for Bcl-2 and PNMT (Table 2). These immunohistochemical staining patterns indicated that the metastatic lung tumors were composed of chromaffin cells with an extra-adrenal phenotype. The right ovarian tumor, resected during the second surgery, exhibited positive staining for both ganglion cell and extra-adrenal chromaffin cell markers (Table 2), although the histology of the tumor resembled that of the left ovarian neuroblastoma.

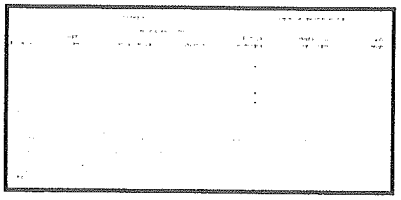

Table 2. Results of Immunohistochemistry*

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FIGURE 2. Immunohistochemical staining of chromogranin A (CGA). **A:** The metastatic left ovarian tumor is positive for CGA only in the neuropils at the center of the rosettes (original magnification, ×50). **B:** The metastatic lung tumor exhibits strong, diffuse cytoplasmic staining for CGA (original magnification, ×50).

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DISCUSSION

The adrenal medulla is derived from neural crest cells with a multilineage differentiation potential and is composed of heterogeneous cell types, including mostly chromaffin cells and a minor population of ganglion cells and Schwann-like supporting cells.[8,20] Reflecting this complex cellular composition, pheochromocytoma, an adrenal medullary tumor of chromaffin cells usually seen in adults, occasionally exhibits a mixed phenotype, such as pheochromocytoma admixed with ganglioneuroma, ganglioneuroblastoma, neuroblastoma, Schwannoma, or melanocytic tumors.[1–3,6,10,14,16,18,19,24] These tumors are called "composite" or "compound" tumors. On the other hand, childhood neuroblastomas are known

to differentiate along a sympathetic neuronal cell pathway with increasing age. However, the potential of neuroblastomas to differentiate along two lineages, not only neuronal cells but also chromaffin cells, has been demonstrated in neuroblastoma cell lines [7] and certain in vivo neuroblastomas [9,12,13]: tumor cells with a chromaffin cell nature, detected as CGA- or IGF-II-positive cells, have been focally found in extra-adrenal neuroblastomas with a lobular architecture.[12] The metastatic lung tumors in our patient arose from the extra-adrenal retroperitoneum and exhibited a lobular architecture and chromaffin cell differentiation, consistent with the above observation. Nevertheless, the conversion of a neuroblastoma to a pheochromocytoma/paraganglioma-like tumor, as seen in our case, is extremely unusual; to the best of our knowledge, a similar transformation has been described in only 1 other patient.[9]

Three cell types in the sympathetic neuroendocrine system, namely, adrenal and extra-adrenal chromaffin cells and sympathetic ganglion cells, can be differentiated using histochemical markers (Table 2). IGF-II is expressed in chromaffin cells but not in sympathetic neuronal cells.[12,13] CGA and Syn are also useful markers of chromaffin cells, since they are strongly and diffusely expressed in chromaffin cells but only focally and weakly expressed in neuroblasts and ganglion cells.[24] Bcl-2 is a marker of sympathetic neurons and is expressed in all neuroblastomas, whereas tumor cells undergoing neuroendocrine differentiation lose this antigen.[11] CD57 (HNK-1) is a marker of fetal adrenal medullary ganglion cells, and its expression in neuroblastomas is uniformly associated with ganglionic differentiation but is lost with differentiation along chromaffin cell lineage.[8,9,13] TH is present in all catecholamine-producing cells, while D[beta]H is expressed only in norepinephrine-producing cells and PNMT is only expressed in human adrenal medulla cells that convert norepinephrine to epinephrine.[20,24] The immunohistochemical results in the present case showed that the metastatic lung tumors were of an extra-adrenal chromaffin cell lineage, although IGF-II was only weakly labeled. On the other hand, the left ovarian tumor, resected during the initial surgery, expressed antigens that were associated with ganglionic differentiation, consistent with a diagnosis of neuroblastoma. Interestingly, the histology of the right ovarian tumor, resected 6 months after the first surgery, was that of an ordinary neuroblastoma, while an immunohistochemical characterization revealed the features of both ganglionic and extra-adrenal chromaffin cells. Thus, this tumor exhibited intermediate characteristics of neuroblasts and chromaffin cells, indicating that the functional maturation of the chromaffin cells preceded any morphologic transformation.

The occurrence of an extra-adrenal pheochromocytoma as a secondary malignancy in an adolescent 15 years after the patient had been treated for a neuroblastoma has been documented.[17] The pheochromocytomatous tumors in our patient, however, occurred as disseminated multiple lesions in bilateral lungs during the course of therapy, indicating that these tumors were metastatic but not a secondary malignancy. The reason why this neuroblastoma patient exhibited such an unusual differentiation pattern in her metastatic lesions, leading to a histology similar to that of a pheochromocytoma/paraganglioma, is not clear. Since the patient received intensive chemotherapy and radiotherapy, these therapies may have caused the unusual differentiation pattern by selecting special tumor clones with the capability of differentiating toward chromaffin cells. Similar phenotypic conversion has been observed in another patient [15]: among the tumors that were treated with a monoclonal antibody against ganglioside G_{D2}, which is abundantly expressed on neuroblastomas, the only tumor that lost G_{D2} expression underwent pheochromocytomatous conversion, indicating a

possible association between tumor differentiation and the therapeutic treatment. The neuroblastoma in the present case was also unusual in that it metastasized to bilateral ovaries. A special genetic background may have been involved in the unique aspects of this case.

