

Title: Latent adrenal Ewing sarcoma family of tumors: a case report

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1 **Abstract**

2 Ewing sarcoma family of tumors (ESFT) is derived from the neural crest, which originates
3 from basal embryo cells in the primitive neural tube. ESFT often arises at the bone, chest
4 wall, and soft tissues of the thoracic region. However, ESFT that arises from the adrenal
5 gland is much rarer and it is usually revealed by clinical symptoms. We report an autopsy
6 case of suicidal hanging, in which adrenal ESFT was incidentally revealed. To our
7 knowledge, this is the first case of latent ESFT arising from the adrenal gland. Autopsy can
8 sometimes reveal latent disease. Some of these latent diseases are very rare and we would
9 not be able to detect them without a complete autopsy. As forensic pathologists, we should
10 attempt to perform a complete autopsy and report new discoveries for the development of
11 medicine.

12

13 **Keywords:** Ewing sarcoma family of tumors, Latent cancer, Adrenal gland tumor

14

15 **1. Introduction**

16

17 The Ewing sarcoma family of tumors (ESFT) is derived from the neural crest, which
18 originates from basal embryo cells in the primitive neural tube. ESFT has a common set of

19 immunohistochemical and cytogenetic characteristics. ESFT is therefore classified as a
20 family of molecularly and histopathologically related small, round, blue cell tumors. ESFT
21 often arises in the bone, chest wall, and soft tissues of the thoracic region. However, ESFT
22 that arises from the adrenal gland is rarer and is often associated with clinical symptoms [1].
23 We report an autopsy case of suicidal hanging, in which ESFT of the adrenal gland was
24 incidentally revealed. To our knowledge, this is the first case of latent ESFT arising from the
25 adrenal gland.

26

27 **2. Case report**

28

29 A 26-year-old man was found dead on the stairs of a hotel, hanging by the neck
30 with his belt. The hanging was complete; the feet had not landed on the floor, with the knot
31 of the ligature in the upper, posterior part of the head. He had depression and left a suicide
32 note. With case investigation, the manner of death was thought to be suicidal.

33

34 **3. Autopsy findings**

35

36 The deceased was 169 cm tall and weighed 61.0 kg. There was no external injury

37 except for around the neck. On examination of the neck, a furrow was present, which did not
38 completely encircle the neck. Focal cutaneous hemorrhages and blisters were present
39 above and below the furrow. The skin, underlying fat, and soft tissue in the area of the
40 ligature marks were dark brown and dry.

41 Subpleural petechial hemorrhages, acute lung emphysema, and liquid blood in the
42 heart were found on internal examination, indicating general autopsy signs of asphyxia.
43 Intra-muscle hemorrhages of the neck were revealed and the hyoid bone was fractured. The
44 weight of the left and right lung was 532 and 636 g, respectively. We also found an 8-cm
45 diameter, whitish-yellow tumor in the right retroperitoneum. The tumor was completely
46 separated from right kidney (Fig. 1). No other pathological change was found.

47 On microscopic examination, the tumor was composed of malignant, small, round
48 cells (Fig. 2A). As the tumor was located in the right adrenal area and had a cortical rim (Fig.
49 3), the tumor was presumed to have arisen from the adrenal gland. Immunohistologically,
50 the tumor was positively stained for Cluster of Differentiation 99 (CD99) (Fig. 2B) and
51 vimentin, but negatively for synaptophysin, desmin, WT1, CD3, CD20, and CD34. Therefore,
52 the cause of death was hanging and a latent ESFT of the adrenal gland was diagnosed.

53

54 **4. Discussion**

55

56 ESFT includes Ewing sarcoma of the bone, extraskeletal Ewing sarcoma,
57 peripheral primitive neuroectodermal tumor (PNET), and Askin tumor (thoracopulmonary
58 PNET) [2]. PNET was first described in 1918 by Stout in a 42-year-old man with ulnar nerve
59 tumors. Then, in 1921, Ewing sarcoma was described in a 14-year-old boy with osteoclasia
60 in the ulna. In 1973, both tumors were defined as PNETs. In 1979, Askin tumors were
61 defined as PNETs in the thoracic cavity [1]. They are, now, collectively termed as ESFT.
62 ESFT is always derived from the primitive neural crest, which originates from basal embryo
63 cells in the primitive neural tube.

