CASE REPORT

Adrenal Ewing’s Sarcoma in an Elderly Man

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Abstract:
Ewing’s sarcoma usually arises in the bones of children and adolescents. We herein report a 74-year-old man with Ewing’s sarcoma in the adrenal gland. The diagnosis was confirmed by a genetic test, pathological studies, and several imaging studies. He already had multiple liver metastases when he was transferred to our hospital and died on the 37th day. The diagnosis was further confirmed by autopsy studies. Adrenal Ewing’s sarcoma is very rare, and our patient was older than other reported cases. Ewing’s sarcoma should be considered even in elderly patients with adrenal tumors.

Key words: adrenal gland, Ewing’s sarcoma, elderly

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Introduction
Adrenal incidentalomas are defined as adrenal tumors identified by imaging studies without clinical suspicion of adrenal diseases. Adrenal incidentalomas have been detected in approximately 4% of patients that underwent high-resolution imaging studies (1). A critical point in dealing with adrenal incidentaloma is determining whether or not the tumor is malignant. It is recommended that malignancy be considered when the tumor is larger than 4 cm (1, 2).

Ewing’s sarcoma is the second-most common bone tumor in children and adolescents and affects 250-400 patients in the United States each year. The peak age of onset is 15 years, and 80% of cases are diagnosed before 18 years of age. Chemotherapy has greatly improved the survival rate for patients with localized tumors in recent years, but the prognosis remains poor in those with metastasis or recurrent tumors (3, 4).

We herein report our findings in treating a 74-year-old man with Ewing’s sarcoma in the adrenal gland. The diagnosis was confirmed by a genetic test, pathological studies including autopsy, and several imaging studies. To our knowledge, our patient is the oldest case of adrenal Ewing’s sarcoma.

Case Report
A 74-year-old man visited another hospital because of abdominal pain on his right side in July 2013. Computed tomography (CT) demonstrated a tumor on his right adrenal gland (Fig. 1A). The tumor was 6.7 cm in size and appeared heterogeneous, which is not consistent with benign adrenal incidentaloma. 18F-fluorodeoxyglucose-positron emission tomography (FDG-PET) revealed the enhanced uptake of the tracer in the tumor, suggesting that the tumor was malignant (Fig. 1B). The maximum standardized uptake value (SUVmax) was 7.6. No significant uptake was observed in other organs, suggesting that the adrenal tumor was not a metastatic lesion of malignant tumors in other organs. The tumor appeared to be hypointense on T1-weighed magnetic resonance imaging (MRI) (Fig. 1C). The T2-weighed image confirmed that the internal signal was heterogeneous (Fig. 1D). Metaiodobenzylguanidine (MIBG) scintigraphy findings were negative (Fig. 1E). In September, the patient underwent open surgery, but the pathological diagnosis was...
obscure. In November, he suffered from a slight fever and general fatigue. FDG-PET/CT studies in December revealed multiple recurrence of the malignant tumor in the liver (Fig. 1F). The patient was transferred to our hospital in January 2014.

His Eastern Cooperative Oncology Group (ECOG) performance status was 1 on admission. He did not present any abnormal findings on a physical examination, except for a slight fever. His blood pressure was well-controlled by can-desartan. He did not have any symptoms of Cushing’s syndrome or phaeochromocytoma. Blood tests demonstrated anemia, elevated levels of liver enzymes, C-reactive protein (CRP), neuro-specific enolase (NSE), and pro-gastrin-releasing peptide (ProGRP) (Table). His urinary free cortisol level was not elevated, although the levels of corticotropic and cortisol in the plasma were slightly high, probably due to stress. His aldosterone and catecholamine levels were within normal limits.

Table. Laboratory Findings on Admission.