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Key Words: neuroblastoma; pheochromocytoma; paraganglioma; differentiation; chromaffin cell

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Accession Number: 00000478-200404000-00016

Pediatric Surgery International

10.1007/s00383-005-1404-y

Case Report

Recurrent yolk sac tumor following resection of a neonatal immature gastric teratoma

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Accepted: 1 April 2004 **Published online:** 1 June 2005

Abstract Gastric teratomas are very rare and usually benign. Only a few cases of gastric teratomas with malignant components have been reported. This report describes recurrence of a yolk sac tumor following resection of a neonatal immature gastric teratoma. Gastric teratoma recurring as a malignant lesion has not been previously reported. Recurrence of immature gastric teratomas should be considered, and a periodic follow-up check with alpha-fetoprotein level should be mandatory.

Keywords Gastric teratoma - Immature teratoma - Yolk sac tumor

Introduction

Gastric teratomas are very rare, with a reported incidence of less than 1% of all pediatric teratomas [*1*]. As of 2002, only 107 cases had been reported in the English literature [*2–7*] and 54 cases in the Japanese literature [*8*, *9*]. Gastric teratoma patients exhibit characteristic differences in gender (90% are male), age (less than 1 year of age), and malignant behavior compared with patients with teratomas originating in other organs. Malignant gastric teratomas are especially rare, with only a few cases reported [*10–12*]. We describe a case of immature gastric teratoma that recurred as yolk sac tumor (YST) 2 years after the resection. To our knowledge, this report is the first of its kind in the literature.

Case report

A 4-day-old male infant was admitted with vomiting and fever. Abdominal examination revealed a firm, elastic, mobile mass with an irregular contour in the left upper quadrant. Upper gastrointestinal tract contrast radiography revealed a gastric tumor with irregular contour (Fig. 1). Computed tomography (CT) showed a calcified, low-density tumor involving the stomach wall and extending toward the retroperitoneum. The serum alpha-fetoprotein (AFP) level was appropriate for age at 80,050 ng/ml, beta human chorionic gonadotropin concentration was <0.1 ng/ml (standard <0.1 ng/ml), and a neuron-specific enolase level was 13.2 ng/ml (standard <10.0 ng/ml) (Table 1).

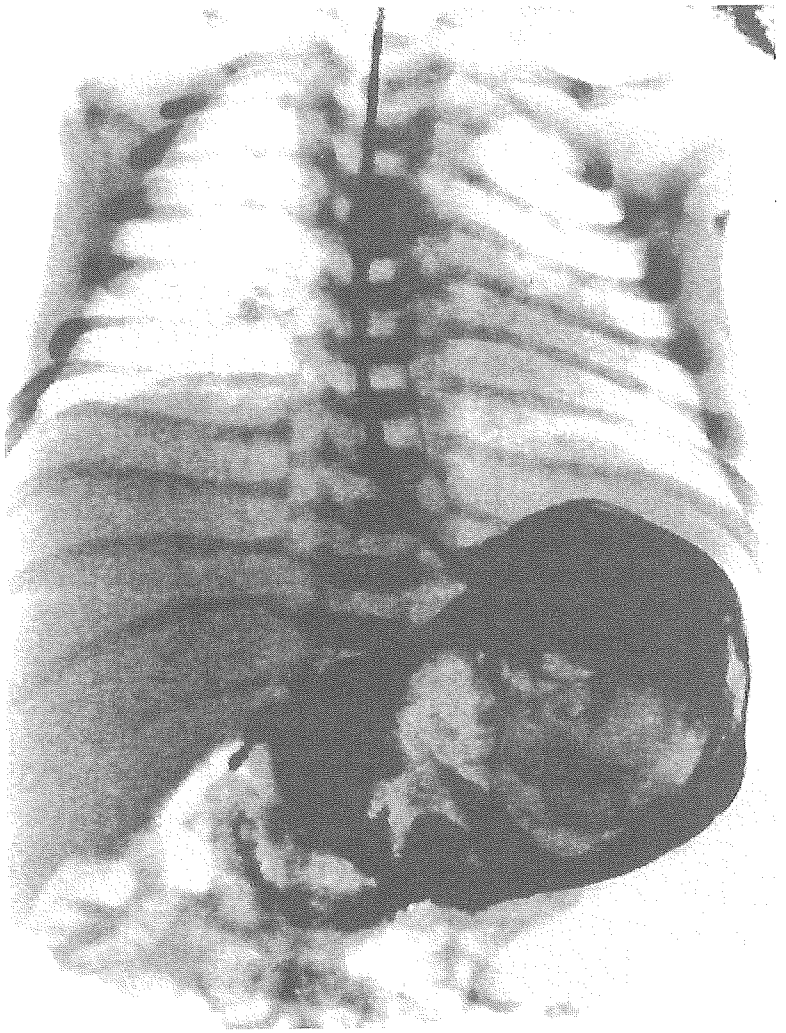

Fig. 1 Upper gastrointestinal contrast study shows a large space-occupying mass with irregular contour in the stomach

Table 1 Serum tumor marker levels on admission (*AFP* alpha-fetoprotein, *HCG* human chorionic gonadotropin, *Beta-HCG* beta human chorionic gonadotropin, *NSE* neuron-specific enolase, *VMA* vanillylmandelic acid, *Cr* creatinine, *HVA* homovanillic acid, *CEA* carcinoembryonic antigen)