64 In the present case, the tumor was located in the right retroperitoneum. It was
65 completely separated from the right kidney and had a cortical rim, suggesting a primary
66 adrenal tumor. Malignant, small, round cells include neuroblastoma, rhabdomyosarcoma,
67 Wilms tumor, desmoplastic small round-cell tumor, malignant lymphoma solitary fibrous
68 tumor, or ESFT during differential diagnosis. Immunohistochemical examination in our case
69 revealed that the tumor was positively stained with CD99, which is consistent with ESFT.
70 The other tumors are ruled out by negative staining for synaptophysin, desmin, WT1, or
71 CD34. We therefore diagnosed primary adrenal ESFT on the basis of pathological
72 examination. ESFT of adrenal gland is a very rare disease and only a few cases have been

73 reported so far [1,3-11]. Molecular analysis of ESFT reveals a reciprocal translocation of t
74 (11; 22) (q24; q12) and t (21; 22) (q22; q12) [12]. In the present case, however, we could not
75 perform molecular analysis because of postmortem changes. We should have preserved a
76 frozen sample of the tumor.

77 In the previously descriptions of adrenal ESFT in the literature (Table 1), most
78 patients had complained of abdominal pain and the tumors were subsequently discovered.
79 ESFT progresses rapidly and some patients already had metastasis by the time the primary
80 tumor was found. However, in the present case, the deceased had no symptoms and did not
81 notice that he had the tumor. Autopsy incidentally revealed the tumor and such a case is
82 very uncommon. To our knowledge, this is the first report of latent adrenal ESFT.

83 With respect to determination of the cause of death, especially in cases of trauma,
84 we may be able to detect the cause of death using only external examination, as in the
85 present case of hanging. However, autopsy can sometimes reveal latent disease [13]. Some
86 of these latent diseases are very rare and we would not be able to detect them without a
87 complete autopsy. As forensic pathologists, we should attempt to perform a complete
88 autopsy and report new discoveries for the development of medicine.

89

90 5. Conflict of interest

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92 The authors have declared no conflict of interest.

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94 **References**

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131

132 **Figure legends**

133

134 Fig. 1. Macroscopic examination of the kidney. An 8-cm diameter, whitish-yellow tumor was
135 found in the right retroperitoneum (A). The tumor was completely separated from the right
136 kidney (B).

137

138 Fig. 2. Microscopic examination of the tumor. The tumor was composed of malignant, small,
139 round cells (A, H&E staining) and stained positively for Cluster of Differentiation 99 (CD99)
140 (B, CD99 staining).

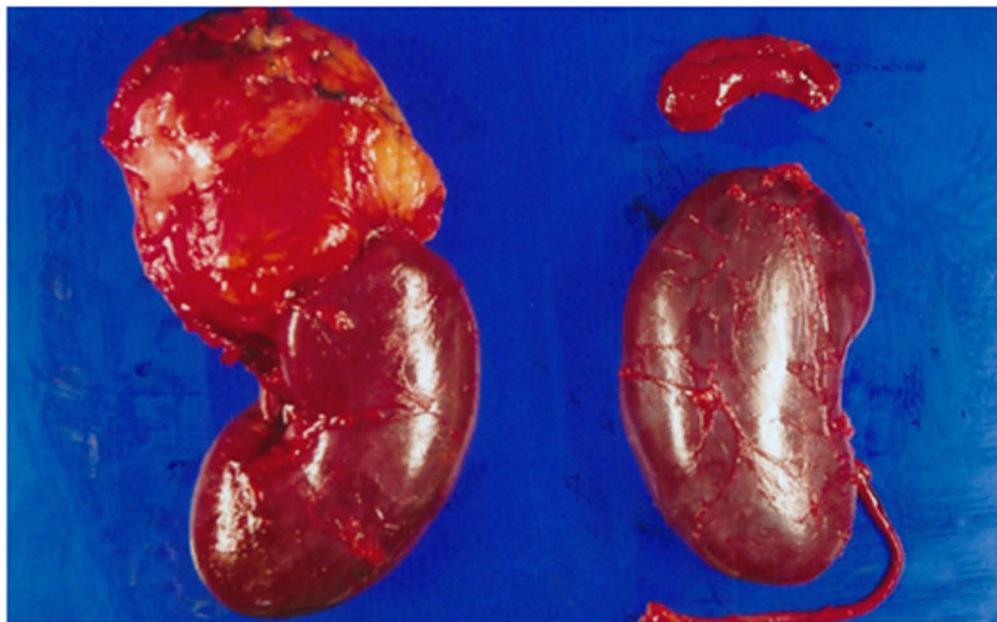
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142 Fig. 3. Microscopic examination of the tumor. The tumor was located in the right adrenal
143 area and had a cortical rim. (H&E staining)

