Malignant peripheral nerve sheath tumors (MPNSTs) of the bilateral adrenal glands: are they metachronous primary tumors—A case report

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Key Words: MPNST; Adrenal gland

Most malignant peripheral nerve sheath tumors (MPNSTs) arise in association with major nerve trunks. Their most common anatomic sites are the proximal portions of the upper and lower extremities and the trunk. MPNSTs have rarely been reported to occur in the adrenal gland and all of the reported cases were associated with neurofibromatosis, pheochromocytoma or ganglioneuroma.1-4 We present here a case of MPNST occurring in the bilateral adrenal glands and the patient had no history of neurofibromatosis or combined tumor.

CASE REPORT

A 31-year-old woman was admitted to our hospital because of a sudden onset of severe epigastric pain. The pain was stinging and continuous and it radiated to back. Her past medical history and family history did not suggest any remarkable disease including neurofibromatosis. The physical examination didn’t reveal any pigmented skin lesion, and there was no palpable mass or nodule found in the cervical area. However, tenderness and mild rebound tenderness was noted in the epigastric area. The initial laboratory studies were nearly normal, but the hemoglobin level decreased from 12.8 g/dL on the first hospital day to 7.9 g/dL on the fourth hospital day. A chest x-ray revealed no specific abnormality. CT showed a 4 cm-sized lobulated, slightly enhancing mass in the left adrenal gland without any evidence of metastasis (Fig. 1A). There was a fluid collection in the rectovaginal pouch, and this was suggestive of hemoperitoneum. No abnormal findings were observed in the other organs, including the pancreas. A mass was noted in the left adrenal gland when performing laparotomy. There was about 300 mL of collected blood in the intraabdominal cavity. There was no evidence of metastatic disease. Left adrenalectomy was done. The resected left adrenal gland measured 6×4.8×2.2 cm and it weighed 31 g. It revealed a 5 cm-sized ruptured tumor that showed a gray pink color and a soft consistency. Extensive hemorrhage was noted around the rupture site (Fig. 2). Twelve blocks were made from the tumor. Microscopically, the tumor cells ranged from spindle to ovoid in shape. They were arranged in sweeping fascicles (Fig. 3A). Mitotic figures were frequently found.
(more than 20 per 10 high power fields). On immunohistochemical staining, the tumor cells were positive for S-100 protein and vimentin (Fig. 3B). No immunoreactivity for c-kit, CD34, cytokeratin, actin, desmin, chromogranin, synaptophysin, and HMB 45 was identified. The ultrastructural findings showed spindle cells with long cytoplasmic processes (Fig. 4A). The cells were focally surrounded by a basal lamina and they were joined by primitive junctional complexes (Fig. 4B). After discharge, the patient did not visit the hospital for follow-up. Three years later, she was admitted to the hospital again because of a similar sudden onset of severe epigastric pain. CT also showed a similar mass in the right adrenal gland (Fig. 1B). The resected right adrenal gland measured $8 \times 6 \times 4$ cm and it weighed 45 g. It revealed a 4 cm-sized ruptured tumor. It was similar to the previous left adrenal tumor for the gross, microscopic and immunohistochemical findings (Fig. 3C, D). The patient is taking prednisolone to prevent adrenal insufficiency and she is undergoing postoperative chemotherapy with vinblastine, ifosfamide, and cisplatin. The postoperative laboratory test didn’t reveal any abnormal

Fig. 1. CT shows a lobulated mass in the left adrenal gland (A). Three years later, similar mass is found in the right adrenal gland (B).

Fig. 2. Sectioned surface of the left adrenal gland shows an ill defined gray pink tumor. Rupture with extensive hemorrhage is noted.

Fig. 3. Left adrenal tumor consists of dense fascicles of spindle cells (A). Immunohistochemically, the tumor cells are of focally positive for S-100 protein (B). Right adrenal tumor shows similar histological and immunohistochemical findings (C, D).
findings. The T3 level was 123.66 ng/dL and the cortisol level was 0.62 μg/dL. Other laboratory studies for detecting endocrine diseases were not done.

**DISCUSSION**

We describe here a woman with unusual bilateral adrenal tumors that consisted of dense fascicles of spindled cells. The immunohistochemical and electron microscopic findings showed the features of neural differentiation. We interpreted these tumors to be MPNSTs that arose from the bilateral adrenal glands. MPNST arising from the adrenal gland is extremely rare with only four such cases having been reported in the English literature.\(^1\)\(^-\)\(^4\) All the reported cases were so-called composite MPNSTs, that is, MPNSTs with other neural crest-derived cell constituents such as pheochromocytoma and ganglioneuroma. MPNSTs commonly occur in the setting of von Recklinghausen’s disease. One of the reported cases with pheochromocytoma-MPNST had a history of von Recklinghausen’s disease.\(^1\) In our case, no combined adrenal tumor was present and there was no family history of von Recklinghausen’s disease. We cannot find a previous report of bilateral adrenal MPNSTs without a combined adrenal tumor or a family history of von Recklinghausen’s disease (Table 1). The histogenesis of various kinds of neuronal tumors is based on the concept of neurocristopathy, as described by Bolande,\(^5\) which is characterized as the results of divergent differentiation of neural crest cells. In the embryonal stage, neural crest-derived cells migrate and differentiate into melanocytes, the adrenal medulla, root ganglia, Schwann cells, and so on. Migration disturbance, developmental arrest or maldevelopment of neural crest-derived cells may result in various types of neoplasms. In support of this concept, bizarre clinical syndromes of multiple neuroendocrine adenomatosis or composite tumors of the sympathetic ganglia and adrenal medulla have been reported. Although we cannot conclude whether this is a case of bilateral primary tumors that has adrenalotropism or a primary tumor that has metastasized from one adrenal gland to the other one, we think that the case represents extremely rare, metachronous primary bilateral adrenal MPNSTs that originated from neural crest derivatives at the same level of the somites for the following reasons: 1) the bilateral adrenal tumors were localized; they had neither extension beyond the midline nor distant metastasis; 2) the right adrenal tumor appeared 3 years after the left adrenalectomy; most of the previous reports of the adrenal MPNSTs showed metastasis within several months (Table 1). We think that MPNSTs in the bilateral adrenal glands without a composite tumor, like our case, are within the spectrum of neurocristopathy.

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