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NOTE

Pathology

Malignant peripheral nerve sheath tumor originating from the adrenal gland in a dog

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ABSTRACT. A large abdominal mass was found in a dog. Histopathologically, the surface of the mass was covered with compressed adrenal gland tissue. The neoplastic cells showed typical features of malignant peripheral nerve sheath tumor (MPNST), including Antoni type A and type B pattern, and nuclear palisading. Immunohistochemically, these cells were positive for S100 protein, nerve growth factor receptor, nestin and claudin-1. The dog was euthanized because of the developing multiple metastatic lesions. The metastatic cells showed quite similar histopathological and immunohistochemical features as those in the original tumor. Although MPNST can develop at many body sites, this is the first report of MPNST originating from the adrenal gland in a dog.

KEY WORDS: adrenal gland, dog, malignant peripheral nerve sheath tumor

Malignant peripheral nerve sheath tumor (MPNST) is rare and has a poor prognosis under the site of occurrence [6, 15]. Metastasis occurs with high percentage in human [2], however, this is rare in dogs. It is widely accepted that MPNST arises from the connective tissue surrounding peripheral nerves, including Schwann cells, perineural cells, and internal intraneural fibroblasts. Although MPNST can develop at many body sites, almost of all MPNST are observed in the brachial or lumbar plexus, nerve roots, and peripheral nerves in dogs [1, 13, 15]. Since MPNST is fundamentally classified as a soft tissue sarcoma with marked morphological variations, it is difficult to differentiate MPNST from neurofibroma and other sarcomas [4, 5]. Immunohistochemically, expression pattern of nerve growth factor receptor (NGFR) and α-smooth muscle actin (α-SMA) were reported to be useful cell markers for differential diagnosis of MPNST [1]. To our knowledge, this is the first report of MPNST originating from the adrenal gland in a dog.

A 7-year-old, 10.7 kg, intact male beagle was referred with refractory vomiting and anorexia. On computed tomography (CT), a large abdominal mass (73 × 66 × 96 mm) was found in the anteriomedial area of the right kidney, indicating the right adrenal gland (Fig. 1a and 1b). No metastatic lesions were detected on CT image. Two weeks after the admission, the mass was surgically resected as a unit of the right adrenal gland, showing a large, firm, and well circumscribed round mass. Tissue samples were fixed in 10% neutral buffered formalin, processed routinely, and embedded in paraffin wax. Sections cut at 4 μm thick were stained with hematoxylin and eosin (HE), and were used for immunohistochemistry. Immunohistochemical staining was performed for evaluation of MPNST markers, including S100 protein (S100), NGFR, nestin, claudin-1, cytokeratin, and α-SMA [1, 3–5, 7, 10]. Antigen retrieval was performed for S100, claudin-1, and cytokeratin by autoclaving sections in citrate buffer (pH 6.0) at 121°C for 10 min. The primary antibodies were replaced with Tris-buffered saline (TBS) to produce a negative control. The endogenous peroxidase activity in the sections were inactivated with 3% hydrogen peroxide in methanol at room temperature (RT) for 5 min. To block nonspecific reactions, the sections were incubated with 8% skimmed milk in TBS at 37°C for 30 min. The sections were then incubated at 4°C for overnight with each primary antibody: rabbit polyclonal anti-S100 (1:4,000, DAKO Japan, Tokyo, Japan), mouse monoclonal anti-NGFR (ME20.4) (4 μg/ml, Abcam, Cambridge, U.K.), rabbit polyclonal anti-nestin (1:60, IBI Scientific, Dubuque, IA, U.S.A.), rabbit polyclonal anti-claudin-1 (1:200, Abcam), mouse monoclonal anti-cytokeratin (AE1/AE3) (1:50, DAKO Japan), and mouse monoclonal anti-α-SMA (1A4) (1:100, DAKO Japan). After 3 washes with TBS, the sections were treated with Dako EnVision+ System-horse radish peroxidase (HRP)-labeled polymer anti-mouse or anti-rabbit secondary antibodies (DAKO Japan) at 37°C for 40 min. The chromogen consisted of 0.05% 3-3′-diaminobenzidine and 0.03% hydrogen peroxide in Tris-HCl buffer. The sections were counterstained with Mayer's hematoxylin.