144

Figure 1

A



B

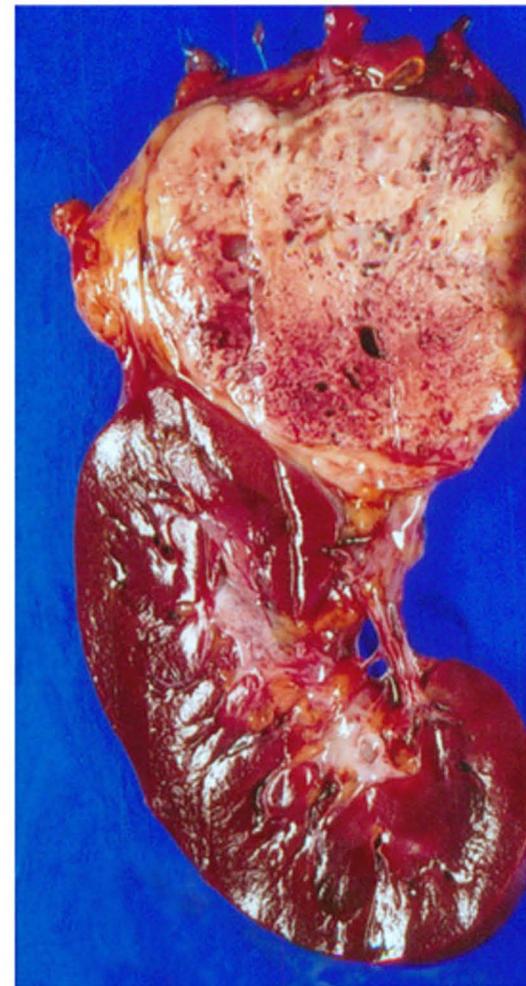
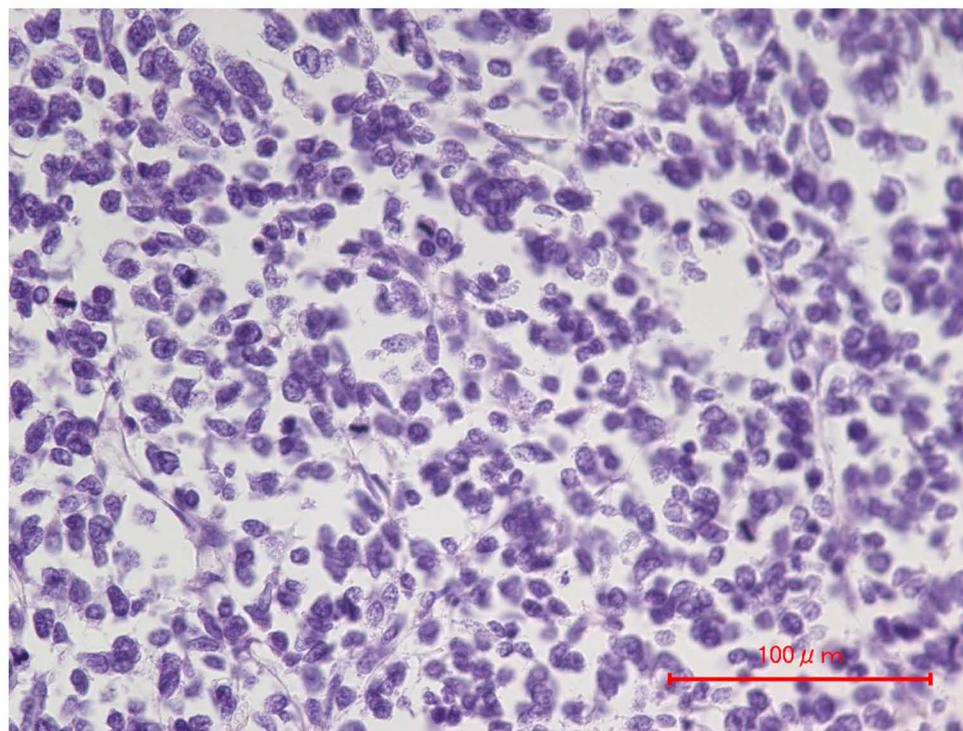