	This case	Standard
AFP(day 5)	80,050.0 ng/ml	
HCG	<0.4 mIU/ml	<0.7 mIU/ml

Beta-HCG	<0.1 ng/ml	<0.1 ng/ml
NSE	13.2 ng/ml	<10.0 ng/ml
VMA/Cr	7.7 mg/gCr	
HVA/Cr	18.9 mg/gCr	
CEA	<0.9 ng/ml	<2.5 ng/ml
Ferritin	96.1 ng/ml	3120 ng/ml

Laparotomy confirmed a well-encapsulated solid tumor arising from the lesser curvature of the stomach and extending into the lumen and retroperitoneum. The tumor was not adherent to adjacent structures. Resection of the tumor was performed, with a 0.5-cm gastric wall margin taken. The tumor was positive in the surgical margin near the esophagogastric junction (EGJ) by intraoperative pathological assessment. Additional resection was performed for the margin. The tumor was 5.5×4.4×4.0 cm in size and weighed 70 g. Histological examination demonstrated an immature teratoma with a variety of components derived from endoderm, ectoderm, and mesoderm, including mature cartilage, alimentary tract epithelium, and immature central nervous system. No yolk sac histology was observed.

The infant's postoperative course was uneventful. Serum AFP levels decreased to <10 ng/ml by 7 months after the operation and were maintained at 7.3 ng/ml for 12 months. However, at the child's 24-month check-up, AFP had risen to 356.2 ng/ml. CT and magnetic resonance imaging (MRI) revealed an enhanced tumor under the left lobe of the liver and the right side of the spleen (Fig. 2). These findings prompted a second-look laparotomy, which was performed 26 months after the initial surgery. The recurrent tumor originated from the greater curvature of the stomach, locally invading the lumen and more growing toward the retroperitoneum surrounding the stomach. The recurrent tumor origin was near the surgical margin of the first operation. It was adherent to the spleen and the left lateral lobe of the liver. The tumor was removed en bloc with the spleen, the left lateral lobe of the liver, and regional lymph nodes. The pathologic diagnosis was YST without any area of immature teratoma (Fig. 3). By standard histologic microscopic evaluation, no invasion was observed to the spleen or the liver. Likewise, no metastasis was seen to any regional lymph nodes.

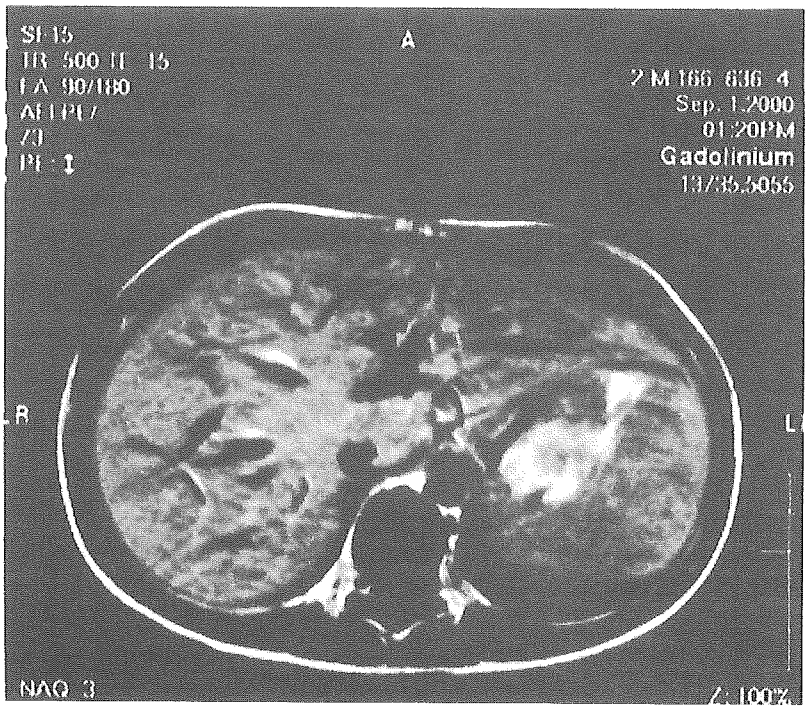

Fig. 2 Magnetic resonance imaging clearly outlines a tumor of high signal intensity on gadolinium-enhanced T1-weighted images (*T1WI*) 2 years after the first operation

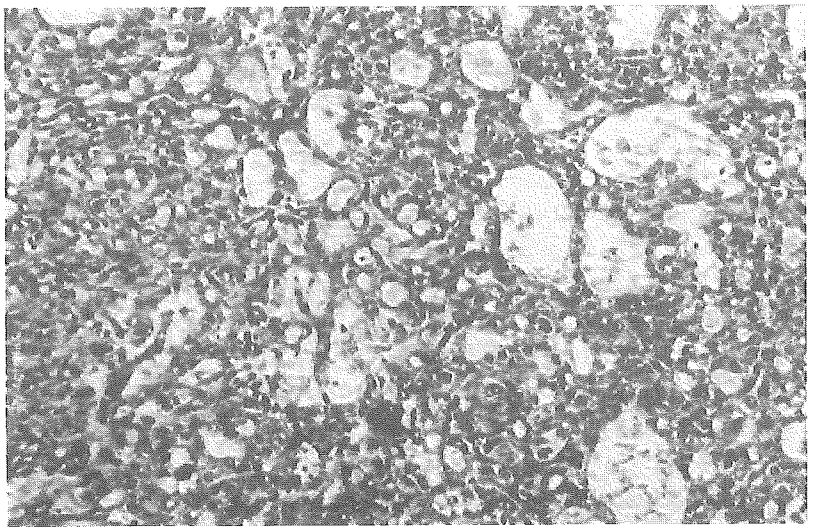

Fig. 3 Photomicrograph of the tumor resected at the second operation. The pathological diagnosis was pure yolk sac tumor (*YST*) without immature teratoma components (hematoxylin and eosin staining, original magnification ×100)

