Cerebrospinal Fluid and Therapy of Isolated Angiitis of the Central Nervous System

Vitor Oliveira, MD; Pedro Póvoa, MD; Adília Costa, MD; José Ducla-Soares, PhD

Background Serial cerebral angiograms, computed tomography, and magnetic resonance imaging are among the proposed methods for monitoring disease activity and response to therapy in isolated angiitis of the central nervous system. Cerebrospinal fluid has not proved to be useful in monitoring clinical course.

Case Description We describe a 45-year-old man with histological diagnosis of isolated angiitis of the central nervous system that was treated with prednisone plus azathioprine and monitored for 2 years. Samples of the cerebrospinal fluid were obtained for cytological and routine chemical examination, as well as albumin and immunoglobulin content. Before treatment, cerebrospinal fluid showed marked plasmatic transudation of albumin and intrathecal synthesis of immunoglobulins. During the first year of immunosuppression no events were noticed, and the previously abnormal aspects of the cerebrospinal fluid showed improvement. During the weaning of azathioprine, a new stroke occurred in conjunction with a marked deterioration of cerebrospinal fluid parameters. Immunosuppression was resumed at previous levels, and during the following year no further events occurred. Once again, abnormal cerebrospinal fluid values improved significantly.

Conclusions We report a case of isolated angiitis of the central nervous system in which the serial cerebrospinal fluid examinations (albumin and immunoglobulin content) showed a close correlation with clinical course. This method may be useful in monitoring response to therapy. (Stroke. 1994;25:1693-1695.)

Key Words • central nervous system • cerebrospinal fluid • angiitis

Isolated angiitis of the central nervous system (CNS) is a very rare segmental necrotizing vasculitis, which may or may not be granulomatous, involving vessels of the CNS and almost always sparing vessels located elsewhere in the body. The most common laboratory finding is an abnormal cerebrospinal fluid (CSF) that shows a mononuclear pleocytosis and/or increased protein levels. Therapy relies on immunosuppression either solely with steroids or in association with cyclophosphamide or azathioprine.

Until now, there has been no satisfactory way of assessing disease activity and response to therapy. Some authors have proposed serial cerebral angiograms as a guideline, but these findings are nonspecific and may even be normal. Serial brain computed tomography (CT) and magnetic resonance imaging (MRI) have also been used with good clinical correlation. So far, no laboratory test has been reported as reliable in the assessment of disease activity.

We report a case of isolated angiitis of the CNS that was treated with immunosuppression and monitored for 2 years. Serial CSF studies revealed a close correlation between disease activity, immunosuppression, and CSF abnormalities.

Received March 17, 1994; final revision received May 9, 1994; accepted May 9, 1994.

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Cerebrospinal Fluid Before and During Immunosuppression

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<td>1230</td>
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<tr>
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<td>48</td>
<td>5</td>
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</table>

AZA indicates azathioprine; PRD, prednisone; CSF, cerebrospinal fluid; TProt, total protein; PTAlb, plasmatic transudation of albumin; and ITSIg, Intrathecal synthesis of immunoglobulins.

Reference values are as follows: TProt, 200-550 mg/L; PTAlb, 0 mg/L; and ITSIg, (IgG, IgA, IgM), 0 mg/L.

globulin content (IgG, IgA, and IgM). Results were compared with albumin and immunoglobulin content in serum. Plasmatic transudation of albumin and intrathecal synthesis of immunoglobulins were assessed according toourtellote et al. and Schuller et al. CSF samples withdrawn before therapy showed a normal cell count, increased total CSF protein, marked plasmatic transudation of albumin, and intrathecal synthesis of immunoglobulins (Table).

On admission brain CT showed a right temporal and a left parietal hematoma. The MRI scan showed the same lesions plus several bilateral hemorrhagic lesions at different stages. Celiac and renal angiograms were normal. Cerebral and leptomeningeal biopsies were performed. Histology revealed multiple granulomatous lesions with lymphocytes and giant cells involving the whole thickness of the wall of the small cerebral vessels and perivascular infiltration of mononuclear cells in the leptomeninges (Figure). A diagnosis of isolated angitis of the CNS was established.

Treatment with prednisone 60 mg/d and azathioprine 150 mg/d was initiated in June 1990. For 1 year of immunosuppression no further events were noticed. Two CSF samples withdrawn during that period showed a normal cell count, reduction of total CSF protein, normalization of plasmatic transudation of albumin, and a marked reduction of intrathecal synthesis of immunoglobulins (Table).

During the weaning of therapy (prednisone 60 mg/d and azathioprine 50 mg/d) a new hemorrhagic stroke occurred in June 1991, and the CSF analysis revealed a marked deterioration of total protein, plasmatic transu-
dation of albumin, and intrathecal synthesis of immunoglobulins (Table). The cell count was normal. Immunosuppressive therapy was resumed at previous levels. No further events were noticed, and the CSF examination once again showed a decrease in the total protein as well as in plasmatic transudation of albumin and no intrathecal synthesis of immunoglobulins (Table). CSF cell count remained normal.

One year later (July 1992) the patient was admitted to our hospital because of bilateral pneumonia. He developed septic shock and died 4 days later.

Discussion

Several therapeutic agents have been tried in isolated angiitis of the CNS, but only steroids and cytotoxic agents have demonstrated some success.\(^1\)\(^\text{-}^\text{10}\) Accepted therapeutic approaches consist of the combination of steroids plus cyclophosphamide or azathioprine. The clinical and laboratory course (serial CSF analyses) in our patient suggested that azathioprine plus prednisone was an effective drug association. The initiation of azathioprine resulted in clinical stabilization, and its weaning was followed by a flare-up of the disease, which once again became quiescent when brought to previous levels.

Monitoring of therapy is also a matter of debate; however, the lack of specificity and the lack of sensitivity of the proposed methods are serious drawbacks.\(^4\)\(^\text{-}^\text{57}\) Angiograms are normal in half of the cases, and CSF, although usually abnormal, has never been used.\(^1\)\(^\text{-}^\text{2}^\text{-}^\text{6}\)

In this case pretreatment CSF showed a marked plasmatic albumin transudation and intrathecal synthesis of immunoglobulins, mainly IgG. Serial CSF analyses showed a clear relation between clinical course and immunosuppression. After therapy was started, both plasmatic transudation of albumin and intrathecal synthesis of immunoglobulins showed a significant decrease. Weaning of azathioprine was followed by another stroke and CSF deterioration. The readministration of azathioprine at previous levels was followed by an improvement in clinical condition as well as CSF parameters. Thus, in our patient serial CSF analyses showed a close correlation between clinical course and immunosuppression.

Serial CSF analyses seem to be a reliable marker of the CNS inflammatory process and therefore a guideline for monitoring disease activity and response to therapy.

Acknowledgments

We are indebted to Dr. António Magalhães, Department of Neurology, Santa Maria Hospital, Lisbon, for performing and discussing CSF analyses and to the Laboratory of Neuropathology, Department of Neurology, Santa Maria Hospital, Lisbon, for processing of the brain and leptomeningeal biopsies.

References

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*Stroke*. 1994;25:1693-1695
doi: 10.1161/01.STR.25.8.1693

*Stroke* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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