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Case report

Rhabdomyosarcomas developing in association with mediastinal germ cell tumours

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Summary. Two mediastinal rhabdomyosarcomas that arose in association with germ cell tumours are reported. One presented as a small component of a mixed germ cell tumour with yolk sac and immature teratomatous elements. The other appeared as a large mass 4 months after diagnosis of a yolk sac carcinoma that had been treated with chemotherapy. The first patient was alive and free of disease 7 years later, whereas the second died of tumour 3 months post-operatively. The proportion of rhabdomyosarcoma within the germ cell tumours appears to have influenced the prognosis of these patients. This observation emphasizes the necessity of performing a thorough search for sarcomatous elements and quantifying their relative proportion in germ cell tumours of the mediastinum.

Key words: Germ cell tumour – Rhabdomyosarcoma – Mediastinum

Introduction

Apart from the hepatic and enteric differentiation that occurs in almost half of germ-cell tumours with a yolk sac carcinoma component, the development of sarcomatous elements in these neoplasms is a recently recognized and uncommon phenomenon (Ulbright et al. 1984). Its occurrence can make histological classification difficult and influence therapeutic decisions. Although its exact nature remains controversial, two theories have been proposed: (1) differentiation from pluripotential germ cells into somatic tissues with concomitant malignant transformation, and (2) malignant transformation of pre-existing teratomatous elements (True et al. 1988; Ulbright et al. 1984, 1985, 1990).

In this article we report the clinicopathological features of two patients with rhabdomyosarcomas arising from mediastinal germ cell tumours. The two cases were found after reviewing a series of 24 extra-gonadal germ cell tumours.

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Materials and methods

Twenty-four cases of extra-gonadal germ cell tumours from our surgical pathology files collected over the last 13 years (1976–1990) were reviewed. Tissue samples of each case were fixed in 10% neutral buffered formalin and embedded in paraffin. Haematoxylin and eosin stained sections and clinical reports were available in each case. In some cases, special stains were prepared including periodic-acid Schiff before and after diastase digestion. Immunohistochemical stains for determination of alpha-fetoprotein (AFP) (BioGenex, San Ramon, Calif.; diluted 1:800), actin (Enzo, New York N.Y.; 1:12800), hCG (Amersham, UK; 1:3), keratins CAM 5.2 (Becton Dickinson, Erembodegen, Belgium; 1:10), desmin (Merck, Darmstadt, FRG; 1:2), vimentin (Dako, Copenhagen, Denmark; 1:50) and myoglobin (Bioyeda, Tel Aviv, Israel; 1:500) were also performed following the avidin-biotin peroxidase complex (ABC) method.

Case reports

Case 1

An asymptomatic 61-year-old man was found to have a pulmonary nodule on routine check-up. Computed tomography (CT) revealed a lobulated mediastinal mass, 3.0 cm in diameter, and several smaller pulmonary nodules. The mediastinal tumour was resected and a biopsy from a pulmonary nodule was taken. Grossly, the cut surface of the mediastinal mass appeared solid, whitish-brown with foci of haemorrhage and necrosis. Microscopically it contained teratoma (Fig. 1A), yolk sac carcinoma and a small focus of sarcoma composed of large elongated cells with hyperchromatic and pleomorphic nuclei and abundant eosinophilic cytoplasm (Fig. 1B). No cross-striations were seen. Immunoperoxidase stains for myoglobin, actin and desmin were positive in the large eosinophilic cells. The biopsy of the pulmonary nodule showed fibrosis and tumour embolism in blood vessels. The patient received chemotherapy including different combinations of methotrexate, vincristine, bleomycin, VP16, actinomycin D, cyclophosphamide and prednisone with complete response. He was alive without evidence of disease 7 years post-operatively.