After the operation, chemotherapy with four courses of PVB regimen (cisplatin, 20 mg/m^2 ×5 days; vinblastine, 0.2 mg/kg ×2 days; bleomycin, 15 mg/m^2 ×1 day) was administered. No recurrence has been observed 3.5 years after the second operation and 3 years after the end of chemotherapy.

Discussion

At birth, teratomas present mainly as coccygeal tumors, whereas in the first 6 months teratomas are predominantly localized in the testis. Later, between the ages of 9 and 15 years, ovarian teratomas are seen [*13*]. Gastric teratomas are very rare and exhibit distinguishing characteristics compared with teratomas from other organ sites. For example, most gastric teratoma patients are male (90%) [*2*], whereas the other teratomas predominate in females. Most gastric teratomas described in previous papers were in infants less than 1 year of age. In addition, gastric teratomas have predominantly exhibited benign behavior. Only a few cases of gastric teratomas with malignant components have been reported [*10–12*]. A case of malignant transformation in an adenocarcinoma arising from immature teratoma in an 83-year-old male was reported [*14*]. Gastric teratoma recurring as a malignant lesion has never been reported.

Our patient's teratoma was diagnosed as an immature teratoma. Immature teratomas are the most controversial and least well-characterized germ cell tumors in children [*15*]. The prevalence of microscopic foci of YST is said to be directly related to the grade of the malignant potential and to be the only valid predictor of recurrence in pediatric immature teratoma. Researchers have reported that elevations of serum AFP concentration greater than 100 ng/dl almost always indicated the presence of foci of YST [*15*]. In our case, the concentration of serum AFP was 80,050.0 ng/ml, within the normal range for a 5-day-old patient. Positive AFP immunoreactivity was not found in the tumor resected at the first operation. However, because clusters of YST cells may be very small or associated intimately with immature neural tissue, or both, and because they frequently do not stain positively for AFP, they are easily overlooked [*16*]. In one series, half of relapsing patients showed highly malignant tumor histology at relapse (mainly YST and in a few cases embryonal

carcinoma) [13]. Relapses were observed for patients with mature as well as immature teratomas. Tumors have had foci of YST in immature teratoma. The recurrent YST in our patient originated near the initial surgical margin but was apart from the EGJ that was positive by intraoperative pathological assessment.

The most common germ cell tumors of childhood are sacrococcygeal teratomas, which have been reported to have a malignant potential of 17% [17]. A case of sacrococcygeal teratoma with immature elements was reported with local recurrence as malignant teratoma [18]. Without coccygectomy, local recurrence of sacrococcygeal teratomas has been reported and was postulated to have arisen from the microscopic remnants of the primary tumors [19]. Our observations suggest that this mechanism may have led to relapse in our patient. This is the first time gastric teratoma has been reported to recur locally with a malignant histology.

The serum concentration of AFP was a good indicator for tumor recurrence in our patient. The AFP concentration—which had been 7.3 ng/ml 12 months after the operation, indicating normal range for the patient's age—was abnormally elevated compared with age-appropriate normal controls when found to be 356.2 ng/ml 24 months later, and CT and MRI confirmed tumor recurrence. MRI was useful in that it made the tumor contour stand out against surrounding viscera. MRI clearly indicated a tumor of low T1 but high T2 signal intensity, with gadolinium enhancement (Fig. 2). A gallium and bone scintigram were negative.

For treating the recurrent tumor, we selected en bloc surgical resection together with surrounding viscera firmly adherent to the tumor. Complete surgical resections are recommended as the most effective treatments for teratomas with or without malignant elements [20].

After the surgery, we chose the PVB (cisplatin, vinblastine, and bleomycin) regimen as an antineoplastic chemotherapy. Vincristine, actinomycin D, vinblastine, bleomycin, doxorubicin, cisplatin, and etoposide have proved effective in treating various tumors of germ cell origin [16]. Cisplatin and its incorporation into combination regimens has resulted in a substantial increase in disease-free survival. VP16 may cause secondary leukemia [21], and ifosfamide may cause severe multiorgan toxicity [22]. Thus, we chose PVB, expecting stronger effects than regimens without cisplatin and weaker side effects than regimens with VP16 or ifosfamide. Four courses of the same PVB regimen that we used are the standard therapy for stage 1 YST in Germany, where favorable outcomes are reported [23].

Our patient has been free of recurrence for 3.5 years after the second operation. Although immature gastric teratomas are considered to have benign behavior, a pediatric surgeon should consider the possibility of recurrence, and periodic follow-up checks with AFP tumor marker measurement should be mandatory.

Acknowledgements We thank C. Haqq, University of California, San Francisco, for critically reviewing the manuscript.

