ELEVATION OF THE SERUM CA125 LEVEL IN EPITHELIOID SARCOMA

*Hoshino M; **Ogose A; *Kawashima H; *Hotta T; *Kado N; *Endo N; *Umezu H; **Hatano H; **Morita T; ***Kawai A; ****Hatori M; ****Kato H; 
*****Yazawa Y; ******Nishio J; ******Iwasaki H

+*Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan
aogose@med.niigata-u.ac.jp

INTRODUCTION
Epithelioid sarcoma is a rare tumor, which was recognized to be a distinct clinicopathologic entity by Enzinger in 1970. The histogenetic origin of epithelioid sarcoma is unknown, and immunohistochemical studies have been performed by previous investigators to characterize this tumor. However, no specific marker for the diagnosis of epithelioid sarcoma has yet been established. According to a literature review, there have been two cases with elevated serum CA125 levels in epithelioid sarcoma according to a report by Kato et al. (1). Although the reason for the elevation of CA125 in epithelioid sarcoma unclear, these authors suggested that CA125 could potentially be a useful marker for diagnosing epithelioid sarcoma and monitoring its clinical course, and an immunohistochemical study demonstrated that the tumor cells in both cases expressed CA125. Kato et al. (2) conducted a subsequent study on 11 cases of epithelioid sarcoma and 10 of their 11 cases showed strong immunoreactivity for CA125 in the tumor cells. These studies clearly demonstrate the specificity and positivity of CA125 in epithelioid sarcoma, thus indicating that CA125 may be a useful marker for diagnosing epithelioid sarcoma. We herein report our experience of 10 epithelioid sarcomas and their serum CA125 levels while, in addition we also performed an in vitro study to investigate the CA125 expression in epithelioid sarcoma cells and a cultured supernatant using three epithelioid sarcoma cell lines.

METHODS
In a clinical study, the serum CA125 levels of 10 epithelioid sarcoma patients were examined at multiple time points. Three epithelioid sarcoma cell lines, ST257, SFT86-06 and NEPS were established in our laboratory and used for an in vitro examination. The concentration of CA125 in the blood serum or conditioned culture medium was measured by an Electrochemiluminescence Immunoassay (ECLA). A reverse transcriptase-polymerase chain reaction (RT-PCR) was used to compare the expression patterns of MUC16 mRNA which encodes the peptide of CA125, and an anti-CA125 Western blot was used to examine the CA125 expression in each cell lysate.

RESULTS
The clinical data of each case were summarized in Table 1. In 7 of 10 cases, the serum CA125 level was elevated and changed with the progression of the tumor growth. The average value was extremely high (950.2 U/ml) in comparison to the normal value (≤35 U/ml) and it was also high in both male and lung metastasis, and the CA125 level was higher than in females or in patients without lung metastasis, respectively. We also tried to reveal whether the CA125 is secreted by epithelioid sarcoma cells themselves like ovarian tumor cells or by the other cells as an oncologic reaction using three established epithelioid sarcoma cell lines. Each cell was seeded on a culture plate, and after 72 hours incubation, the conditioned medium was then collected and the concentration of CA125 was measured. In ST257 and SFT86-06 cells, CA125 value was 259 U/ml and 252 U/ml, respectively and 6 U/ml in NEPS cells. We next, examined the expression of the MUC16 gene encoding CA125 sequence by the RT-PCR method using MUC16 specific primer (Figure 1). As a strong expression of MUC16 mRNA was shown in ST257 and SFT86-06 cells and a weak band also was appeared in NEPS cell. In addition, we also examined the CA125 protein expression in each cell lysate by Western blot using anti-CA125 clone OC125 antibody (DakoCytomation, Kyoto, Japan) and a thick band was thus observed at around 250 kDa only in ST257 and SFT86-06 cells.

DISCUSSION
CA125 is most commonly used as a serum marker for monitoring the disease response and for estimating the prognosis in ovarian cancer. As a result of this clinical analysis, the elevation of CA125 reflected the disease progression in 7 of 10 epithelioid sarcoma patients and it was also more clearly shown in patients with lung metastasis. According to the results of in vitro experiments, it supposed that CA125 was secreted by epithelioid sarcoma cells themselves in some cases. These results suggest that epithelioid sarcoma cells may therefore produce and secrete CA125 into the blood serum and an elevation in the serum CA125 value may therefore correlate with the disease progression. We therefore conclude that measuring the serum CA125 level may thus be useful for diagnosing and monitoring the clinical response to treatment in patients with epithelioid sarcoma.

<table>
<thead>
<tr>
<th>Case</th>
<th>Serum CA125</th>
<th>Tissue</th>
<th>Case</th>
<th>Serum CA125</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>16</td>
<td>M</td>
<td>2</td>
<td>40</td>
</tr>
<tr>
<td>3</td>
<td>21</td>
<td>M</td>
<td>4</td>
<td>29</td>
</tr>
<tr>
<td>5</td>
<td>25</td>
<td>M</td>
<td>6</td>
<td>26</td>
</tr>
<tr>
<td>7</td>
<td>30</td>
<td>M</td>
<td>8</td>
<td>46</td>
</tr>
<tr>
<td>9</td>
<td>38</td>
<td>F</td>
<td>10</td>
<td>29</td>
</tr>
</tbody>
</table>

Table 1: Clinical data of 10 epithelioid sarcoma patients.

The median age was 30 y.o. and size of the tumor varied in each case. The average of serum CA125 value was 950.2 U/ml (normal ≤35 U/ml).

Figure 1: MUC16 mRNA expression in epithelioid sarcoma cell lines. CA125 peptide encoding MUC16 gene was highly expressed in ST257 and SFT86-06 cells, while a relatively low expression was seen in NEPS cell.

REFERENCES

**Niigata Cancer Center Hospital, Niigata, Japan; **National Cancer Center Hospital, Tokyo, Japan; ****Tohoku University, Miyagi, Japan; *****Tochigi Cancer Center, Tochigi, Japan; ******Fukuoka University Hospital, Fukuoka, Japan