Placental alkaline phosphatase as a tumor marker for primary intracranial germinoma

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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.

KEY WORDS: brain neoplasm, placental alkaline phosphatase, tumor marker, enzyme-linked immunosorbent assay, immunohistochemistry, germinoma

In cases of primary intracranial germ-cell tumors, alpha-fetoprotein (AFP), which is specific for yolk-sac tumor, and human chorionic gonadotropin (HCG), which is specific for choriocarcinoma and syncytiotrophoblastic giant cells, are utilized in biochemical diagnostic examinations of the serum and cerebrospinal fluid (CSF) in clinical evaluation of the effect of various treatments and as a check on the recurrence of tumors.1,2,13 Until recently, germinoma, which is the most frequent type of intracranial germ-cell tumor, has not been identified as having a specific biochemical tumor marker.3-6 However, during an immunohistochemical study, placental alkaline phosphatase (PLAP) was reported as a specific tumor marker for primary intracranial germinoma.32 Studies have distinguished PLAP from common tissue alkaline phosphatases (ALP's) by its heat resistance and its inhibition by L-phenylalanine.8,23

Immunohistochemical PLAP studies have been reported for testicular seminoma, which is histopathologically identical to primary intracranial germinoma.3,9,24,27-29,31,35,38 In addition, serum PLAP levels in testicular seminoma patients were measured by enzyme-linked immunosorbent assay (ELISA), which verified that PLAP is a useful tumor marker for seminoma not only histopathologically but also biochemically.15 From a neurosurgical point of view, it seemed important to examine PLAP levels in serum, CSF, or intratumoral cyst fluid to determine the efficacy of PLAP as a tumor marker for primary intracranial germinoma.

In this study, we established a highly sensitive "sandwich ELISA" using a polyclonal antibody to PLAP for assessing PLAP which we used to measure serum, CSF, and intratumoral cyst fluid concentrations of PLAP in various brain tumor patients. The clinical courses of three germinoma patients, in whom PLAP was examined, are reported and the significance and problems of PLAP measurement are discussed.

Clinical Material and Methods

Patients with Germinoma

The clinical summary of three patients with primary intracranial germinoma is presented in Table 1. The patients were aged 12, 15, and 22 years, and included...
TABLE 1

Clinical summary of three cases of primary intracranial germinoma*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Location of Tumor</th>
<th>Pretreatment Status</th>
<th>Tumor Marker in Pretreatment State†</th>
<th>Treatment</th>
<th>Histology‡</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>PLAP (IU/liter)</td>
<td>HCG (IU/liter)</td>
<td>AFP (ng/ml)</td>
</tr>
<tr>
<td>1</td>
<td>15, M</td>
<td>suprasellar region, pineal region, bilateral thalami, 4th ventricle</td>
<td>emaciation, diabetes insipidus, disturbed ocular movement</td>
<td>3.78</td>
<td>&lt; 1.0</td>
<td>&lt; 10</td>
</tr>
<tr>
<td>2</td>
<td>12, F</td>
<td>basal ganglia</td>
<td>right hemiparesis, intellectual deterioration, slow physical movement</td>
<td>0.52</td>
<td>603</td>
<td>120,000</td>
</tr>
<tr>
<td>3</td>
<td>22, M</td>
<td>suprasellar region, ventricular walls</td>
<td>bitemporal hemianopsia, disturbed visual acuity, diabetes insipidus</td>
<td>2.11</td>
<td>9.83</td>
<td>30</td>
</tr>
</tbody>
</table>

* Abbreviations: PLAP = placental alkaline phosphatase; HCG = human chorionic gonadotropin; AFP = alpha-fetoprotein; CEA = carcinoembryonic antigen; CSF = cerebrospinal fluid.
† The normal ranges of serum levels of HCG, AFP, and CEA are < 5.0 IU/liter, < 20 ng/ml, and < 5.0 ng/ml, respectively.
‡ Immunohistochemical study findings. Staining grade (% of all tumor cells staining positive): +++ = >80%; ++ = 50%-80%; + = 20%-50%; 0% = 0%.