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Eur J Pediatr (2005) 164: 616–620
DOI 10.1007/s00431-005-1728-6

ORIGINAL PAPER

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Granulocytic sarcoma of the spine in a child without bone marrow involvement: a case report and literature review

Received: 8 March 2005 / Accepted: 18 May 2005 / Published online: 13 July 2005

Abstract We report a 2-year-old Japanese boy without bone marrow involvement who developed a primary granulocytic sarcoma in his spinal canal. Tumour cells were positive for myeloperoxidase, MIC2, CD56 and, CD68 on formalin-fixed, paraffin-embedded tissue sections and CD13, CD33, CD45, and CD64 on acetone-fixed fresh frozen sections. Nine months after the initiation of treatment, the tumour had significantly regressed and the patient was able to walk with help. *Conclusion*: Our patient is the youngest case of granulocytic sarcoma of the spine without bone marrow involvement. Immunohistochemical methods are very helpful in establishing a diagnosis of granulocytic sarcoma.

Keywords Granulocytic sarcoma · Myeloid sarcoma · Spinal cord compression · Without bone marrow involvement

Abbreviations AML: acute myeloid leukaemia · GS: granulocytic sarcoma

Introduction

Granulocytic sarcoma (GS), also termed extramedullary myeloid tumour, myeloid sarcoma or chloroma, is a malignant, solid tumour consisting of myeloblasts or immature myeloid cells occurring in extramedullary sites [1]. GS has often been described in association with acute myeloid leukaemia (AML), chronic myeloid leukaemia, or myeloproliferative disorders [1]; however, GS rarely presents in the absence of other haematological disease. Many of these cases are misdiagnosed as small round cell tumours such as malignant lymphoma, rhabdmyosarcoma or Ewing sarcoma [1]. GS may occur in almost any part of the body, but is most commonly seen in the skin, lymph nodes, and bone [1, 21,26]. Spinal cord compression is an uncommon symptom.

Here we report the youngest case of a primary GS occurring in the spinal canal and causing severe spinal compression in a child without bone marrow involvement. The importance of immunohistochemical studies in the diagnosis of GS without bone marrow involvement is discussed.

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Case report

A 2-year-old Japanese boy was taken to a local hospital complaining of external genital and lower extremity pain for a month; the patient had difficulty standing or walking. As MRI showed an epidural mass filling the spinal canal below the L3 level and extending into the left abdominal cavity (Fig. 1a, b), he was referred to our hospital for further evaluation and treatment. Although an open biopsy was planned to enable a diagnosis, his mother refused the procedure and the patient was discharged because of her decision. Three months later, however, the patient's lower extremities became paralysed and he developed bladder and bowel problems; he was thus readmitted to our hospital. On physical examination at the time of the second admission, he could not move his legs by himself and his lower extremities were more atrophic than at the previous examination. The deep tendon reflexes in his lower extremities were disturbed. A sensory assessment revealed hyperaesthesia below the level of L3. A complete blood count at the time of the second admission

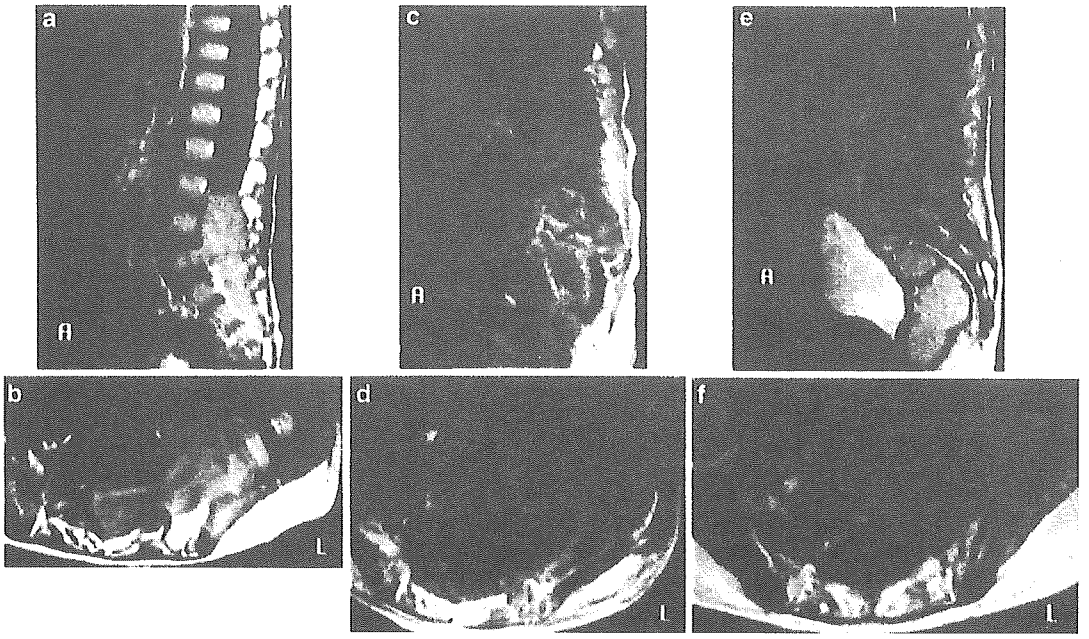

Fig. 1 a,b At the time of the initial admission, sagittal and coronal T1-weighted MRI scans showed an epidural mass filling the spinal canal below L3 and extending into the left abdominal cavity. **c,d** At the time of the second admission, the tumour had increased in size, compared to the images obtained 3 months earlier. **e,f** The size of the tumour shrunk remarkably after six courses of chemotherapy