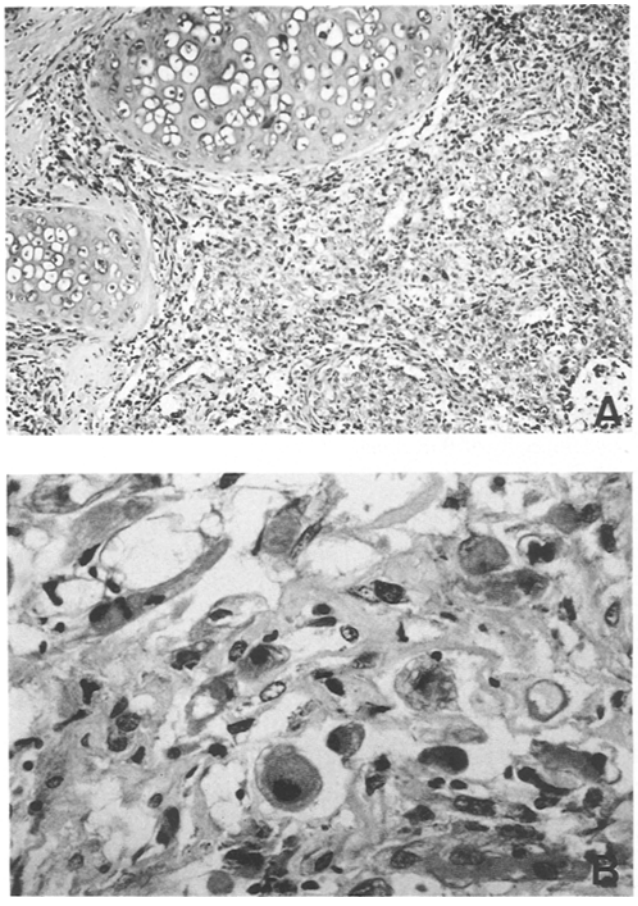

Fig. 1 A, B. Case 1. Rhabdomyosarcoma in mediastinal teratoma. **A** A focus of sarcoma close to two islands of fetal-type cartilage. H & E, ×200. **B** Rhabdomyoblasts showing elongated and round eosinophilic cytoplasm. H & E, ×400

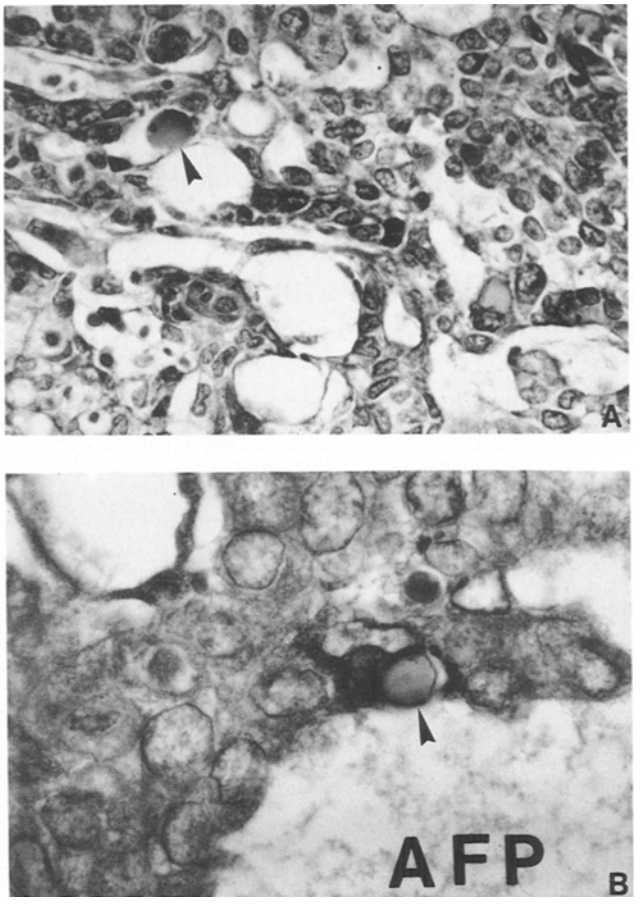

Fig. 2 A, B. Case 2. Yolk sac carcinoma metastatic to the bone marrow. **A** The tumour shows reticular architecture and contains hyaline globules (*arrow*). H & E, ×400. **B** Positive cytoplasmic stain for alpha-fetoprotein. Notice negative hyaline globule. ABC, ×600

