cryptococcosis: Cryptococcosis is a rare opportunistic mycosis, located preferentially in the neuro-meningeal,[3] more commonly in cases of HIV infection, diabetes, Hodgkin's disease and prolonged therapy with corticosteroids or other immunosuppressive drugs.[3]

It is thought that individuals infected by HIV, 5 to 10%, will develop CNS cryptococcosis.

Cryptococcus are encapsulated, ubiquitous, and only *Cryptococcus neoformans* is pathogenic for man. Pigeons epidemiologic role is well-defined for serotypes A and D, with the contagion made by their excrements through the respiratory tract.[3]

Physiopathologically, there is a meningeal inflammatory infiltration spreading along the Virchow-Robin perivascular spaces to the cerebral parenchyma, cerebral trunk and cranial nerves roots.[3,19]

The most commonly found clinical syndrome is meningoencephalitis of insidious evolution, with an initial meningeal stage, followed by infectious encephalitis.[8,18] The cranial nerves are involved in around one third of cases,[2,3] the most frequently affected are the oculomotor and the optical nerve (with papilloedema and optical nerve atrophy).[2] Meningeal cryptococcosis, throughout its evolution, can complicated itself with hydrocephalus and cerebral vascular accidents.

For the diagnosis is fundamental the CSF study, presenting in most cases a pleocytosis (PMN or mononucleate), protein in the CSF slightly increased or hypoglycorrhachia. The agent direct identification with China ink is possible, but can be falsely negative in 60% of cases. [3] Cryptococcus culture, from the CSF, is usually slow. The latex particles agglutination test detects antigens in the serum or in the CSF of patients infected in around 90 to 100% of cases.[20] Frequently there is not a matching image for this situation being hydrocephalus and diffuse abscesses the most commonly observed aspects (although rare).

The aspects of a bad prognosis are an absence of cells in the CSF (more frequently found in AIDS cases), the syndrome of inadequate secretion of antidiuretic hormone, hypoglycorrhachia and high opening pressure. In AIDS cases, even with adequate therapy, the survival average time is nine months. [2]

Neurobrucellosis: Brucellosis is an endemic disease in Portugal and in countries around the Mediterranean area and Middle East. In such countries, it seems to be a predominance of infection by *Brucella melitensis*, while in other regions where the disease is not endemic most of the human infections are caused by *Brucella Suis* and *Brucella abortus*.[21]

During the acute infection, the neurologic involvement is unspecific, consisting of headaches, fatigue and myalgia. Neurobrucellosis occurs in around 5% of diagnosed cases, being a form of chronic infection. Its clinical presentation can be diverse, simulating different neurological diseases (such as neurosyphilis and neurotuberculosis).[21, 22, 23, 24]

Clinically, chronic meningitis cases (rarer form of neurobrucellosis) manifest themselves frequently by headache and papilloedema, translating an increase of intracranial pressure. Seldom there is fever, meningeal signs and focal signs in the neurological exam.[21] In a revision of 24 cases, Bouza et al.[2] refer that brucellosis symptomatology was present in those patients for periods ranging from 4 to 7 months and that less than 50% of patients with chronic meningitis presented meningeal syndrome.

In the CSF is frequent a lymphocytic pleocytosis, hypoglycorrhachia, increased protein in the CSF and the existence of oligoclonal IgG bands (translating protein intrathecal synthesis). ADA is usually high, posing prognosis problems with neurotuberculosis, as the clinic similarities and the changes in the CSF are evident.[13] Antibody detection for *Brucella* in the CSF is always an indicator of local infection[22] and can be made through Rose of Bengal, Wright or immunofluorescence tests. The last seems to be the most reliable, with the first two poorly sensitive to CSF titers.

Different from most cases of chronic meningitis, neurobrucellosis seems to present a good prognosis, being the low mortality and not always clearly related with brucellosis.[22]

Lyme disease: It is an infection caused by a Spirochaetes, *Borrelia burgdorferi,* transmitted by a tick bite, usually *Ixodes dammini* or another one of the same group.[25, 26] It has universal distribution, with some special features seeming to differentiate the American from the European form. In the North Hemisphere most infections are acquired from May to July, although the appearance of symptomatology may occur in any time of the year.[8]

As all the infections by Spirochaetes, Lyme disease presents several clinical stages, with remissions and exacerbations. Its clinical preservation can be classified in three stages:[26]

Stage 1 – The condition starts with a migratory chronic erythema, which can be followed by fever, fatigue, general malaise, myalgia, arthralgia and meningism.

Stage 2 – Weeks or months later, neurologic changes (meningitis, cranial neuritis, peripheral neuritis, encephalitis, hemiparesis, chorea, cerebellum ataxia), heart changes (alterations in the intracardiac

conduction, myocarditis, pericarditis, heart failure) or osteoarticular.