showed a white blood cell count of 10,500 cells/μl with a normal differential, an haemoglobin level of 12.4 g/dl, and a platelet count of 289,000 cells/μl. Bone marrow aspiration showed normocellular bone marrow with no evidence of leukaemia. An MRI examination showed that the tumour had increased in size (Fig. 1c, d). An open biopsy was performed and a small round-cell-like tumour was observed in the biopsy sample. To establish a definitive diagnosis, immunohistochemical studies were performed. At this time, the tumour cells tested positive for myeloperoxidase, MIC2 (CD99), CD56, and CD68 and negative for c-Kit (CD117) and CD43 using immunohistochemical techniques on formalin-fixed, paraffin-embedded tissue sections (Fig. 2). Additional immunohistochemical studies using acetone-fixed, fresh-frozen sections revealed that the tumour cells were also positive for CD13, CD33, and CD64, all of which are markers for myeloid-lineage cells, and CD45 but negative for CD3 and CD79a (Fig. 3). Therefore, a histopathologicla diagnosis of GS was made.

First of all, we performed three courses of AML chemotherapy using etoposide, cytarabine, mitoxantron, and idarubicin (1st course: etoposide 150 mg/m^2, days 1–5, cytrabine 200 mg/m^2, days 6–12, mitoxantron 5 mg/m^2, days 6–10; 2nd course: cytarabine 3 g/m^2×2/day, days 1–3, etoposide 100 mg/m^2, days 1–5, idarubicin 10 mg/m^2, day 1; 3rd course: etoposide 150 mg/m^2, days 1–3, cytarabine 200 mg/m^2, days 4–8, mitxantron 5 mg/m^2, days 4–6). Despite this regimen, an apparent regression of the tumour was not observed. We then changed the chemotherapy to four additional courses of ifomide, pirarubicin, etoposide, and carboplatin (4th-7th course: ifomide 3 g/m^2, days 1, 2, pirarubicin 30 mg/m^2, days 4, 5, etoposide 400 mg/m^2, day 3, carboplatin 100 mg/m^2, days 1–5). In total, seven courses of chemotherapy were performed 9 months after the initiation of treatment. A subsequent MRI examination showed that the tumour had significantly regressed (Fig. 1e, f), and the patient was able to walk again with assistance.

Discussion

GS without bone marrow involvement is rare and only a few cases have presented with spinal involvement. Yamauchi et al. [26] summarised 74 GS patients without bone marrow involvement, two of their own and 72 previously reported cases; 13 out of 102 tumours (13%) in these patients had head or spinal cord involvement. Tsimberidou et al. [21] summarised GS patients without bone marrow involvement treated at the MD Anderson Cancer Center between 1990 and 2002 and reported that 4 out of 21 patients (19%) with GS without bone marrow involvement had CNS involvement. Our literature survey found only 25 GS cases without bone marrow involvement causing spinal cord compression since 1950, including the above reports (Table 1) [2, 3, 5, 7, 8, 9, 10, 11, 12, 13, 15, 16, 17, 18, 19, 20, 22, 23, 24, 25,28]. The age distribution of these patients ranged from 12 to 73 years (mean 32.2 years). Since our patient was 2 years old, he is the youngest GS patient without bone marrow involvement of the spine to be reported. 1

In our literature review including our case, the symptoms of GS causing spinal cord compression were variable depending on the patient and tumour location. Local pains were present in 88% of the patients, with