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two males and one female. The histopathological diagnoses in Cases 2 and 3 were defined as germinoma by hematoxylin and eosin staining and by immunohistochemical staining for PLAP. Case 1 was diagnosed by the clinical findings and course.

**Serum Testing**

Control serum specimens were obtained from: 40 normal adult men ranging in age from 20 to 34 years; 20 nonpregnant patients ranging in age from 1 to 79 years with histologically verified glioma (two cerebellar pilocytic astrocytomas, two fibrillary astrocytomas, nine anaplastic astrocytomas, and seven glioblastomas); 14 nonpregnant patients ranging in age from 36 to 74 years with histologically verified meningioma; 11 nonpregnant patients ranging in age from 42 to 76 years with histologically verified acoustic neuroma; and seven nonpregnant patients with histologically verified germ-cell tumor (the three germinomas studied in this report, one suprasellar teratoma in a 23-year-old woman, two pineal teratomas in 12- and 17-year-old boys, and one vermic metastatic chorioncarcinoma from the testes of a 23-year-old man). In the germinoma study, more than one sample was taken from each patient in order to monitor changes during the clinical course. Serum samples from 21 women at various months of gestation were prepared as positive controls. These human serum samples were obtained in a fasting state and stored at −80°C until they were assayed.

**Intratumoral Cyst Fluid Testing**

The intratumoral cyst fluid of a right thalamic germinoma with cysts (Case 2) was obtained during surgery and stored at −80°C until it was assayed.

**Hepatic and Intestinal Alkaline Phosphatase Testing**

A normal liver and small intestine were obtained at autopsy within 24 hours postmortem from a 72-year-old woman who had died of cerebral infarction without malignant or systemic disease. Nonparenchymal tissue was removed from the liver, and excess blood was washed away with phosphate-buffered saline (PBS). The luminal surface of the small intestine was washed with PBS, and the mucosal tissue was scraped off. The tissue of each specimen was homogenized in PBS and centrifuged at 5000 rpm for 1 hour. The supernatants were stored at −80°C until they were assayed.

One international unit (IU) of enzyme activity is defined as hydrolyzing 1.0 μmol of p-nitrophenolphosphate per minute, at 37°C (pH 9.8). The normal value of human serum enzyme activity for ALP is defined at the Special Reference Laboratories Co., Ltd., Tokyo, Japan, as 68 to 220 IU/liter at 37°C by kinetic rate assay with p-nitrophenolphosphate as a substrate.
Electrophoresis was performed using 1% agar gel in a tray at 4°C. Purified PLAP* and the supernatant of the homogenized small intestine and liver were tested for 75 minutes at a constant current (30 mA/plate). After the run, the gel was stained with p-toluidinium 5-bromo-4-chloro-3-indoxyl phosphate at 37°C for 1 hour. In the presence of magnesium, ALP catalyzes the hydrolysis of p-toluidinium 5-bromo-4-chloro-3-indoxyl phosphate to a corresponding indol, which is then oxidized by air to indigo blue.

**Coupling of Anti-PLAP IgG to Horseradish Peroxidase**

Rabbit anti-human PLAP immunoglobulin G (IgG)† was labeled with horseradish peroxidase (HRP) using the method first described by Nakane and Kawaoi. This procedure was conducted at the Medical and Biological Laboratories Co., Ltd., Nagoya, Japan.

**Sandwich ELISA for PLAP**

A slight modification of the ELISA technique of Millán and Stigbrand was employed in this study. Microtitration 96-well plates‡ were coated with 200 μl of rabbit anti-human PLAP antiserum (dilution 1/200) for 24 hours. After treatment with 300 μl of normal bovine albumin§ (dilution 1/40) for 30 minutes, each well was washed twice with PBS containing Tween 20 surfactant (0.5 ml/liter). Purified PLAP, serving as the standard, was diluted with PBS, and 200 μl of each dilution was dispensed into half the wells in triplicate. Each clinical sample was heat-treated at 65°C for 20 minutes; 200 ml was then dispensed into the other wells in triplicate undiluted, or diluted if the PLAP content was expected to exceed 13.9 IU/liter. Samples and standards were incubated in antibody-coated wells for 2 hours at room temperature. After being washed three times with PBS containing Tween 20 surfactant (0.5 ml/liter), 200 μl of a 1000-fold dilution of rabbit anti-human PLAP-HRP conjugate was prepared in PBS containing normal bovine albumin (0.3 gm/liter), then dispensed into each well. The plate was left for 2 hours at room temperature. Enzyme activity was determined using citrate-phosphate buffer (0.1 mol/liter, pH 5.0) containing H₂O₂ (0.1 ml/liter) and o-phenylenediamine (0.4 gm/liter). The solution was reacted for 30 minutes at room temperature in a dark place, after which the color was recorded using an automatic ELISA reader¶ with a 482-nm filter.

