Epithelioid Sarcomas with Elevated Serum CA125: Report of Two Cases

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Epithelioid sarcoma (ES) is a musculoskeletal malignant tumor with epithelioid appearance. It is a relatively rare soft tissue neoplasm, the histological diagnosis of which is difficult and the histogenesis is still obscure. Like many other musculoskeletal tumors, according to the literature, ES has no useful tumor marker to be monitored in the serum. We experienced two ES patients with elevated serum CA125 level. One patient was a 29-year-old woman with ES in her pubic area and the other a 26-year-old man with a tumor in his right calf. Laboratory examination revealed that the CA125 values of both patients were high and changed in accordance with the progress of the tumor growth. An immunohistochemical study demonstrated that the tumor cells in both cases expressed CA125. These results suggest that CA125 can be used as a useful tumor marker for diagnosing and monitoring tumor progress.

Key words: epithelioid sarcoma – CA125 – immunohistochemistry – tumor marker

INTRODUCTION

There have been a few reports linking raised serum CA125 level with sarcomas and other musculoskeletal tumors (1–6). An extensive literature survey revealed that there have been no reports of CA125 in relation to epithelioid sarcoma (ES). We report two cases of ES with high serum levels of CA125.

CASE REPORTS

CASE 1

A 29-year-old woman was admitted to our hospital with a subcutaneous tumor in the medial aspect of the left thigh in January 1996. She had no history of trauma or other illness. Her family history was unremarkable. On admission, the patient had a tumor measuring 2 × 4 cm in diameter in the left thigh near the pubic region. There was no pain or tenderness. Blood analyses revealed the data to be within normal limits except for a marked elevation of CA125. The serum CA125 level was 840 U/ml (normal: <35 U/ml). Magnetic resonance (MR) imaging revealed a lesion in the subcutaneous region in her left proximal medial thigh.

Microscopic examination of the biopsy specimen revealed a nodular growth pattern with central necrosis, composed of compact sheets of round to oval cells (Fig. 1). In parts, aggregates of rhabdoid cells were observed. Histological diagnosis was epithelioid sarcoma. Immunohistochemical study showed that the tumor cells were reactive with CA125 antibody. CA125 was diffusely positive in the cell membranes (Fig. 2). Tumor cells also expressed vimentin, cytokeratin, epithelial membrane antigen (EMA) and carcinoembryonic antigen (CEA). The tumor was widely excised in February 1996. Subsequently, four courses of chemotherapy of ifosfamide were administered. However, 3 years after operation, the tumor recurred in the pelvic cavity extending towards the medial side of her left thigh in March 1999. The serum CA125 level was elevated at 526 U/ml. In June, the recurrent tumor was excised and postoperative irradiation was performed. Combination chemotherapy with cisplatin and adriamycin was performed. The serum CA125 level decreased to 150.0 U/ml in September and 43.2U/ml in November 1999. However, since April 2000, the serum CA125 increased to 83.1 U/ml in April, 102.7 U/ml in May, 138.9 U/ml in June and 1808.0 U/ml in August. Computed tomography (CT) revealed local recurrence of ES in the peritoneum and the serum CA125 level was 7609.0 U/ml in September 2000. The tumor grew rapidly, causing ascites. On
December 1, 2000, the serum CA125 level was 14,020.0 U/ml. The patient died because of disease progression (Fig. 3).

CASE 2

The patient was a 26-year-old man. In November 1991 he noticed a thumb-sized mass in his right calf. In May 1992, an ulcer and pus appeared at the same site. The ulcer disappeared but later recurred. MRI demonstrated a mass in the ulcer with low signal intensities on T1 weighted images and high signal intensities on T2 weighted images. Histological examination of the biopsy specimens confirmed ES in April 1994.

The tumor cells showed epithelioid features, arranged in nodules with central necrosis. The tumor was composed of large, round to polygonal, partially plump spindle-shaped cells with deeply eosinophilic cytoplasm, showing focally rhabdoid features (Fig. 4). Immunohistochemically, the tumor cells were reactive with CA125 antibody (Fig. 5). The tumor cells expressed vimentin, cytokeratin and EMA. CEA was absent. In July, right thigh amputation was performed after chemother-

Figure 1. Microphotographs of the biopsy specimen showing compact sheets of round to oval cells in nodular growth pattern with central necrosis (×4).