Fig. 3. Case 2. Mediastinal rhabdomyosarcoma. The solid tumour, resected 4 months after diagnosis of yolk sac carcinoma, appears focally haemorrhagic and necrotic

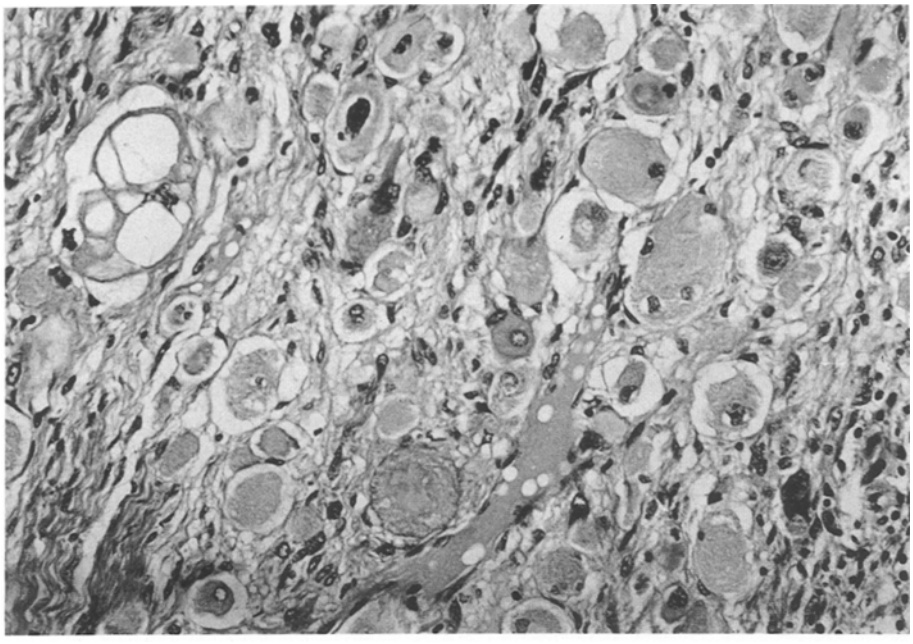

Fig. 4. Case 2. Mediastinal rhabdomyosarcoma. The tumour was composed of numerous large round rhabdomyoblasts. H & E, ×400

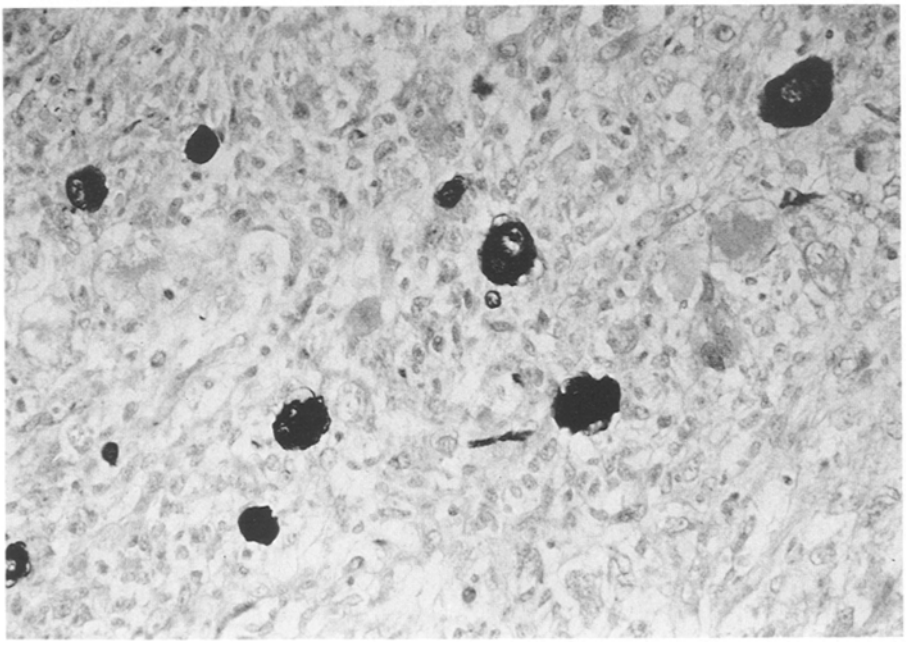

Fig. 5. Case 2. Mediastinal rhabdomyosarcoma. Positive stain for myoglobin. ABC, ×400

