European Review for Medical and Pharmacological Sciences 2012; 16: 977-982

A large calcified retroperitoneal extraskeletal osteosarcoma with consequent bilateral hydronephrosis

M. UCCELLO*, M. MALAGUARNERA*, M. GIORDANO*, F. LEGGIO*, V.E. CATANIA**, A.S. CONSOLI**, M. TRAINITI**

*Research Center "The Great Senescence", Senescence, Urological, and Neurological Sciences Department, University of Catania, Catania (Italy)
**Department of General Surgery, University of Catania, Catania (Italy)

Abstract. – Extraskeletal osteosarcoma (ESOS) is a rare malignant mesenchymal neoplasm that accounts for less than 4% of all osteosarcomas and approximately 1-2% of all soft tissue sarcomas. The tumor is typically located in the deep soft tissues, without attachment to skeletal bones. Although ESOS has been found to develop virtually in every organ, its most common locations are the limbs. In the case of abdominal or pelvic lesions the diagnosis can be very difficult, thus it necessarily requires confirmation after exploratory laparotomy and histopathology. Such tumors may reach enormous sizes before detection because the enlarging mass may not be associated with pain. ESOS may be one of the differential diagnoses to be considered in the case of calcified masses arising in retroperitoneal space. Here we describe a bulky, bilateral, metastatic ESOS arising from the retroperitoneum and causing obstructive uropathy with consequent hydronephrosis.

Key Words:

Osteosarcoma, Extraskeletal, Extraosseous, Retroperitoneal.

Introduction

Extraskeletal osteosarcoma (ESOS) is a rare malignant mesenchymal neoplasm that accounts for less than 4% of all osteosarcomas (OSs) and approximately 1-2% of all soft tissue sarcomas[1]. The criteria for the diagnosis of primary ESOS provided by Allan et al[2] include: its soft tissue origin and no attachment to the bone or periostium; the uniform morphological pattern of sarcomatous tissue that excludes the possibility of a mixed malignant mesenchymal tumor; the production of malignant osteoid, bone or cartilage matrix by the sarcomatous tissue. Skeletal OS is the most common primary malignant bone neoplasm which typically occurs in the metaphysis of long bones in young subjects[3] while ESOS most commonly occurs in patients older than 50 years, with a slight male predominance of 1.9:1[1,4,5]. Although it has been reported that ESOS may develop virtually in every organ, its most common locations are the limbs[5,6]. In the case of abdominal or pelvic lesions the diagnosis can be very difficult, thus it necessarily requires confirmation after exploratory laparotomy and histopathology[7,8]; such tumors may reach enormous sizes before detection, because the enlarging mass may not be associated with pain[1,8,9]. Here we describe a bulky, bilateral, metastatic ESOS arising from the retroperitoneum and causing obstructive uropathy.

Case Report

A 66-year-old woman was hospitalized for a right hypochondrium colicky pain radiating to the ipsilateral subscapularis region. The pain had appeared during the previous weeks and had persisted despite nonsteroidal anti-inflammatory medication. Moreover, it was not related to food and posture. At the anamnesis, she reported hysterectomy for fibroids six months earlier. Clinical examination showed that the patient performance status was like to be good, but the abdomen appeared swollen by the right iliac fossa because of the presence of voluminous palpable mass that was hard, fixed to the deep layers and sore to the touch. The abdominal ultrasound (US) examination revealed a liver with gallbladder stones, with normal biliary tract and without

Corresponding Author: Mario Uccello, MD; e-mail: mario_uccello@hotmail.it

space-occupying lesions in the liver parenchyma; there was also found a heterologous formation in the right iliac fossa with internal calcification, that compressed the iliac vessels, and a bilateral hydronephrosis, more marked on the right than on the left. The laboratory tests revealed a significant increase of alkaline phosphatase (ALP) 1460 U/L (normal range, 34-270 U/L), blood urea nitrogen (BUN) (196.2 mg/dl) and creatinine (7.89 mg/ml) values. The blood pressure was above 180 mmHg. The chest X-ray showed the presence of multiple metastases placed in both lung fields. Total body CT scan without contrast confirmed the presence of lung metastases, bilateral hydronephrosis, and mass in right iliac fossa invading the ureter and the iliac artery just before the subdivision. There was also a sort of mass similar to the previous one but with a reduced size in the left iliac fossa invading the psoas muscle. The internal structure of the masses was homogeneous, apart from the centrally located amorphous high-attenuation areas; this finding was consistent with calcifications. There was no fat inside the lesion. The patient underwent hemodialysis and then an exploratory laparotomy. The exploration of the abdominal cavity detected a retroperitoneal mass in the right iliac region which besides compressing the iliac vessels and infiltrating the ureter, it involved the last ileal loop. Another mass in the left iliac fossa caused a compression of the left iliac vessels and ureters without infiltration. Because of the inoperability of the mass in the right iliac region, it was performed an ileotransversostomy with enucleation of the left mass and cholecystectomy. The histological examination performed on the mass diagnosed an ESOS infiltrating the psoas muscle, the internal iliac artery and the bladder wall. Macroscopically the mass was of hard consistency, whitish-gray in color, and there were large central calcified parts and areas of hemorrhagic-necrotic tissue. It was of the osteoblastic histological type, consisting of osteoblasts producing osteoid (Figure 1). The lesional cells showed great cytological atypia, high mitotic activity and permeative growth pattern. After surgery BUN and creatinine values returned within normal limits. After the hospital discharge, which took place in the fifteenth day, the patient was sent to a Cancer Center for chemotherapy.