Figure 2

A



B

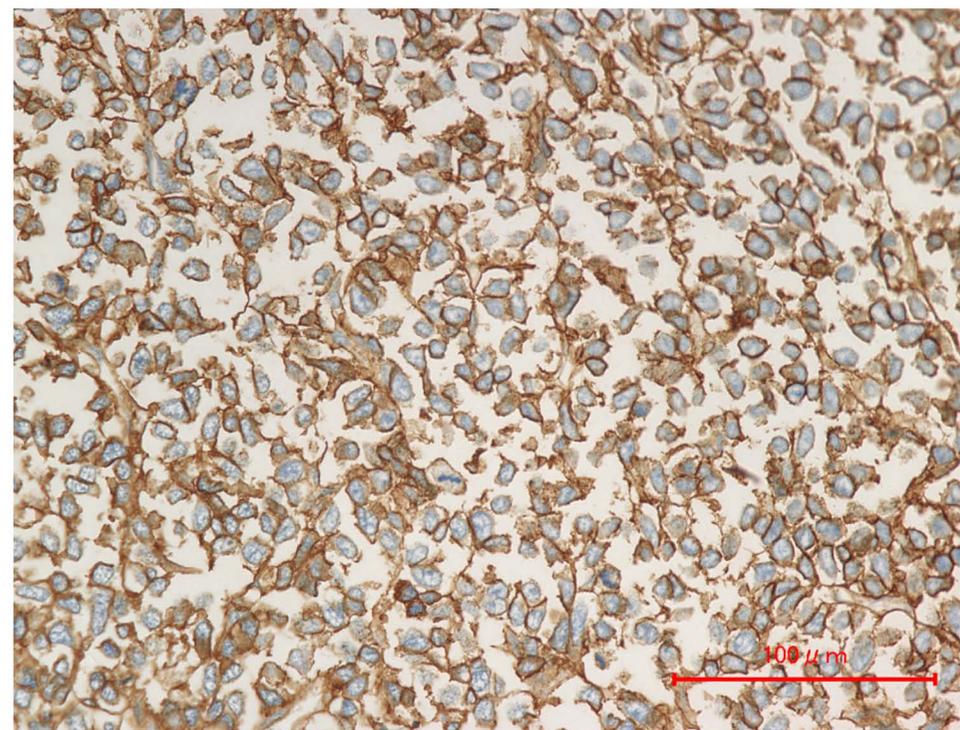


Figure 3

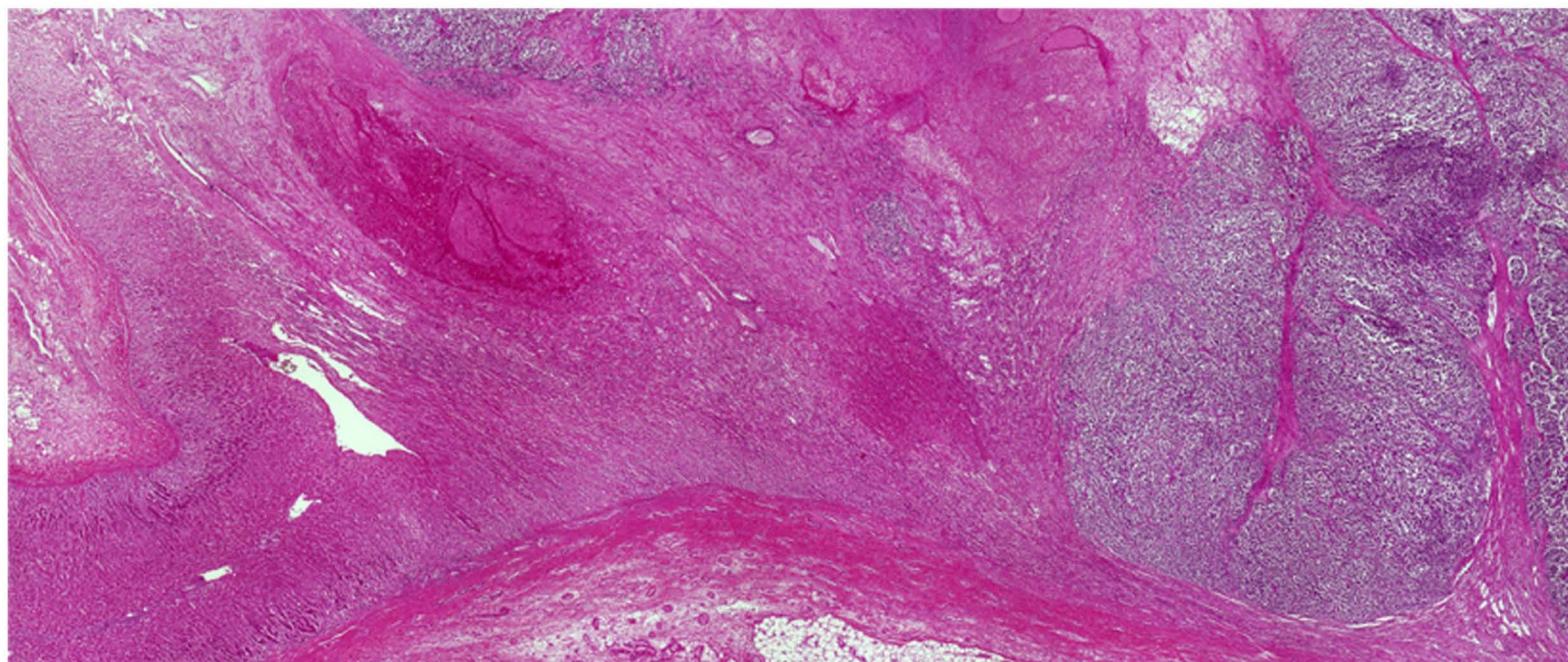


Table 1

Adrenal Ewing sarcoma family of tumors: summary of case reports.

Authors [reference]	Age (yr)/sex	Outcome*	CD99	Clinical symptoms	Tumor size
Marina et al. [3]	17/F	Dead	NR	NR	NR
	7/M	Dead	NR	NR	NR
	4/M	Dead	NR	NR	NR
Renshaw et al. [4]	46/F	NR	+	NR	NR
	20/F	NR	+	NR	NR
	48/F	NR	+	NR	NR
Matsuoka et al. [5]	32/F	Dead at 5 mo.	+	Abdominal pain	10 cm
Pirani et al. [6]	57/M	NR	+	Lower extremity pain	15 cm
Kato et al. [7]	11/M	Dead at 15 mo.	+	NR	13 cm
Komatsu et al. [8]	53/F	Alive at 10 mo.	+	Health screening	3 cm
Ahmed et al. [9]	28/F	NR	+	NR	10 cm

Kim et al. [10]	25/F	NR	+	Abdominal pain	15 cm
	24/F	NR	+	Flank pain	8 cm
Zhang & Li [1]	30/M	Dead at 8 mo.	+		12 cm
	21/F	Dead at 6 mo.	+	Abdominal pain or discovery	10 cm
	24/F	Alive at 13 mo.	+	by imaging tests	9 cm
	22/M	Alive at 1 mo.	+		17 cm
Stephenson et al. [11]	17/F	Alive at 14 mo.	+	Flank pain	5 cm
Current report	26/M	Dead	+	Latent cancer	8 cm

*Time after initial presentation

Abbreviations: F, female; M, male; mo., months NR, not recorded