Case 2

A 29-year-old man had chest pain and cough for 8 months. CT revealed a mass, 6.0 cm in diameter, in the anterior mediastinum. Clinical diagnosis was lymphoma and the patient received chemotherapy including cyclophosphamide, vincristine, Adriamycin and prednisone without obvious response. A mediastinal biopsy revealed extensively necrotic yolk sac carcinoma. Metastases were identified on a bone marrow biopsy (Fig. 2). AFP levels of 100 mg/l returned to normal after a new chemotherapeutic treatment with seven alternating cycles of BOMP (bleomycin, vincristine, methotrexate and prednisone), EAC (VP16, actinomycin D and cyclophosphamide) and PAV (cisplatin, Adriamycin and vinblastine). However, no decrease of tumour size was evident on the CT scan and it was excised 4 months after the initial presentation.

The resected specimen was a solid greyish-white mass, 6.5 cm in diameter (Fig. 3). The cut surface showed white and pink areas with foci of haemorrhage and necrosis. On microscopic examination there were intersecting bundles of immature spindle cells and collections of large round-to-oval elements with large hyperchromatic nuclei and abundant eosinophilic cytoplasm of fibrillary appearance (Fig. 4). There were numerous abnormal mitoses. Immunoperoxidase stains for actin, desmin and myoglobin were positive (Fig. 5). Ultrastructurally, actin-myosin filaments and Z bands were seen (Fig. 6). The patient received radiotherapy but he died 7 months later. Serum AFP had remained negative.

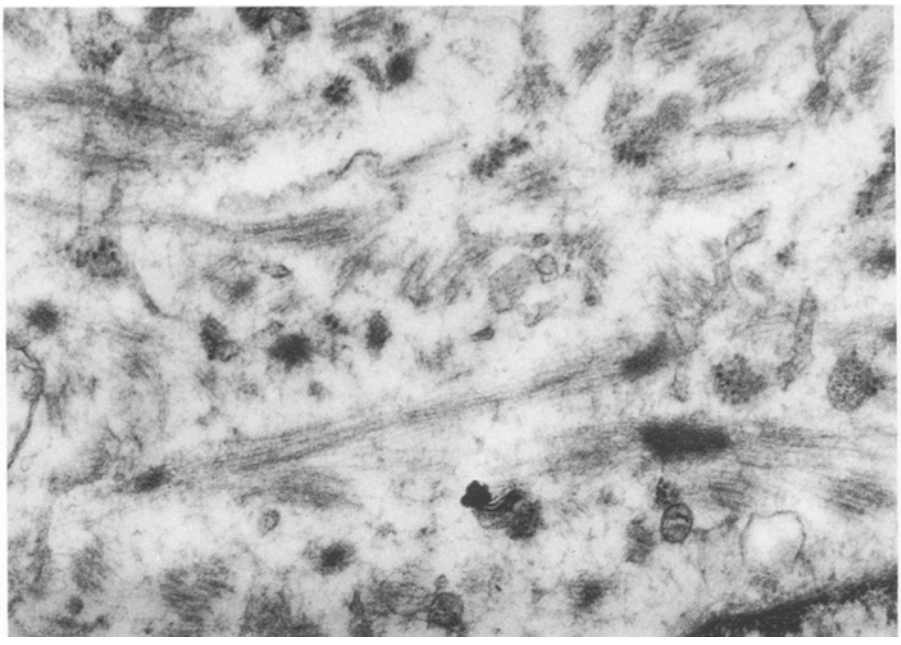

Fig. 6. Case 2. Mediastinal rhabdomyosarcoma. Thick myosin filaments and Z bands. EM, ×80000