| Hematology          | Blood Chemistry          | Hormones                        |
|---------------------|--------------------------|--------------------------------|
| Hematocrit 25.6 %   | Total protein 6.2 g/dL   | Corticotropin 73.9 pg/mL        |
| Hemoglobin 8.6 g/dL | Albumin 3.0 g/dL         | Cortisol 24.9 μg/dL             |
| Red blood cell 295 ×10⁹/μL | Aspartate aminotransferase 37 IU/L | DHEA-S 1,475 ng/mL            |
| Platelet 20.8 ×10⁹/μL | Alanine aminotransferase 30 IU/L | Urinary free cortisol 19.3 μg/dL |
| White blood cell 6,000 /μL | Lactate dehydrogenase 471 IU/L | Plasma renin activity 0.4 ng/mL/h |
| Neutrophil 66.5 %   | Alkaline phosphatase 493 IU/L | Aldosterone 58.2 pg/mL          |
| Eosinophil 2.3 %    | γ-glutamyl transpeptidase 121 IU/L | Adrenaline 0.02 ng/mL           |
| Basophil 0.5 %      | Blood urea nitrogen 15 mg/dL | Noradrenaline 0.50 ng/mL        |
| Monocyte 0.6 %      | Creatinine 0.66 mg/dL    |                                |
| Lymphocyte 20.7 %   | Sodium 131 mEq/L         | Tumor markers                   |
| Coagulation 380 mg/dL | Potassium 4.7 mEq/L     | Neuro-specific enolase 135.0 ng/mL |
| Prothrombin time 86 % | Chloride 98 mEq/L      | ProGRP 1,120.0 pg/mL           |
| APTT 34.1 sec       | Glucose 115 mg/dL        |                                |
| FDP 22.7 μg/mL      | Hemoglobin A1c 7.6 %    |                                |
| D-dimer 8.7 μg/mL   | Total cholesterol 120 mg/dL |                                |
|                     | C-reactive protein 7.34 mg/dL |                                |

APTTr: activated partial thromboplastin time, FDP: fibrin/ fibrinogen degradation product, DHEA-S: dehydroepiandrosterone sulfate, ProGRP: pro-gastrin-releasing peptide
We obtained the removed tumor tissue from his former hospital, and the specimen was subjected to pathological studies. The tumor was surrounded by normal adrenal tissue, suggesting that the tumor arose in the adrenal gland. Tumor cells with round nuclei and pale cytoplasm, as well as the formation of rosette structures, led us to suspect Ewing’s sarcoma (Fig. 2A). Immunohistochemistry revealed that the tumor cells were positive for CD99 (×20 magnification). C: Immunohistochemistry revealed that the tumor cells were positive for Nkx2.2 (×20 magnification). D: Separation of the red signal and green signal (arrows) by fluorescence in situ hybridization reveals Ewing’s sarcoma breakpoint region 1 gene rearrangement of the tumor cells, while the yellow signal (arrowhead) shows the normal allele.

Discussion

Ewing’s sarcoma predominantly arises in the bones of children and adolescents; 80% of cases are diagnosed before the age of 18 (4). Clinical manifestations include pain, a fever, and bone fracture. Anemia and an elevated level of CRP are frequently observed, which is consistent with the laboratory findings in our patient. Treatment strategies include surgery, radiation, and chemotherapy. One commonly used protocol for chemotherapy consists of vincristine, doxorubicin, cyclophosphamide plus ifosfamide, and etoposide (VDC-IE) (7). Recent progress in chemotherapy has greatly improved the survival rate of patients with localized tumors, but the prognosis remains poor in those with metastasis or recurrent tumors (3, 4).

Ewing’s sarcoma is regarded as a bone tumor in general, but the cell of origin remains elusive. One proposed hy-
Ewing’s sarcoma arises at extraskeletal sites in 20-30% of the patients (3, 15, 16). The frequent primary sites include the trunk, extremities, head and neck, and retroperitoneum (17). The oldest reported case was 85 years old for skeletal Ewing’s sarcoma and 77 years old for extraskeletal sarcoma (18, 19). In general, Ewing’s sarcoma with extraskeletal origin is more frequent in elderly patients, and both elderly and extraskeletal cases are associated with a poor prognosis (15, 20, 21). However, some recent reports have shown that the prognoses of these cases were not severe (22, 23). It is speculated that recent advances in chemotherapy have gradually improved the prognoses in these cases. Only 13 cases of Ewing’s sarcoma with adrenal origin had been reported, according to a literature review published in 2013 (24). The mean age of patients was 22.8 years, and the oldest patient was 57 years old. Recently, additional reports regarding adrenal Ewing’s sarcoma have been published (25-31), and the oldest case among those was 63 years old. Therefore, to our knowledge, the present 74-year-old patient is the oldest reported patient with adrenal Ewing’s sarcoma. This case suggests that we need to consider Ewing’s sarcoma when encountering adrenal tumors, even if the patient is an elderly person. Although the prognosis of adrenal Ewing’s sarcoma is poor, the early diagnosis by CD99 staining and analyses for EWSR1 gene arrangement can result in a better outcome.

The authors state that they have no Conflict of Interest (COI).

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Figure 3. Autopsy studies. A: The right lobe of the liver had been mostly replaced by tumor tissue (yellow circle). B: The liver tumors contained CD99-positive cells (×20 magnification).
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