Figure 2. Microphotograph showing that the tumor cells were reactive with CA125 antibody. CA125 were diffusely positive in the cell membranes.

Figure 3. Clinical course of case 1 and change of CA125 value.
apy. In December 2000, MRI revealed recurrence in the right femoral neck and ilium. CT demonstrated lung metastasis. In March 2001, the serum CA125 value was 1693.0 U/ml. In April 2001, ifosfamide and adriamycin were administered. Temporarily, the CA125 level declined to 1353.0 U/ml. In June 2001, 2 months after chemotherapy, the value increased to 1630.0 U/ml. Lymphokine activated killer (LAK) therapy was performed. The CA125 values were 1302.0 U/ml on July 24, 1426.0 U/ml on August 6 and 1480.0 U/ml on September 21. The patient died in November 2001 (Fig. 6).

**DISCUSSION**

Epithelioid sarcoma is a relatively rare type of sarcoma, first described by Enzinger in 1970 (7). This neoplasm is a unique soft tissue sarcoma which typically pursues an indolent, relent-
less clinical course with numerous recurrences and frequently culminates in regional lymph nodes or pulmonary areas. Chase and Enzinger reported a retrospective review of 241 cases of epithelioid sarcoma and reaffirmed the propensity of this tumor to occur in the distal extremities of young adults. The tumor was generally firm and non-tender and involved the dermis, subcutis or deeper soft tissues, particularly fascial planes, aponeuroses and tendon sheaths (8). This tumor typically contains nodular aggregates of epithelioid and spindle cells with zonal necrosis (7). ES is often misinterpreted pathologically as non-neoplastic granuloma (rheumatoid nodule, necrobiosis lipoidica) and often may be confused with other malignancies, especially squamous cell carcinoma and synovial sarcoma (7,8). Therefore, exact histological diagnosis is mandatory.

Many kinds of immunohistochemical studies have been performed by previous investigators in order to characterize this tumor. Most ES stain for cytokeratins, epithelial membrane antigen and vimentin (7–11) and about 60% of epithelioid sarcoma stain for CD34 (12). These immunohistochemical patterns were the same as for other sarcomas with an epithelioid appearance.

CA125 is a high molecular mass glycoprotein (13,14). It is a differentiation antigen associated with coelomic epithelium and its normal and neoplastic derivatives. CA125 has been reported to be immunoreactive with various normal tissues such as esophageal epithelium, pancreatic exocrine glands, hepatocytes, etc. (15). CA125 was found to be a serum antigen used as a marker for epithelial ovarian carcinoma. Radioimmunoassay for serum CA125 demonstrated elevated levels of antigen in cases of ovarian carcinoma. Rising or falling levels of CA125 correlated with progression or regression of disease, hence its widespread use as a serum tumor marker (16).

An elevated serum CA125 level has been found in patients with stage III, IV endometriosis (17), pancreatic carcinoma, liver carcinoma, carcinoma of the biliary tree and liver carcinoma (18). These pathologies are of epithelial origin. Patients with disseminated carcinomas had significantly higher levels than patients with localized carcinomas. The nature of the antigen detected by the CA125 antibody remains under investigation.

Normal smooth and striated muscle cells and chondrocytes gave positive reactions with CA125. Therefore, the immunoreactivity of a tumor with CA125 does not necessarily indicate its epithelial and ovarian origin (5).

There have been a few reports of elevation of CA125 levels in mesenchymal tumors (1,3,4,6). Whiteley and Marshall reported a case of leiomyoma with elevated serum CA125 level (1). Chiarle et al. (3) and Holcomb et al. (6) reported alveolar rhabdomyosarcoma with raised serum CA125. Ordonez and Sahin reported a case of desmoplastic small round cell tumor (DRCT) with raised serum CA125 (4). Zetter et al. reported that immunohistochemical staining showed reactivity for CA125 within the four of 15 sarcomas (5). An extensive literature survey revealed there have been no reports of CA125 with respect to ES. No serum tumor markers have been available for ES. It is noteworthy that elevation of CA125 was observed in the present two cases of ES and that the values corresponded well with the progress of this disease and that immunohistochemically ES tumor cells expressed CA125. These results strongly suggest that CA125 could be a useful tumor marker for diagnosing ES and monitoring its clinical course.

References