Discussion

Although malignant transformation of epithelial elements in teratomas is a well-known event, the development of sarcoma in germ cell tumours has rarely been described (Ahlgren et al. 1984; Matoska and Talerman 1990; Preissig et al. 1979; True et al. 1988; Ulbright et al. 1984, 1985, 1990). Ulbright and co-workers reported 11 non-seminomatous germ cell tumours of the testis and mediastinum in which malignant mesenchymal components were found (Ulbright et al. 1984). Most contained rhabdomyosarcoma. In half of their cases the mesenchymal components were found when the tumours were first resected; in the other half they appeared in recurrences. The authors postulated that the sarcomatous elements had developed from foci of teratoma because most cases contained teratoma in both the initial and the recurrent tumours. Furthermore, they considered the possibility of malignant transformation of residual teratomatous elements unaffected by chemotherapy after elimination of the immature germ cells. They preferred such an explanation over the idea that the chemotherapy effect exerted on the pluripotential germ cells would cause them to differentiate into somatic cells.

Manivel and co-workers (1986) also reported the occurrence of sarcomas in 7 germ cell tumours of the mediastinum. They included 4 rhabdomyosarcomas, 2 angiosarcomas and the simultaneous presence of both in 1 case. Because of the occasional co-existence of the sarcomas and the immature teratomas, these investigators also suggested that the sarcomatous elements might derive from the immature mesenchyma of the teratomas, namely the vascular and skeletal muscle components. Indeed, in some cases it may be difficult to determine the boundaries between immature teratoma and sarcoma.

Recently, Ulbright and co-workers (1990) studied 14 male patients with testicular and extra-testicular germ cell tumours, in whom distinctive mesenchymal neoplasms composed of spindle to stellate cells were seen. Thirteen had received prior chemotherapy. They contended that many, if not all, of these tumours represented proliferation of a spindle cell component of yolk sac carcinoma. The presence of transitional areas in some cases provided circumstantial evidence that the spindle cell tissue may be the substrate for the development of sarcomas in patients with germ cell tumours. However, sarcomatous elements have been described in a spermatocytic seminoma of the testis (Matoska and Talerman 1990; True et al. 1988) and since this tumour is seldom associated with teratomatous and other germ cell components, the development of sarcoma can best be explained as a differentiation from totipotential germ cells rather than malignant transformation of teratomatous elements. Nevertheless, it has also been claimed that such a change may be secondary to anaplastic dedifferentiation, similarly to what occurs in chondrosarcomas and liposarcomas.

Out of a series of 24 extra-gonadal germ cell tumours we found 2 with rhabdomyosarcomatous components. Both were located in the mediastinum. In 1 case, the sarcomatous elements constituted a minor component; in the other the initial biopsies showed yolk sac carcinoma but the resected mediastinal mass contained only rhabdomyosarcoma. Since neither of these 2 neoplasms exhibited major foci of teratoma, the origin of rhabdomyosarcoma from poorly differentiated germ cells appears most likely. It is probable that the amount of sarcomatous tissue in these tumours might have influenced the prognosis of the patients. Whereas the patient whith the large rhabdomyosarcomatous mass died 3 months after surgery, the other – who only had a small focus of sarcoma – is alive and free of disease after 7 years; both patients had metastatic disease and both received chemotherapy. The different outcome underscores the need of a thorough search for sarcomatous components

in germ cell tumours of the mediastinum as well as an estimate of the relative proportions of tumour tissues. However, as in most of such cases a small diagnostic biopsy is usually followed by chemotherapy, it can be very difficult to identify the sarcomatous elements. Nevertheless, the possibility of a sarcoma arising from a germ cell tumour should be borne in mind in cases with poor response to chemotherapy. The aggressive behaviour of these neoplasms justifies the establishment of a modified chemotherapeutic protocol including antisarcoma drugs.

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