**Results**

**Electrophoresis**

Zymograms of purified PLAP and the supernatant of the homogenized small intestine and liver are shown in Fig. 1. The electrophoretic mobility of the ALP's was different in each of these three samples. Based on a definite site for the band of purified PLAP on ALP4, the main bands of the samples from the small intestine and liver were located on ALP5 and ALP2, respectively.

**Sensitivity of ELISA**

A standard curve was generated by the sandwich ELISA. The minimum detectable concentration in this assay was 0.11 IU/liter of PLAP (a concentration sig-

**TABLE 2**

Reproducibility of ELISA for PLAP in three different concentrations*

<table>
<thead>
<tr>
<th>Assay</th>
<th>PLAP (IU/liter)</th>
<th>CV (%)</th>
<th>Mean CV (%)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>within-assay</td>
<td>0.43</td>
<td>7.94</td>
<td>7.5 ± 2.0</td>
</tr>
<tr>
<td>(5 different plates)</td>
<td>1.74</td>
<td>5.33</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6.94</td>
<td>5.98</td>
<td></td>
</tr>
<tr>
<td>between-assay</td>
<td>0.43</td>
<td>9.63</td>
<td>7.0 ± 2.3</td>
</tr>
<tr>
<td>(5 separate days)</td>
<td>1.74</td>
<td>5.98</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6.94</td>
<td>5.40</td>
<td></td>
</tr>
</tbody>
</table>

* Abbreviations: ELISA = enzyme-linked immunosorbent assay; PLAP = placental alkaline phosphatase; CV = coefficient of variation.
† Mean ± standard deviation.

**Heat Treatment**

Heat treatment is known to inactivate all ALP iso-enzymes except PLAP. The effect of heat treatment to diminish cross-reactions between the rabbit anti-human PLAP antiserum used in this study and other ALP iso-enzymes, particularly intestinal ALP, was examined. Purified PLAP and the supernatant of the homogenized small intestine and liver were each divided into two samples. One series of these samples was used directly for ELISA and the other was heat-treated at 65°C for 20 minutes before ELISA.

**Fig. 1.** Zymograms of purified placental alkaline phosphatase (A) and the supernatant of the homogenized small intestine (B) and liver (C). The electrophoretic mobility of the alkaline phosphatases (ALP's) was different in each sample.
significantly different from 0 at the 95% confidence level). The within-assay precision was tested on different plates in the assay run by parallel measurements of five dilution curves. The mean coefficient of variation for determination of purified PLAP was 7.5% \( \pm \) 2.0% (\( \pm \) standard deviation) (Table 2). The between-assay precision was tested on five different days. The mean coefficient of variation for determination of purified PLAP was 7.0% \( \pm \) 2.3% (Table 2).

**Heat Inactivation**

The dilution curves of purified PLAP and the supernatant of the homogenized small intestine and liver, with and without heat treatment, are shown in Fig. 2. Following heat treatment, the dilution curve of purified PLAP showed no precipitation. A cross-reaction between samples from the small intestine without heat treatment and the rabbit anti-human PLAP antiserum was observed at concentrations of 90, 45, and 22.5 IU/liter in samples from the small intestine. The dilution curve of samples from the small intestine with heat treatment showed a significant precipitation in comparison with those without heat treatment, although a weak reaction was revealed at concentrations of 90 and 45 IU/liter. The dilution curves of samples from the liver with and without heat treatment showed an almost horizontal plane. The liver sample did not react in the ELISA used in this study.