Stage 3 – months or years later, chronic cutaneous (chronic atrophic acrodermatitis), neurologic (encephalopathy, polyneuropathy, encephalomyelitis and cerebral vascular accidents) and joints changes appear.

Regarding the meningeal involvement, irritation signs developed in an initial stage of the disease are not usually followed by any CSF alteration. In stage two, the most frequent neurologic complication is lymphocytic meningitis, evolving for weeks or months and not followed by cranial and/or peripheral neuritis (Bannwarth Syndrome). The VII pair paralysis is particularly frequent. [25, 26]

Serology for *Borrelia*, made by ELISA or Western Blot, reveals in the serum an increase of specific IgM titer from the third to the sixth week whilst the specific IgG titer rise for months or even years. The CSF, in cases of meningeal involvement, is compatible with lymphocytic meningitis (mononuclear pleocytosis, increased protein in the CSF, and glycorrachia within normal values, as well as the opening pressure). Determining intrathecal production of antibodies (IgM, IgG or IgA) specific for *Borrelia* is crucial to confirm a diagnosis of meningitis.[26, 27] Serology can be falsely negative in the first weeks of the disease, or in patients treated earlier with appropriate antibiotic therapy. False positives are found in many situations as syphilis, Rocky Mount fever, autoimmune diseases as SLE and amyotrophic lateral sclerosis.[25]

Non-infectious causes

Neoplastic chemical meningitis: within such group, it is considered a meningeal metastization of CNS primary and secondary being the most frequent the first one under the form of meningeal carcinomatosis. The most frequently involved tumors are breast adenocarcinoma, lung, stomach, melanoma and leukaemias in children.[8,29]

Meningeal metastization by glial cells, complicates around 20% of supratentorial gliomas being symptomatic only in 4% of cases. It emerges frequently in the absence of the primary tumor recurrence being the meningeal primary involvement very rare. Craniopharyngioma with cystic transformation may, through the liberation of cystic contents, lead to an inflammatory response manifested under the form of a chemical meningitis.[30]

For the diagnosis is of crucial importance the CSF evaluation, where around 50% of cases presents a high opening pressure and pleocytosis with lymphocytic predominance, as an inflammatory reaction to the tumor. Crucial also is the research of neoplastic cells and carrying out a CT scan or NMR to exclude intracranial expanding lesions.[28, 29]

Neurosarcoidosis

Sarcoidosis is followed by the CNS involvement in just one to 10% of cases (depending on the series), [30, 31] being rare its manifestation in the absence of signs and/or systemic symptoms.

Pathophysiologically there is a granulomatous infiltration of the meninges and adjacent parenchyma, more prominent in the bases.[8]

Clinically, it is presented in a subacute or chronic form, with visual alterations caused by lesions of the optical nerve and chiasma, polydipsia, polyuria, drowsiness and obesity, due to the involvement of the hypothalamus and pituitary. Hydrocephalus, convulsive crisis, cranial nerves paresis, pyramidal and cerebellum signs are also frequent manifestations. Seldom can it cause recurrent or chronic meningitis. [8]

The diagnosis is based in biopsies with evidence of sarcoid granulomas, from lymphatic ganglia, skin, lungs and bone tissue. Analytically, in 2/3 of cases there is a serial increase on the angiotensin-converting enzyme and a high calcaemia. In the CSF test is frequent the existence of moderate lymphocytic pleocytosis, increased protein in the CSF and sometimes hypoglycorrhachia. Image wise, there is a increased uptake of contrast by the meninges, more marked in the bases and sometimes hypothalamic and the pituitary ((more easily observed by NMR).[8,30]

Final considerations

Chronic meningitis is nowadays a growing problem with importance in terms of public health due to its increasing frequency in some risk groups, namely in immunodepressed patients.

Before the multiplicity of underlying causes and their different therapeutic approach, the differential diagnosis of such situations becomes of critical importance and must be established as early as possible. Sometimes this is not possible in spite of resorting to multiple tests and supplementary investigations being essential to formulate non-infectious aetiologic hypotheses. ■

References

1. Smith J, Aksamit A. Outcome of Chronic Idiopathic Meningitis. Mayo Clinic Proc 1994; 69 : 548 – 556.

2. Garrit JA, Herman DC, Imes R, Fries P, Hughes CF, Campbell RJ. Optic nerve sheath decompression for visual loss in patients with acquired immunodeficiency syndrome and cryptococcal meningitis with papilloedema. Am J Ophthalmol 1993; 116: 472 – 478

3. Donnet A, Graziani N, Harlé JR, Durand JM, Touta A, Grisoli F. Formes neurologiques de la cryptococcose. A propos de 2 cas atypiques chez des patients non infectés par le VIH. Rev. Neurol (Paris). 1993; 149: 326 – 330

4. Carpentier AF, Sanson M, Kujas M, Giroud M, Poisson, Delattre JY, Gliomatose meningée primitive. Rev Neurol (Paris) 1994; 150:232 – 235

5. Swartz MN. Chronic meningitis; many causes to consider. N Eng J Med 1987; 317: 957 – 959.

6. Infectious, subdural empyema and epidural abscess in Osborn AG, Tong KA (ed), Handbook of neuroradiology: Brain and Skull, 2nd edition, 429 – 430, Mosby, St. Louis, 1996.

