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Letter to the Editor

AFP Index, a Parameter for the Detection of Brain Metastases in Non-seminomatous Germ Cell Tumours of the Testis

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THE DETERMINATION of alpha$_1$foetoprotein (AFP) has been accepted as a reliable parameter for diagnosing and monitoring patients with a non-seminomatous testicular tumour (NSTT) [1, 2]. The prognosis of NSTT patients has considerably increased since the application of the chemotherapeutic regimen according to Einhorn and Donohue [3]. Early detection of recurrence and/or metastases based on increasing serum AFP values contributed substantially to this achievement.

Metastases to the central nervous system (CNS) are the most common neurologic complication of disseminated germ cell tumours of the testis. Schold *et al.* [4] reported an incidence of approximately 40% in autopsy specimen. Measuring tumour markers in the cerebrospinal fluid (CSF) could provide an early sign for the development of brain metastases. Increased permeability of the blood-CSF barrier due to pathological conditions will result in overall increased concentrations of serum proteins in the CNS. In order to discriminate between barrier damage and synthesis within the CSF as a cause for elevated levels of AFP, it is necessary to determine the AFP index. This index—defined as the quotient between the CSF/serum AFP ratio and the CSF/serum albumin ratio—is expected to increase when AFP is synthesized within the central nervous system.

Our study population comprised thirty-one NSTT patients; one patient had an extragonadal brain teratoma tumour. AFP and albumin were measured in the sera and CSF—sampled on the same day—of these patients. Samples were taken during periods with or without AFP production at the time of sampling, but always before institution of chemotherapy. AFP levels were established by means of an enzyme immunoassay (Abbott Diagnostics, Wiesbaden, F.R.G.). Albumin was measured by 'rocket immunoelectrophoresis', using antisera and standard human serum from Behringwerke (Marburg, F.R.G.).

Figure 1 depicts the results. Apparently, only serum AFP values exceeding 1000 μg/l contributed to a reliable AFP value in the CSF, as indicated by the linear relationship between serum and CSF AFP values ($Y = 0.006X - 13.76$; $r = 0.994$; $n = 8$; $P < 0.001$).

As a mean CSF/serum ratio for albumin we found 4.0×10^{-3}, range $2.4\text{–}6.2 \times 10^{-3}$, which is in accordance with the literature [5]. As a CSF/

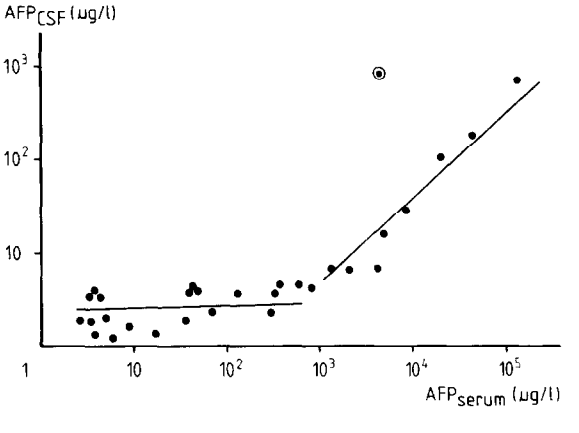

Fig. 1. AFP concentrations in serum and cerebrospinal fluid (CSF) from patients with non-seminoma testicular tumours. ◉ Patient with extragonadal brain teratoma tumour.

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serum ratio for AFP a mean value of 4.2×10^{-3} was obtained (range $3.1-5.6 \times 10^{-3}$) for the group of patients having serum values above 1000 μg/l. At serum AFP concentrations below 1000 μg/l the percentage transmitted through the blood–brain barrier is too low to give reliable values in the assay used.

The above-mentioned ratios for albumin and AFP in turn lead to a mean AFP index of 1.07 (range 0.78–1.42), a value which can be expected for two proteins with equal molecular weight and other physicochemical characteristics.

At low (<1000 μg/l) serum AFP values, a CSF AFP value of above 20 μg/l—depending on the sensitivity of the assay used—can be taken as an early indicator for deterioration of the process. At higher serum values the AFP concentration in the CSF should be judged in relation to the accompanying serum value (samples taken at the same day).

The only one in our group of patients with an AFP index (43.5) clearly above the upper limit indeed had local production of AFP due to his extragonadal brain teratoma tumour. His CSF/serum albumin ratio (4.6×10^{-3}) fell within the normal limits, thus barrier damage could be excluded. Demonstration of elevation of AFP in serum of patients with primary intracranial germ cell tumor has been reported [6].

An AFP index above 1.42 in our hands can be taken as an indicator for local synthesis in the central nervous system and primary secretion into the CSF. Bagshawe and Harland [7] have demonstrated that determination of chorionic gonadotrophin (HCG) has considerable value in early diagnosis and subsequent management of brain metastases in trophoblastic tumours. On the use of AFP, however, they were more sceptical [8].

In summary, determination of the AFP index could be a valuable parameter in establishing the presence of AFP producing brain metastases in NSTT patients. One should not, however, rely on a single CSF AFP level but include the albumin ratio in order to account for possible damage of the blood–brain barrier.

REFERENCES

1. Javadpour N. The value of biological markers in diagnosis and treatment of testicular cancer. *Semin Oncol* 1979, **6**, 37–47.
2. Willemse PHB, Sleijfer DTh, Schraffordt Koops H *et al.* Tumor markers in patients with non-seminomatous germ cell tumors of the testis. *Oncodev Biol Med* 1981, **2**, 117–128.
3. Einhorn LH, Donohue JP. *Cis*-diammine-dichloroplatinum, vinblastine and bleomycin combination chemotherapy in disseminated testicular cancer. *Ann Intern Med* 1977, **87**, 293–298.
4. Schold S, Vugrin D, Golbey R, Pasner J. Central nervous system metastases from germ cell carcinoma of the testis. *Semin Oncol* 1979, **6**, 102–109.
5. Tibbling G, Link H, Öhman S. Principles of albumin and IgG analyses in neurological disorders. I. Establishment of reference values. *Scand J Clin Lab Invest* 1977, **37**, 385–390.
6. Nørgaard-Pedersen B, Lindholm J, Albrechtsen R, Arends J, Diemer NH, Rhshede J. Alpha fetoprotein and human chorionic gonadotrophin in a patient with primary intracranial germ cell tumor. *Cancer* 1978, **41**, 2315–2320.
7. Bagshawe KD, Harland S. Immunodiagnosis and monitoring of gonadotrophin producing metastases in the central nervous system. *Cancer* 1976, **38**, 112–118.
8. Kaye SB, Bagshawe KD, McElwain TJ, Peckham MJ. Brain metastases in malignant teratoma: a review of four years' experience and assessment of the role of tumour markers. *Br J Cancer* 1979, **39**, 217–223.