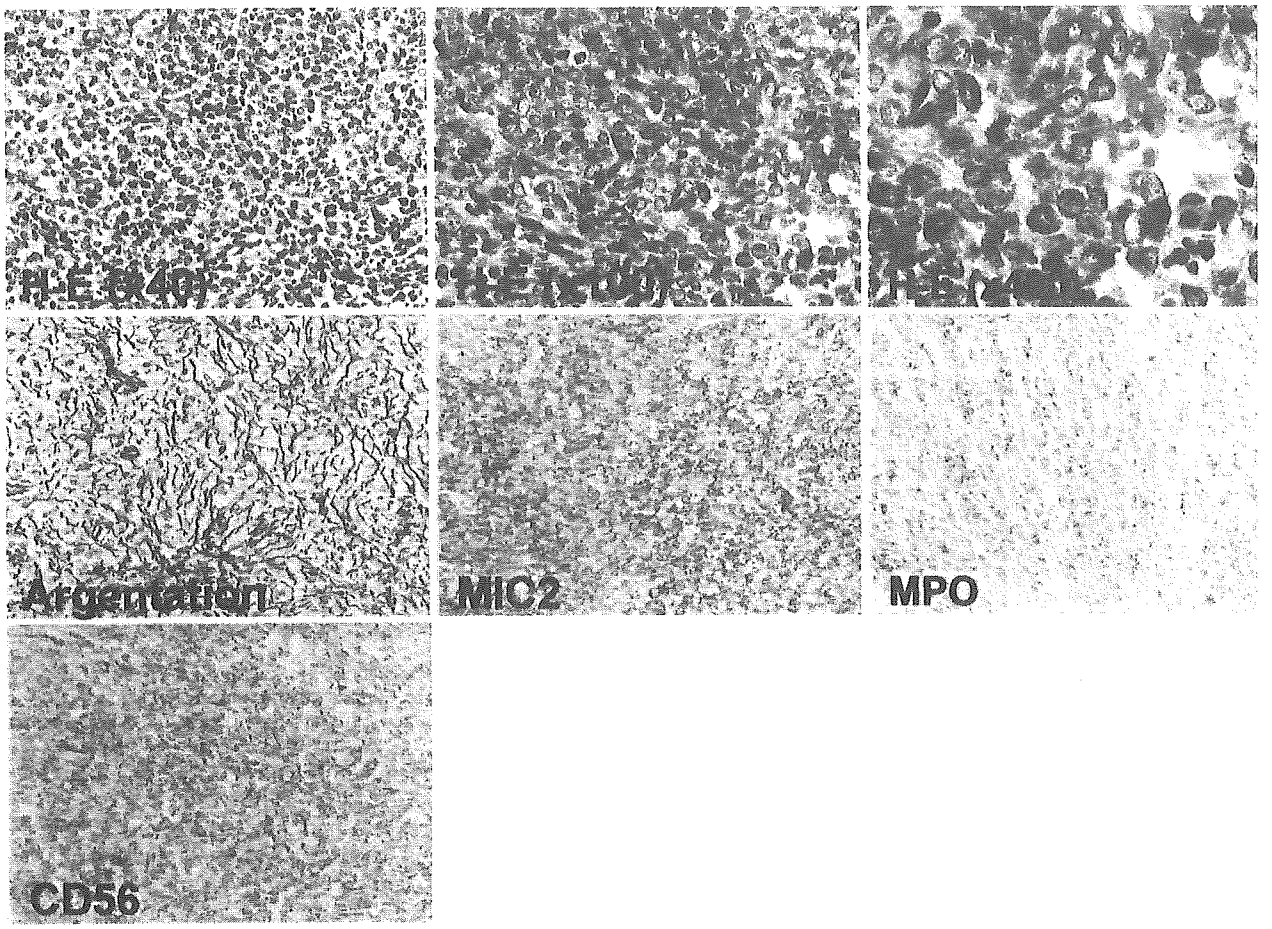

Fig. 2 Haemotoxylin and eosin and immunohistochemical staining of paraffin sections. On the stained sections, myeloid cells with round or oval nuclei, and scanty cytoplasm were generally observed. The nuclei were homogeneous, and exhibited atypia and karyomitosis. The nucleoli were obscure. On argentation, argentaffine fibres were observed twisted around the cells. On immunohistochemical-stained sections, MIC2, myeloperoxidase, CD56, and CD68 tested positive

Fig. 3 Immunohistochemical staining of acetone-fixed, fresh-frozen sections; CD13, CD33, CD45, and CD64 tested positive

