FURTHER OBSERVATION ON KASAHARA ISOENZYME IN PATIENTS WITH
MALIGNANT DISEASES

Kazuya HIGASHINO, Shunjiro KUDO, Richiko OHTANI, and Yuichi YAMAMURA
Third Department of Internal Medicine, Osaka University Medical School*

The Kasahara isoenzyme of alkaline phosphatase was found in cancer tissues
from patients with gastric carcinoma, maxillary carcinoma, pulmonary carcino-
ma, and carcinoma of the urinary bladder, in addition to hepatoma. This fact
suggests that the Kasahara isoenzyme may not be a specific marker protein of
liver cancer but could occur in a variety of neoplasms.

We have reported previously that an alka-
line phosphatase (EC 3.1.3.1) which occurs
in hepatoma patients is similar in enzymic
properties to one of the alkaline phosphatases
in FL-amnion cells⁴,⁵) and we designated this
enzyme the Kasahara isoenzyme after the
name of our first patient. However, this en-
zyme seems to be the same as a variant alka-
line phosphatase found originally in hepa-
toma by Warnock and Reisman.¹³) We have
also reported that serum or tissue with the
Kasahara isoenzyme came only from patients
with hepatocellular carcinoma.⁶)

This communication presents subsequent
observations on the occurrence of the Kasa-
hara isoenzyme in serum and carcinoma tis-
sue in patients with various malignant
tumors.

Materials and Methods

Cancer tissue, liver, intestine, and other speci-
mens were obtained by autopsy and stored at
-20° until use. Alkaline phosphatase was ex-
tracted from the tissue with 1-butanol and frac-
tionated with acetone as described previously.³)
Electrophoresis of alkaline phosphatase³) was
carried out in a horizontal polyacrylamide gel
plate in Tris-HCl buffer (pH 8.9) with 0.3M
borate buffer (pH 8.0) as an electrode buffer, at
a constant current (1 mA/cm) for 3.5 hr at 4°.
The gel was stained at the site of enzyme activity
with 1-naphthyl phosphate and Fast Blue BB
salt (Sigma Chemical Co., St. Louis, U.S.A.).
Identification of the Kasahara isoenzyme was
made not only from the electrophoretic pattern,
but also from enzymic properties such as the effect
of amino acids or heat treatment on the activity
examined on the electropherogram and the effect
of neuraminidase on the electrophoretic mobility.

Results and Discussion

Serum Kasahara isoenzyme activity was
found in patients with hepatocellular carci-
noma (5 out of 47 cases tested) but not so
far in patients with metastatic liver carci-
noma (14 cases examined), hepatoblastoma (1
case), melanoma (1 case), pancreatic carci-
noma (5 cases), gall bladder carcinoma (1
case), seminoma (1 case), gastric carcinoma
(9 cases), and pulmonary carcinoma (9 cases).
The carcinoma tissue, in which this enzyme
was found, included hepatocellular carcinoma
(10 positive cases out of 28 cases), gastric carci-
noma (2 out of 7 cases), pulmonary carcino-
ma (1 out of 4 cases), maxillary carcino-
ma (1 case), and carcinoma of urinary
bladder (1 case). Although the number of
cases tested was not large, the purpose of this
communication is to present evidence that
Kasahara isoenzyme could occur in cancers
other than hepatoma. The enzyme was un-
detected in 83 specimens of normal liver, 3

* Fukushima 1-1-50, Fukushima-ku, Osaka 553 (東野一織、工藤俊次郎、大谷理智子、山村雄一).
of fetal liver (12, 16, and 24 weeks of gestation), 3 of fetal intestine (12, 16, and 24 weeks of gestation), 30 of placenta (38–40 weeks of gestation), and 32 of amnion (24 and 38–40 weeks of gestation).

In our previous studies, the prevalence of Kasahara isoenzyme in the sera of patients with hepatocellular carcinoma was about 30%, but in the present studies it has fallen to about 10%. This latter percentage is in approximate agreement with that made by Portugal et al., but is much smaller than that observed by Suzuki et al. This difference between our figure and that of Suzuki et al. might be due to the method of polyacrylamide gel electrophoresis used, since Suzuki and others used disc electrophoresis, while we used thin-layer electrophoresis. The amount of enzyme applied to a disc is usually larger than that to a thin-layer. In the present study, prevalence of the Kasahara isoenzyme in hepatoma tissue was considerably higher than that in serum, suggesting that release of the enzyme into serum from cancer tissue is not obligatory. It was previously reported that the Kasahara isoenzyme-like alkaline phosphatase occurred in gastric carcinoma with or without liver metastasis, pancreatic carcinoma, prostatic carcinoma, and even in benign diseases. These findings as well as the present observations suggest that the Kasahara isoenzyme may not necessarily be a specific marker protein of hepatoma. However, on no occasion did we find the Kasahara isoenzyme in the serum of patients with carcinoma other than hepatoma.

We have noticed that most of the cases with hepatoma having the Kasahara isoenzyme in serum showed extensive necrosis of the tumor and surrounding liver tissues, probably due to the rapid growth of the tumor. Of interest in this connection is the report of Dingjan, Postma, and Stroes who suggested, from their experience in four patients with adenocarcinoma of the stomach or pancreas with liver metastasis, that the enzyme appears in the serum only when there are extensive liver metastasis and necrosis.

Relevance of the occurrence of the Kasahara isoenzyme in serum and/or tumor to the ABO blood group was examined. It was found so far that the Kasahara isoenzyme occurred in subjects with blood types A, AB, and O, but not in type B.

Hoffmann and Dorner reported that the corticosteroid-induced alkaline phosphatase in the serum and liver of dogs was distinctly different from the normal liver enzyme and was identical with the isoenzyme in the liver of a dog with advanced stage of lymphosarcoma, which possessed properties similar to those of the Kasahara isoenzyme. Accordingly, the effect of corticosteroid on the appearance of Kasahara isoenzyme in serum was investigated in patients with various collagen diseases treated with the hormone and in three patients with Cushing disease, but no effect of corticosteroid was observed.

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REFERENCES


