Placental alkaline phosphatase for germinoma

Placental alkaline phosphatase (PLAP) in CSF can provide a very high diagnostic value in cases of intracranial germ cell tumors (GCTs), especially in pure germinomas, to the level of not requiring histological confirmation. Unlike other tumor markers, reliable data analysis with respect to the diagnostic value of PLAP serum or CSF levels has not been available until now.

In the first systematic and comprehensive study examining the diagnostic value of CSF PLAP in patients with intracranial GCTs.

From 2004 to 2014, 74 patients (average age 19.6 ± 10.6 years) with intracranial GCTs were evaluated using PLAP from their CSF and histological samples. Chemiluminescent enzyme immunoassay was utilized to measure CSF PLAP in the following tumor sites: pineal (n = 32), pituitary stalk, suprasellar (n = 16), basal ganglia (n = 15), intraventricular (n = 9), and cerebellar (n = 5) regions. In addition to classifying GCT cases, all patients underwent tumor biopsy for correlation with tumor marker data.

PLAP in combination with other tumor markers resulted in extremely high sensitivity and specificity of the diagnostic value of intracranial GCTs. Intracranial GCT cases were classified into 1) germinomas, both “pure” and syncytiotrophoblastic giant cell types (n = 38); 2) nongerminomatous GCTs, choriocarcinomas (n = 9) and teratomas (n = 4); and 3) nongerminomas, other kinds of tumors (n = 23). Consequently, all patients received chemoradiation therapy based on elevation of PLAP and the histopathological results. It was also speculated that the level of PLAP could show the amount of intracranial germ cell components of a GCT. PLAP was 100% upregulated in all intracranial germinoma cases. The absence of CSF PLAP proved that the tumor was not a germinoma.

The current study is the first systematic and comprehensive examination of the diagnostic value of the tumor marker PLAP in pediatric patients with intracranial GCT. Using the level of PLAP in CSF, we were able to detect the instances of intracranial germinoma with very high reliability, equivalent to a pathological diagnosis [1)].

A sensitive enzyme linked immunosorbent assay (ELISA) was used in a retrospective study of placental alkaline phosphatase (PLAP) levels in serum, cerebrospinal fluid (CSF), and intratumoral cyst fluid in primary intracranial germinoma. The ELISA showed no cross-reactivity with intestinal alkaline phosphatase except in very high concentrations, after samples had been heat-treated. Three patients with germinoma were studied for serum PLAP levels and in all the levels were elevated (3.78, 0.52, and 2.11 IU/liter). Two of the germinoma patients were studied for PLAP levels in the CSF, and both had elevated levels (0.83 and 9.83 IU/liter). The intratumoral cyst fluid in one case of germinoma was tested for PLAP and the level was found to be very high (603 IU/liter). These PLAP levels decreased concomitantly with the reduction in tumor size during irradiation. Serum PLAP levels were measured in 40 control adult male individuals and in the CSF of 20 nonpregnant patients with subarachnoid hemorrhage. The upper normal limits were 0.20 and 0.11 IU/liter in the serum and the CSF, respectively. All PLAP levels measured in the serum of patients with various brain tumors were 0.18 IU/liter or less. This study strongly suggests that PLAP is a clinically useful tumor marker for primary intracranial germinoma. [2)].

A chemiluminescent enzyme assay for Placental alkaline phosphatase (PLAP) was developed using an anti-human-PLAP monoclonal antibody. PLAP concentrations were determined in 37 controls, 36 germinomas, 3 nongerminomatous germ cell tumors, 21 gliomas and 12 other brain tumors.

The assay detection limit was 5 pg/ml. The median PLAP concentration in the control group was below the detection limit. Significantly higher PLAP levels were detected in all 36 germinoma patients, with values ranging from 16 to 3,700 pg/ml. The high PLAP concentrations of 17 germinoma patients decreased to below the detection limit after complete remission had been achieved with radiochemotherapy. The sensitivity and specificity of PLAP for germinomas were 94 and 97%, respectively, with a cutoff value of 30 pg/ml.

The results of this study suggest that the determination of CSF PLAP by the chemiluminescent method described here provides a clinically useful tumor marker for the diagnosis and monitoring of intracranial germinomas [3].

Case reports

2016

Yoneoka et al., present a pediatric case of neurohypophyseal germinoma with a perifocal inflammatory reaction (PIR) with volume fluctuation caused by diagnostic radiation-induced regression (DRIR). On-target biopsy failed to confirm the histology because PIR hardly contained any germinoma cells. DRIR-related fluctuation of the tumor volume disguised germinoma as inflammation. They analyzed the cerebrospinal fluid (CSF) and detected a high level of placental alkaline phosphatase (PLAP), which demonstrated the neurohypophyseal lesion to be germinoma and brought the patient from successful radiochemotherapy up to complete remission. PIR adjacent to the germinoma (PIRAG) disappeared completely following radiochemotherapy, although it contained almost no germinoma cells. Examination of the CSF-PLAP level can complement the diagnosis of germinoma and will decrease the risk of misdiagnosis. Neurosurgeons should keep in mind PIRAG, DRIR, and the diagnostic value of CSF-PLAP when germinoma is suspected [4].

1)
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