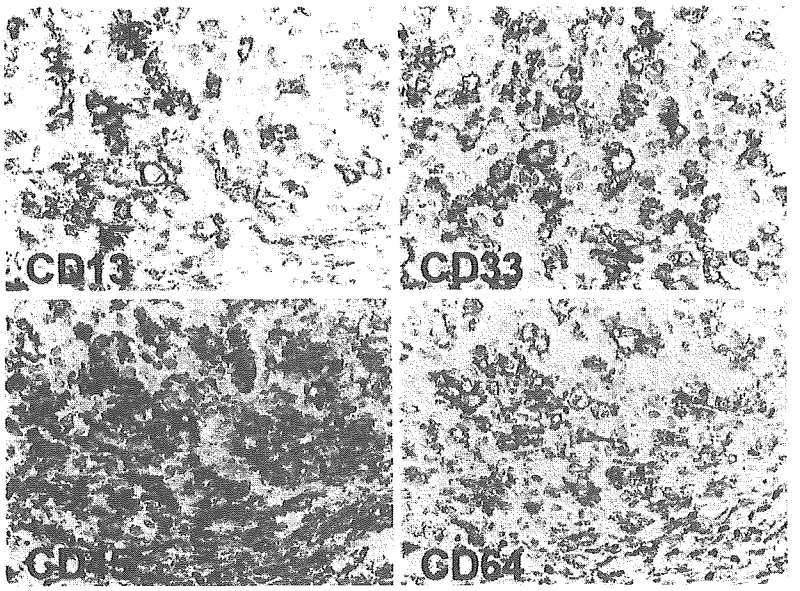

Table 1 Reported cases of GS of the spine without bone marrow involvement

No	Reference	Gender	Age (years)	Site of lesions	Treatment	Progression to leukaemia	Outcome
1	[17]	M	22	T8	Surgical decompression and radiotherapy	Negative	Death at 13 months
2	[24]	F	12	T3–T11	Surgical decompression and radiotherapy	Positive (6 months)	Death at 8 months
3	[12]	M	20	T8	Surgical decompression, radiotherapy, and chemotherapy	Positive (26 months)	Death at 43 months
4	[10]	M	33	T9–T12	Radiotherapy and chemotherapy	Negative	Survival at 14 months
5	[16]	M	21	T4–T8	Surgical decompression	Positive (29 months)	death at 29 months
6	[3]	M	13	T12–L1	Surgical decompression and radiotherapy	Negative	Survival at 72 months
7	[13]	F	29	T9–T12	Surgical decompression, radiotherapy, and chemotherapy and marrow transplantation	Positive (7 months)	Death at 1 year
8	[28]	M	31	T12–L4	Surgical decompression, radiotherapy, chemotherapy, and autologous bone marrow transplantation	Positive (32 days)	Survival at 18 months
9	[18]	M	58	T5–T8	Radiotherapy and chemotherapy	Negative	Death at 3 months
10	[8]	M	70	L2–L3	Surgical decompression, radiotherapy and chemotherapy	Negative	Survival at 3 months
11	[25]	M	49	L3–L5	Chemotherapy	Negative	Not described
12		M	36	S1	Not described	Not described	Not described
13	[23]	M	20	Less than L5	Surgical decompression, and chemotherapy	Positive (5 months)	Survival at 4 months
14	[9]	M	22	T4	Surgical decompression, radiotherapy, chemotherapy, and autologous and HLA-identical bone marrow transplantation	Positive (11 months)	Death at 29 months
15	[19]	M	22	L4–S1	Not described	Positive (4 weeks)	Not described
16	[5]	M	47	C6–C7	Surgical decompression, radiotherapy, and chemotherapy	Negative	Death at 12 months
17		M	49	L3–L4	Surgical decompression and chemotherapy	Negative	Survival at 3 months
18		M	15	L2	Surgical decompression and chemotherapy	Positive (10 months)	Death at 12 months
19	[20]	M	22	L3–S1	Radiotherapy and chemotherapy	Positive (6 weeks)	Death at 4 months
20	[15]	M	29	T2–T4	Surgical decompression, radiotherapy, and chemotherapy	Negative	Survival at 9.5 years
21	[11]	M	73	T4–T6	Surgical decompression, radiotherapy, and chemotherapy	Negative	Death at 4 months
22	[22]	M	13	T11–L1	Surgical decompression	Negative	Death at 12 months
23	[2]	F	35	C4–C5	Surgical decompression, radiotherapy, and chemotherapy	Negative	Survival at 3 months
24	[7]	M	40	S1	Surgical decompression, radiotherapy, and chemotherapy	Negative	Survival at 2 years
25		F	17	T6–T10	Chemotherapy	Negative	Survival at 2 years
26	Present case	M	2	Less than L3	Chemotherapy	Negative	Survival at 1 year

50% of these reporting back pains. Motor deficits ranging from extremity weakness to loss of bowel/bladder function (31%) or paraplegia (27%) were detected in 73% of the patients. Numbness and loss of sensation were recorded in 19% and 35% of the patients, respectively [2, 3, 5, 7, 8, 9, 10, 11, 12, 13, 15, 16, 17, 18, 19, 20, 22, 23, 24, 25,28]. If appropriate early diagnosis and early treatment are done, those symptoms can be reversible. Therefore, GS should be included in the differential diagnosis of extradural spinal cord tumours, regardless of the evidence of leukaemia.

GS is difficult to diagnose in patients without bone marrow involvement because of its rarity. Yamauchi et al. [26], Chen et al. [4], Neiman et al. [16], Eshghabadi et al. [6], and Meis et al. [13] reported that 47%, 48%, 56%, 59%, and 75% of GS patients without bone marrow involvement were initially misdiagnosed, respectively. These cases were most often misdiagnosed as lymphoproliferative disorders. In addition, small round-cell tumours, particularly in children (neuroblastoma, rhabdmyosarcoma, Ewing sarcoma/peripheral neuroectodermal tumour and medulloblastoma) must be included in the differential diagnosis [1]. Immunohistochemical methods have been reported to be helpful in establishing a diagnosis of GS [4,22]. The myelo- and/or monoblasts in GS lesions have antigenic profiles that are similar to the blasts in AML/acute monoblastic leukaemia and express myeloid- and monocytoid-associated antigens, like CD13, CD14, CD33, CD64, CD68, and c-Kit (CD117), as well as lysozyme [1]. In addition,

blasts in the GS also express leukocyte common antigen (CD45), CD43 and MIC2 (CD99). CD45 is useful for distinguishing GS from non-haematopoietic tumours but is not helpful for distinguishing GS from lymphoproliferative disorders because it is expressed in most haematopoietic tumours. CD43 is also expressed in T-cell lymphoma [14]. While MIC2 (CD99) expression has long been used as diagnostic marker for Ewing sarcoma or primitive neuroectodermal tumours; MIC2 (CD99) has also been shown to be expressed by immature myeloid cells and lymphoid cells [14,27]. C-Kit (CD117) is also highly sensitive in GS [4]. In our patient, myeloperoxidase, MIC2 (CD99), CD13, CD33, CD45, CD56, CD64, and CD68 were positive and c-Kit (CD117), CD3, CD43, and CD79a were negative. We emphasise that immunohistochemical methods are very important for the diagnosis of GS, especially the positive reaction of myeloid lineage-specific markers, such as myeloperoxidase, CD33, and CD64. Since some of these markers cannot be examined using formalin-fixed, paraffin-embedded sections, parallel examinations using acetone-fixed, fresh-frozen sections are recommended.

Although no clear relationship between specific treatment modalities and survival was found in a review of the literature [27], most GS patients without bone marrow involvement progress to AML if left untreated [5, 6,26]. In contrast, a reduced risk of developing AML was reported in GS patients without bone marrow involvement receiving chemotherapy for AML. Since early diagnosis followed by appropriate therapy may prevent leukaemic transformation in these cases, GS should be included in the differential diagnosis of extradural spinal cord tumours, regardless of the evidence of leukaemia and immunohistochemical methods are mandatory for a correct diagnosis.

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