**Normal PLAP Levels of Serum and CSF**

Serum samples from 35 normal adult men showed undetectable PLAP levels on testing using ELISA. The highest PLAP level in the serum was 0.20 IU/liter, and this was chosen as the upper normal limit for serum (Fig. 3). In all CSF samples from 20 SAH patients, ELISA showed PLAP concentrations of less than 0.11 IU/liter, and this value was selected as the upper normal PLAP limit for CSF (Fig. 3). The PLAP levels in serum samples from 21 patients with uncomplicated pregnancies were determined by ELISA. The samples were obtained between 5 months of gestation and term. There was an overall increase

![Graphs](image_url)
in the PLAP level with increasing time of gestation (Fig. 4).

**PLAP Levels of Intracranial Tumor Patients**

The pretherapeutic serum PLAP levels of the three germinoma patients were 3.78, 0.52, and 2.11 IU/liter in Cases 1, 2, and 3, respectively (Table 1). In all of the teratoma patients, the PLAP levels before treatment were less than 0.11 IU/liter. The PLAP level of serum from a patient with metastatic choriocarcinoma from the testis was also less than 0.11 IU/liter. In 20 patients with glioma, 14 with meningioma, and 11 with acoustic neurinoma, all serum samples showed PLAP levels of 0.18 IU/liter or less (Fig. 3).

The PLAP levels in the CSF of two germinoma patients (Cases 1 and 3, Table 1) were assayed and found to be 0.83 and 9.83 IU/liter, respectively. In three patients with teratoma and one with metastatic choriocarcinoma, the PLAP assayed levels were less than 0.11 IU/liter (Fig. 3). In one case of germinoma (Case 2, Table 1), the PLAP level of intratumoral cyst fluid obtained at surgery was 603 IU/liter.

**Case Reports**

**Case 1**

This 15-year-old boy had an 18-month history of nausea, vomiting, and continuing appetite loss. His clinical course is summarized in Table 1. Admission computerized tomography (CT) showed a contrast-enhancing mass in the pineal region, extending bilaterally to the posterior part of the thalami, the suprasellar region, and the wall of the fourth ventricle. There was a small cyst in the right thalamus. Obstructive hydrocephalus was also observed (Fig. 5). A ventriculoperitoneal shunt was placed. Although CSF cytological examination revealed no atypical cells, a clinical diagnosis of a primary intracranial germinoma was made based on the CT and clinical findings. Subsequently, because of the patient’s cachexic condition, irradiation was begun without surgical intervention. Follow-up CT scans during irradiation showed that the tumor had disappeared completely (Fig. 6). The patient’s clinical course is summarized in Fig. 7. He was irradiated with a total of 2000 rads to the whole brain and another 2000 rads to the pineal region. At discharge, he had slight diabetes insipidus.

**Case 2**

This 12-year-old girl had suffered from noticeable intellectual deterioration and psychomotor retardation for 2 years before her present admission. Her clinical course is summarized in Table 1. Admission CT showed a contrast-enhancing mass with cysts of various sizes in the left basal ganglia (Fig. 8A). A subtotal resection of...
the tumor was performed with aspiration of the cyst fluid. The histopathological diagnosis was germinoma. On immunohistochemical examination, all tumor cells showed a positive reaction for PLAP, but no tumor cells revealed HCG. The patient received radiation therapy totaling 4340 rads to the whole brain. During radiation therapy, follow-up CT scans showed that the enhanced lesion had become decidedly smaller (Fig. 8B–D). The patient’s clinical course is summarized in Fig. 9. At discharge, she had no physical disturbance except for mild motor weakness of the right extremities.

Case 3
This 22-year-old man had a 4-year history of polyuria and polydipsia and began noticing progressive visual loss over 3 months. His clinical course is summarized in Table 1. Admission CT scanning showed a contrast-enhancing mass in the suprasellar region, with bilateral enhancement along the lateral ventricular walls (Fig. 10). A tumor biopsy specimen was taken from the suprasellar region, and a histological diagnosis of germinoma was made. On immunohistochemical examination of this specimen, all tumor cells showed a positive PLAP reaction, but there was no positive reaction for either AFP or HCG. The patient underwent irradiation with a total of 5000 rads to the whole brain and another 2340 rads to the spine. Follow-up CT scans during irradiation showed the disappearance of the enhanced lesion (Fig. 11). The patient’s clinical course...
is summarized in Fig. 12. At discharge, diabetes insipidus was still present, and his visual disturbance was unchanged.

