CNS lymphoma

To the Editor: Lachance et al. report results in 10 patients treated according to a standardized protocol with standard-dose cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP). Several issues can be raised regarding this report. First, patients with neuroradiographically and pathologically documented parenchymal primary CNS lymphoma (PCNSL) were evaluated for systemic lymphoma. I am unaware of any cases reported.

CNS staging should include slit-lamp examination for possible uveal or vitreous eye disease, CSF cytology for possible lymphomatous meningitis, and spine imaging (either CT-myelography or contrast-enhanced MRI) for LM necessitating either craniospinal irradiation or involved-field radiotherapy and intra-CSF chemotherapy. Spinal drop metastases necessitate a treatment similar to that described for LM.

Also, contrast, careful staging of the CNS is quite relevant to treatment planning of PCNSL. CNS staging should include slit-lamp examination for possible uveal or vitreous eye disease, CSF cytology for possible lymphomatous meningitis, and spine imaging (either CT-myelography or contrast-enhanced MRI) for LM necessitating either craniospinal irradiation or involved-field radiotherapy and intra-CSF chemotherapy. Spinal drop metastases necessitate a treatment similar to that described for lymphomatous meningitis.

First, patients with neuroradiographically and pathologically documented parenchymal primary CNS lymphoma (PCNSL) were evaluated for systemic non-Hodgkin's lymphoma (NHL). Rather, the effectiveness of CHOP in the treatment of immunocompetent patients with PCNSL; in fact, our results argue against its use, and we closed this study early because of the high-risk recurrence rate. The point of our paper was the unusual pattern of intracerebral recurrence at apparently uninvolved sites after an initial response at the primary site.

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References

Cabergoline in Parkinson's disease

To the Editor: Lieberman et al. and Lera et al. concluded that cabergoline can provide continuous dopaminergic stimulation in patients with Parkinson's disease (PD) when taken orally once a day. It is possible, however, that the improvement after cabergoline— for example, the decrease in "off" time in both studies—is partly due to a peak effect in the morning hours following intake of cabergoline.

Four PD patients participating in an open study of cabergoline in PD with motor fluctuations took cabergoline (mean dose, 8.1 mg) at 8 AM for 1 week and at 2 PM for another week. All other medications remained the same. These patients kept diaries of their motor function for 2 weeks from 8 AM until 11 PM by recording at half-hour intervals whether they were "on" or "off." We used t tests to compare 28 days on which cabergoline was taken at 8 AM with 28 days when the daily intake was at 2 PM.

It appears that the timing of cabergoline administration influences the course throughout the day of hours "off" (figure). When cabergoline was taken at 8 AM the number of hours "off" between 8 AM and 2 PM was 1.4 ± 1.0 hours, fewer than the 2.0 ± 1.1 hours recorded when cabergoline was taken at 2 PM (p = 0.004). Intake at 2 PM resulted in 1.4 ± 0.9 hours "off" between 2 PM and 7 PM, fewer than the 2.0 ± 1.1 hours after intake at 8 AM (p = 0.024). The results in the evening hours between 7 PM and 11 PM did not differ significantly according to the time of caber-
When cabergoline is administered at 8 AM (08h), there are fewer hours "off" in the morning than when cabergoline is taken at 2 PM (14h). When taken at 2 PM, there are fewer hours "off" in the afternoon than when cabergoline is taken at 8 AM. This suggests that there is a peak-dose effect of cabergoline that does not last throughout the entire day.

Although the number of subjects is too small to warrant any definite conclusion, our results do suggest a peak-dose effect of cabergoline during the first 5 to 6 hours after administration. This time course matches the course of daily plasma levels of cabergoline (see figure, Lera et al), showing higher levels 5 to 6 hours after cabergoline intake, especially at the higher dose of 7 mg as taken by our patients.

Lera et al reported an improvement of early morning akinesia in all patients, and early morning dystonia practically disappeared. This clearly indicates that cabergoline does exert a long-acting dopaminergic effect after the first 5 to 6 hours, but as matters stand at present, further studies will have to be carried out before one can conclude that the easiest way to administer cabergoline (ie, once a day) is also the most effective therapeutic strategy. Despite cabergoline's long-acting properties, administration two or three times a day may prove more beneficial than once daily because the former strategy also implies the beneficial effects of two or three times a peak-dose effect, especially in higher doses of cabergoline.

Reply from the Author: The study by Horstink et al is interesting although limited in size. Cabergoline may be more effective in some patients when given in two divided doses. In the majority of patients in open studies, the convenience of a once-daily dose outweighs the relatively minor benefit of two divided doses.

References

Beethoven's illness

To the Editor: I read Drake's article on Beethoven's possible neurosarcoidosis with much interest and would like to add the following: "Beethoven was an artist, but a man as well." So wrote Franz Grillparzer in his funeral oration for the composer. Beethoven's music is immortal, but he was endowed with talents and limitations, with strengths and weaknesses of character. He fell in love often and he had several affairs with "well-born, well-bred women. . . . Although Beethoven frequently regretted not having a wife, he sensed that a stable domestic life would have ill-suited his artistic temperament." Nettil gave a thorough and complete account of Beethoven and his relation to the medical profession. In addition to constant contact with his friend Professor Franz Wegeler, Beethoven also consulted J.H. Creveld in Bonn, Johann Nepomuk Hanzczovsky (Mozart's doctor), Dr. Ludwig Freiherr von Turckheim in Vienna, Dr. Johann Peter Frank (with whom he consulted about his deafness and diarrhea), and Dr. Gerhardt von Vering, who was Staff Surgeon in Charge to Emperor Joseph II.

Beethoven wrote to Wegeler: "For several days Vering has been applying, to both my arms, vesicants consisting of some bark or other—I expect you know what I mean. This is a most unpleasant form of treatment, because it always robs me of the use of my arms for several days—until the bark has taken proper effect—and is extremely painful to boot. But I must admit that the buzzing and ringing in my ears is now somewhat fainter, particularly in my left ear. Although so far my hearing has not improved in any way . . . my bowels are now on the mend; when I have taken the lukewarm baths for several days, I feel quite well for a week. . . . Sometimes I take a tonic for my stomach. . . . I am now also following your advice and applying herbs to my belly. . . . Vering won't hear of my taking shower-baths." Beethoven also had the habit of drinking enormous quantities of water, and poured a jug of cold water over his head without drying himself! He felt "hot" at work. He also consulted Johann Adam Schmidt, Johann Malfatti, Rohrich, Andreas Wawruch, Andreas Bertolini, Jakob Staudenheim (who sent him herbs to my belly. . . . Vering won't hear of my taking shower-baths.) Beethoven also had the habit of drinking enormous quantities of water, and poured a jug of cold water over his head without drying himself! He felt "hot" at work. He also consulted Johann Adam Schmidt, Johann Malfatti, Rohrich, Andreas Wawruch, Andreas Bertolini, Jakob Staudenheim (who sent him herbs to my belly. . . . Vering won't hear of my taking shower-baths.)