7. Infection, white matter abnormalities and degenerative diseases in Osborn AG (ed) Diagnostic radiology, 686 – 687, Mosby, St Louis, 1994.

8. Non-viral infections of the nervous system in Adams RD; Victor M (Eds), Principles of Neurology, 5th Edition, 600-609, 617 – 620, McGraw-Hill, New York, 1993

9. Haddock DR. Predominantly tropical and subtropical infections in Swash M; Oxbury J (Eds), Clinical Neurology, Vol. 1, 916 – 917. Churchill Livingstone, New York, 1991.

10. Norris AH, Buckley RM. Central nervous system tuberculosis in Rossman M, McGregor (Eds), Tuberculosis: Clinical Management and New Strategies, 1st edition 159 – 165, McGraw-Hill, New York, 1995

11. Dastur DK, Manghani DK, Udani PM. Pathology and pathogenetic mechanisms in neurotuberculosis. Radiol Clin North Am 1995; 33: 733 – 752.

12. Warren NW, Body BA. Bacteriology and diagnosis in Rossman M, McGregor R (eds), Tuberculosis: Clinical Management and New Strategies, 1st edition, 47 – 52, McGraw-Hill, New York, 1995.

13. Cunha S, Gaspar E, Meliço-Silvestre A, Azevedo-Bernarda R, Costa C: Neurobrucellosis. Another cause of increased adenosine deaminase activity in cerebrospinal fluid. J Infect Dis 1990; 161:156 – 157.

14. Crawfoord JT. New developments for the diagnosis of tuberculosis: the impact of molecular biology in Rossman M, McGregor R (Eds), Tuberculosis: Clinical Management and New Strategies, 1st edition, 259 – 262, McGraw-Hill, New York, 1995.

15. Hook EW, Marra CM. Acquired syphilis in adults. N Eng J Med 1992; 326:1060 – 1069.

16. Goldmeier D, Skinner C. Neurosyphilis: Current drug treatment recommendations. CNS drugs 1995; 3: 328 – 336.

17. Cintron R, Pachner A. Spirochetal diseases of the nervous system. Current Opinion Neurology 1994; 7: 217 – 222.

18. Davis LE, Schmitt J. Clinical significance of cerebrospinal fluid tests for neurosyphilis. Ann Neurol 1989; 25: 50 – 55.

19. Saul TJ, Gallagher JE. Sudden hemiparesis as the presenting sign in cryptococcal meningoencephalitis. Stroke 1986; 17:753 – 754.

20. Chan KH, Mann KS, Yue CP. Neurosurgical aspects of cerebral cryptococcosis. Neurosurgery 1989; 25: 44 – 48

21. Deeb SMA, Yaqub BA, Sharif HS, Phadke J G. Neurobrucellosis: clinical characteristics, diagnosis and outcome. Neurology 1989; 39: 498 – 501.

22. Bouza E, Torre MG, Parras F, Guerrero A, Rodrigues-Creixems M, Gobernado J. Brucellar meningitis. Rev Infect Dis 1987; 9:810 – 822

23.Shakir RA, Al-Din ASN, Araj GF, Lulu AR, Mousa AR, Saadah MA. Clinical categories of neurobrucellosis. Brain 1987; 110: 213 – 223.

24. Bakemuka M, Shemena AR, Panayiotopolous CP, Al-Aska AK, Obeid T, Deif AK. Neurological syndromes of brucellosis. J Neurol Neurosurg Psychiatry 1988; 51:1017 – 1021.

25. Ruel M. Lyme borreliosis: what is new in diagnosis and treatment? Eur J Int Med 1992; 2: 205 – 211.

26. Sigal LH. Current recommendations for treatment of Lyme disease. Drugs 1992; 43: 683 – 699.

27. Kaiser R. Intrathecal immune response in patients with neuroborreliosis: specificity of antibodies for neuronal proteins. J Neurol 1995; 242:319 – 325.

28. Intracranial Neoplasms in Adams R D; Victor M (Eds), Principles of Neurology, 5th edition, 571 – 572, McGraw-Hill, New York, 1993.

29. Currie S. Non-metastatic consequences of malignant disease in Swash M; Oxbury J (Eds), Clinic Neurology, Vol. 2, 1672 – 1673, Churchill Livingstone , New York, 1991.

30. Ludmere KM, Kissane M. Chronic meningitis in a 51-year-old man. Am J Med 1993; 94:85 – 92.

31. Cheng TM, O'Neill BP, Scheithauer BW, Piepgas DG. Chronic meningitis; the role of meningeal or cortical biopsy Neurosurgery 1994; 34:590 – 596.