Histopathologically, the surface of the mass was covered with compressed adrenal cortex and medulla. The neoplastic cells showed a continuity to the adrenal medulla. These cells ranged from spindle to fusiform in shape, and arranged in dense to sparse

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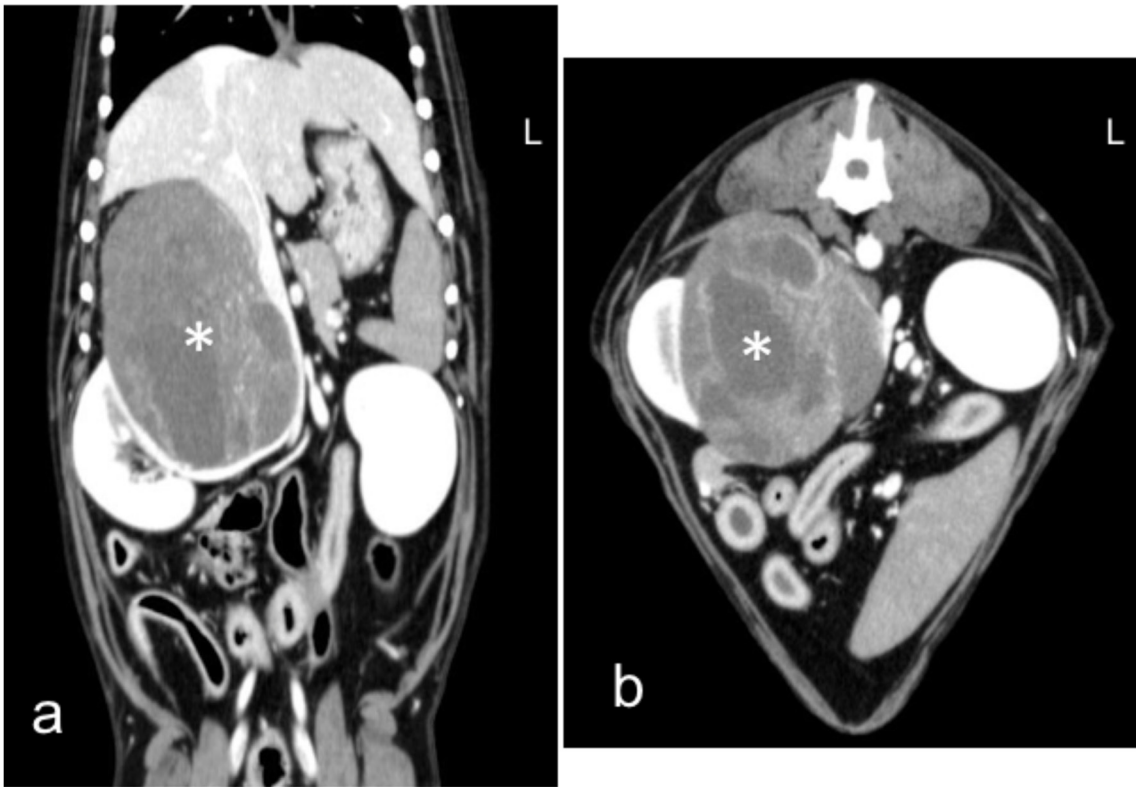

Fig. 1. Reconstructed image of dorsal plane (a) and transverse image of abdominal plane (b) of computed tomography (CT) in the case. A large enhanced abdominal mass (*) is found in the anteriomedial area of the right kidney, indicating the right adrenal gland.