Discussion

Normally, PLAP is expressed on the plasma membrane of syncytiotrophoblasts and germinoma cells, but it has also been identified as an oncodevelopmental protein in various cancer tissues. 7-14,16,20,31,32,37 Many reports have been published regarding various assays of PLAP used in monitoring cancer patients and patients during the course of pregnancy. 5,6,11,12,17,19,21,23,34 Recently, due to the development of a sensitive technique of enzyme immunoassay, more accurate PLAP assay studies have been reported. 17,19,21 Enzyme immunoassay is highly sensitive for assaying minute quantities of various substances and eventually will replace radioimmunoassay. Enzyme immunoassay was first performed for serum PLAP by Millán and Stigbrand 19 in 1981; they reported detecting PLAP as low as 0.4 ng/ml, significantly less than by radioimmunoassay techniques using the same reagents. Soon after, reports of immunoassay for PLAP using monoclonal antibodies to PLAP were published. 6,17,23

A major difficulty in detecting PLAP with polyclonal antisera has always been the cross-reactivity of these antibodies with intestinal ALP.4 The use of a highly specific monoclonal antibody that reacts only with an epitope on PLAP and does not react with all other normal tissue ALP can obviate this inaccuracy. However, using monoclonal antibodies presents a problem. As stated by McLaughlin, et al., 17 monoclonal antibodies may not be able to recognize some infrequent allelic forms of PLAP because of a marked selective reactivity to a specific PLAP. Heat treatment of samples may be another way to prevent cross-reactivity between poly-

**FIG. 6.** Case 1. Contrast-enhanced computerized tomography scans. A: After irradiation with 1400 rads (May 30, 1985), only a small portion of the mass remains in the pineal region. B: After irradiation with 3400 rads (June 13, 1985), there is no tumor shadow.

**FIG. 7.** Diagram showing the clinical course in Case 1. Serial placental alkaline phosphatase (PLAP) levels in serum (filled circles) and in cerebrospinal fluid (CSF) (open circles) are shown. The dotted area indicates the accumulated radiation dosage. V-P shunt = ventriculoperitoneal shunt.

**FIG. 8.** Case 2. Contrast-enhanced computerized tomography scans. A: Admission scan, obtained on April 3, 1986, showing an enhanced mass with cysts of various sizes in the left basal ganglia. B: Scan obtained on May 1, after irradiation with 800 rads, showing a portion of the enhanced mass remaining in the left basal ganglia. C and D: Scans obtained on May 10, after a total of 1640 rads (C) and on May 30, after a total of 4340 rads (D). The contrast-enhanced mass has shrunk, but a small enhanced remnant remains.
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clonal anti-PLAP antibodies and intestinal ALP, based on the biochemical characteristics of ALP isoenzymes. Intestinal ALP has been known to be inactivated by heating, in contrast to the heat resistance of PLAP. Miki, et al., have reported that the ALP activity of the intestine is inactivated almost completely 20 minutes after incubation at 65°C. However, whether the activity of ALP is identical with the antigenicity of ALP or not still remains unclear.

In our study, using a polyclonal antibody for PLAP and incubating the homogenized small intestine supernatant for 20 minutes at 65°C, we have effectively been able to demonstrate decreased cross-reactions with the anti-PLAP antibody, although some cross-reactivity continues at high concentrations of ALP. High levels of serum intestinal ALP have been recorded in patients with liver cirrhosis or idiopathically increased alkaline phosphatemia and also in normal people with blood type O or B. Mössner and Pfleiderer have reported that healthy fasted individuals with blood type O or B showed intestinal ALP values ranging from 2 to 8 IU/liter, and these values increased after a fatty meal, ranging from 10 to 24 IU/liter. They further stated that blood type A donors had intestinal ALP values below 1 IU/liter and displayed an increase from 2 to 7 IU/liter after fat intake (their normal ALP serum value was

Fig. 9. Diagram showing the clinical course in Case 2. Serial placental alkaline phosphatase (PLAP) levels in serum (filled circles) and in cerebrospinal fluid (CSF) (open circle) are shown. The dotted area indicates the accumulated radiation dosage. HCG = human chorionic gonadotropin.