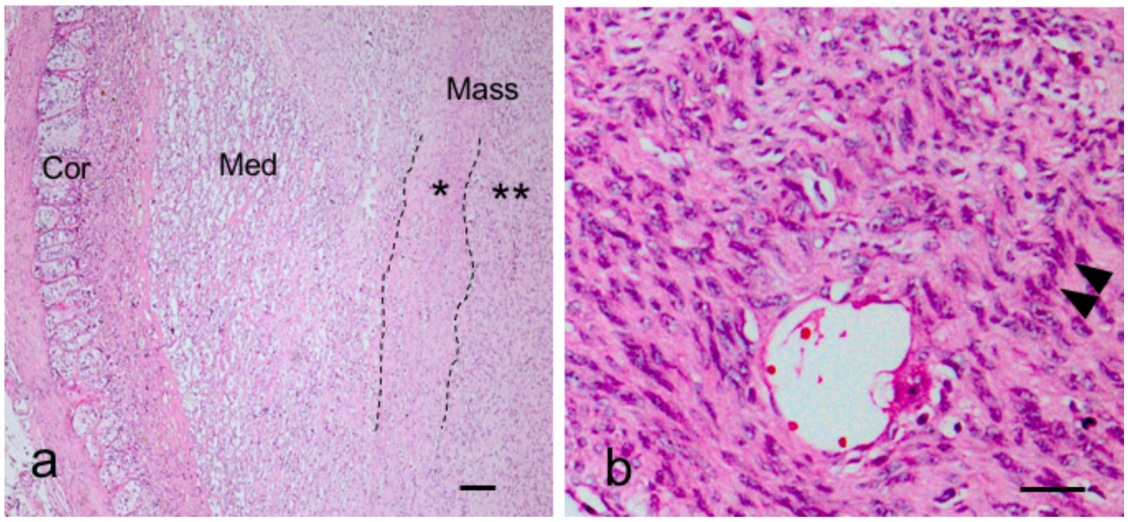

Fig. 2. Histological sections of the mass in the adrenal gland. The surface of the mass is covered with compressed adrenal cortex (Cor) and medulla (Med). The neoplastic cells range from spindle to fusiform in shape, showing a continuity to the adrenal medulla, and are arranged in dense to sparse interwoven bundles with collagenous stroma. Areas of densely packed neoplastic cells (*) (area between dash lines) and loosely packed spindle cells (**) are observed, corresponding to Antoni type A and Antoni type B pattern, respectively (Fig. 2a). HE. Bar=400 μm. Nuclear palisading (arrowheads) around vessels or collagen are occasionally observed (Fig. 2b). HE. Bar=100 μm.

interwoven bundles with collagenous stroma. Two area of densely packed neoplastic cells corresponding to the Antoni type A pattern and loosely packed spindle cells corresponding to the Antoni type B pattern were observed (Fig. 2a). Nuclear palisading around vessels or collagen was occasionally observed (Fig. 2b). Immunohistochemically, the neoplastic cells were positive for

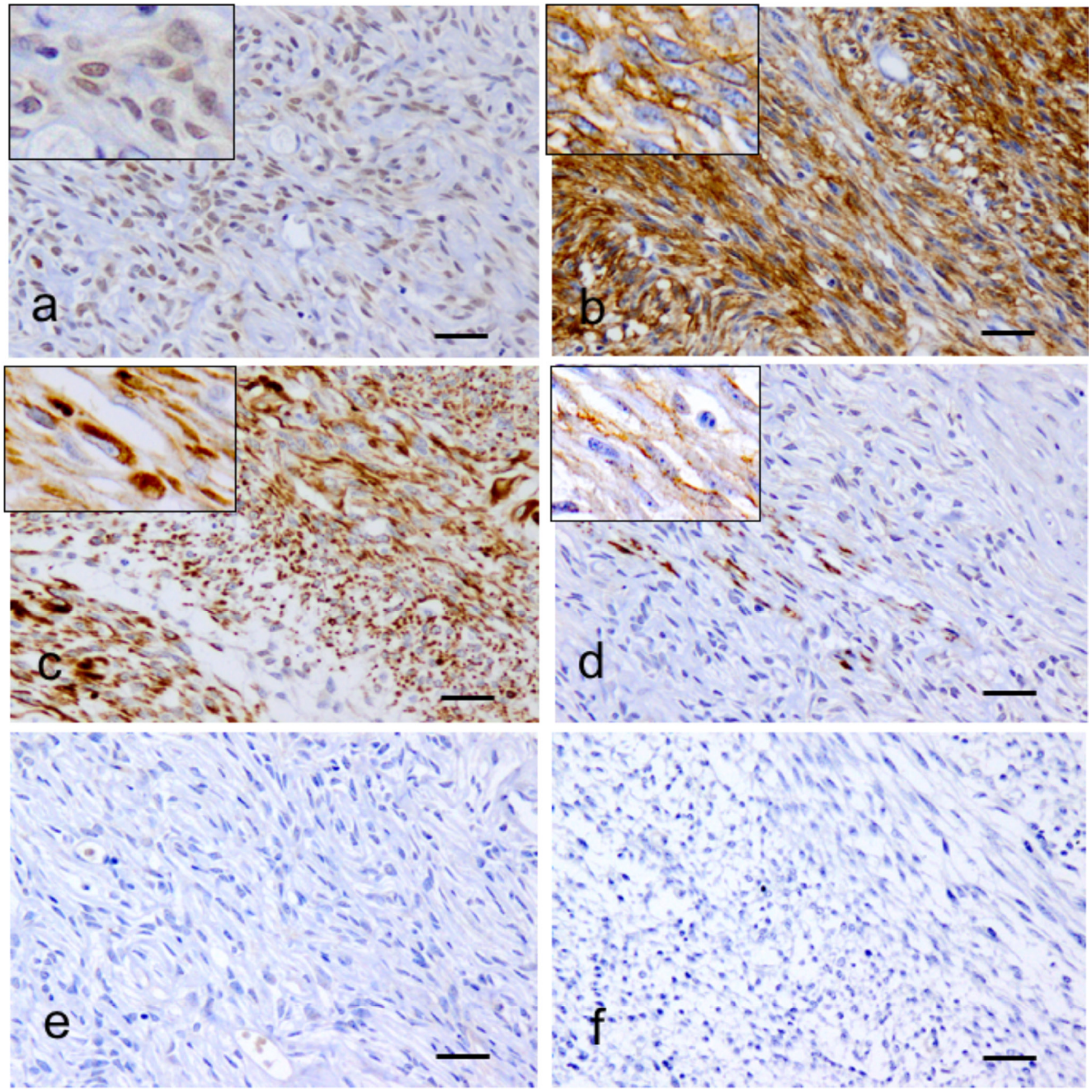

Fig. 3. Immunohistochemical staining of the neoplastic cells in the tumor. Positive reaction against to S-100 (a), NGFR (b), nestin (c) and Claudin-1 (d), and negative reaction against to cytokeratin (e) and α-SMA (f) are observed. IHC. Bar=100 μm.

S100, NGFR, nestin, and claudin-1, and negative for cytokeratin and α-SMA (Fig. 3a–f, respectively). Based on histopathological features and expression pattern of the marker proteins, especially positive reaction for nestin [11], the mass was diagnosed as MPNST arising from the right adrenal medulla.

The dog was in good health for approximate 5 months after the surgery. However, the dog showed anorexia again with hydronephrosis of the right kidney caused by ureteral obstruction on the abdominal ultrasonography (data not shown). A surgical resection was performed again to remove the ureteral tumor and the right kidney. Two months later, the owner decided on euthanasia because of the developing multiple metastatic lesions. At necropsy, white patchy lesions of approximate 10 mm in diameter were observed in the liver, lung, small intestine, and left kidney. The metastatic lesion in the liver showed quite similar histopathological features, especially 2 area of Antoni type A and type B, and nuclear palisading. Immunohistochemical staining patterns were also the same as shown in the neoplastic cells of the original tumor, including positive for S100, NGFR, nestin, and claudin-1.

In this case, the original tumor found in the right adrenal gland revealed histopathologically that the surface of the tumor was

covered with compressed adrenal cortex and medulla. The tumor showed typical morphological characteristics of PNSTs, such as 2 area of Antoni type A and type B pattern [1, 4, 5]. In addition, no septum was observed between the tumor and the adrenal medulla, suggesting the neoplastic cells arose from the adrenal medulla cells. Mohiuddin and Gilliland [8] reviewed adrenal Schwannoma, one of the benign PNSTs, is a rare type of adrenal incidentaloma arising from Schwann cells in the adrenal medulla in human. In addition, a case of adrenal MPNST with pheochromocytoma was also reported in human [9]. Immunohistochemical results of the neoplastic cells in the original tumor were positive for S100, NGFR, nestin, and claudin-1 and negative for cytokeratin and α-SMA. Among them, positive for S100, and negative for cytokeratin and α-SMA are typical expression pattern of PNSTs [1, 4, 5, 8, 10, 13, 15]. In contrast, expressions of NGFR, nestin, and claudin-1 are thought to be an available marker for MPNSTs [1, 3, 7, 11–14]. Briefly, NGFR expressed normally in Schwann cell as a differential marker [1, 7], nestin expressed in neuroectodermal stem cell as a neural cell marker [11, 12], and claudin-1 expressed in Schwann cell and perineurial cell as a neural cell marker [3, 13] are commonly expressed in MPNSTs. In addition, metastatic lesions developed on 7 months after the surgical resection of the original tumor with no infiltration or invasion of the neoplastic cells. The neoplastic cells in the metastatic lesion in the liver revealed quite similar histopathological and immunohistochemical features as those in the original tumor.

Although MPNST can develop at many body sites, this is the first report of MPNST originating from the adrenal gland in a dog, based on the histopathological and immunohistochemical findings.

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