Fig. 10. Case 3. Computerized tomography scans on admission (July 24, 1986), unenhanced scans (upper) and contrast-enhanced scans (lower). An enhanced mass is visible in the suprasellar region and an enhanced outline is seen along the walls of the ventricular system.
40 to 190 IU/liter). On the basis of their study, our ELISA for PLAP was designed to solve the problem of cross-reactivity in low intestinal ALP levels of normal individuals, but not for those patients with liver cirrhosis or other diseases with increased intestinal ALP levels. In addition, to insure more accurate data, serum samples were drawn after patients had fasted.

Serum PLAP concentrations in patients with various neoplasms have been measured by various immunoassays. Based on enzyme immunoassays, elevated PLAP levels have been reported in 9.8% to 14.2% of all cancer patients and in 35% to 40% of patients with ovarian cancer. Among patients with testicular seminoma, elevated PLAP serum levels have been reported in 57.1% by Lange, et al., and in 83.3% by Mössner and Pfeiderer. Lange, et al., also showed that, in six of 10 serial studies, PLAP levels provided clinically useful information not otherwise available, and the levels were never inappropriately elevated. All of this evidence suggests that measuring PLAP levels is useful as a serum tumor marker for seminoma, but it has questionable value in identifying other cancers which rarely show elevated PLAP levels. Until this report, there have been no studies examining either serum PLAP levels in patients with brain tumors or PLAP levels in the CSF of patients with various neoplasms.

Some problems regarding the evaluation of the measured PLAP still remain unclear in primary intracranial germinoma cases. First, it is unknown what size of germinoma is detectable by our ELISA for PLAP in the serum and/or CSF. Further studies must be carried out delineating the minimum size of tumor that can be accurately identified using ELISA for PLAP. Earlier detection of the tumor is highly advantageous, leading to earlier treatment. Therefore, the sensitivity of ELISA for PLAP may have to be increased to detect smaller tumors. One way to obtain a small amount of PLAP may be to withdraw blood from the internal jugular vein. This may prove useful in patients with intracranial tumors.

The second question relates to the location of the tumor. In patients such as Case 2, where the tumor was located in an unusual site for a germinoma, it becomes difficult to make an accurate diagnosis of germinoma based only on the radiological findings. Measuring serum PLAP may be more beneficial in these types of cases. In cases where the tumor has almost no direct contact with the CSF, it may be impossible to verify elevated PLAP levels in the CSF. However, in
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patients such as Case 3, where the tumor has spread along the walls of the ventricular system and has broad contact with the CSF, measuring PLAP levels in the CSF may be more valuable. In fact, we verified high levels of PLAP in CSF obtained from Case 3, even though CSF cytological examination revealed no atypical cells. The third problem concerns the relationship between irradiation dosage and PLAP levels. The PLAP levels decreased concomitantly with the cumulative irradiation dosage in this study. The dosages at the time when serum PLAP levels returned to normal range were 2000 to 3400 rads in Case 1, 800 to 2540 rads in Case 2, and 1600 to 4000 rads in Case 3. These values correspond to previously reported irradiation dosage associated with the disappearance of germinomas on CT scans. Verification of a critical total irradiation dosage may be necessary, requiring further related studies of many germinoma cases.

Primary intracranial germinoma is recognized as being radiosensitive, and the present therapy of choice calls for irradiation without surgical intervention or histopathological diagnosis. However, neurosurgeons require detailed and reliable information in making an accurate diagnosis of germinoma to eliminate any unnecessary and possibly damaging treatment. This preliminary study has established that PLAP is a clinically useful tumor marker for primary intracranial germinoma and suggests that PLAP will become a clinical diagnostic tool in the future. Measuring PLAP may also be helpful in making an earlier diagnosis of germinoma, in evaluating the effects of various types of treatment, or in monitoring for tumor recurrence.

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References