Discussion

ESOS is a high-grade malignant mesenchymal neoplasm with a very aggressive behavior[9]. The tumor is typically located in the deep soft tissues, without attachment to skeletal bones it is shown by the radiographic examination or the inspection performed during surgery[10]. The most common affected site is the thigh (42.3%-52%), followed by the upper extremities (11.5%), the retroperitoneum (11.5%), and the buttocks (7.7%)[1]. Moreover, in previous case reports ESOS has been shown to develop in unusual sites, such as mediastinum[11], hand[12], cerebellum[13], heart[14], skin[15], pleura[16], larynx[17], scalp[18], tongue[19], penis[20], gallbladder[21], breast[22], and mesentery[7]. The aetiology of ESOS is essentially unknown, even if cases of radiation-induced ESOS, a history of previous trauma or intramuscular injection at the tumor site and malignant transformation of myositis ossification have been reported[1,9,10,23]. In our patient there was no history of radiation or trauma, but there was an anamnestic finding of hysterectomy just six months before the diagnosis of ESOS.

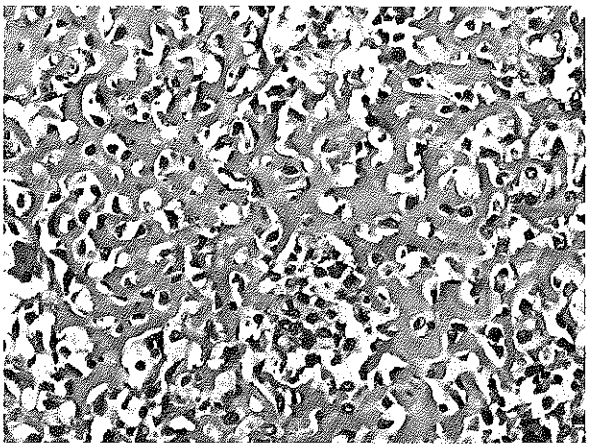

Figure 1. Round and multinucleated cells separated by osteoid material (EE 200X).

The most common presentation of ESOS is a gradually enlarging mass that not always implies pain. The size varies from 1 cm to 50 cm in diameter. Very large and bulky tumors often develop in the retroperitoneum before their detection as in our case[10]. Thus, the size is the major prognostic factor as patients with very large lesions have a worse clinical outcome. Other poor prognostic factors are the presence of metastatic lesions and the patient age[1,24,25]. An increase of ALP is often found in ESOS, and constitutes an established prognostic factor[26]. In general, the prognosis of ESOS is poor, with a 5-year overall survival rate less than 37%[5,9]. Approximately 50% of such tumors recur locally, and 60% develop lung metastasis[27]. The lung is, therefore, the primary site of metastasis although the liver, bone lymph nodes and soft tissue represent other common sites of metastases[1,9,10]. In our patient case the tumor massively invaded the abdominal cavity and metastasized in both lung fields. According to these parameters our patient was in a very poor prognostic subgroup, owing to a very bulky and high growth rate tumor that was only partially resectable, and because she was over sixty and presented multiple metastatic lesions, a multi-organ impairment and increased ALP levels. CT scan, as it was the case with our patient, typically shows large soft tissue masses with focal or massive areas of calcification, with no osseous involvement[5,9]. MR images are not specific, showing an intermediate signal intensity on T1-weighted images, and a low- to hyperintense signal on T2-weighted ones[28]. Since other neoplasms such as soft tissue sarcomas and carcinosarcoma may present wide areas of calcification[29,30] as well as ESOS may not present radiologically visible ossification, a histological biopsy is required to correctly address the diagnosis[5,9]. The histological features of ESOS are similar to those of skeletal OS though most tumors are poorly differentiated and of high grade. There are six different histological subtypes of ESOS: the most common is the osteoblastic type (1), followed by (2) fibroblastic, (3) chondroid, (4) teleangectatic, (5) small cell and (6) well differentiated ones[31]. In our patient the diagnosis of osteoblastic ESOS was confirmed by the tumor confination within the soft tissue, without attachment to the bony structures, and by the presence of abundant osteoid produced by the malignant neoplastic cells, morphologically identical to that of skeletal OS. A retroperitoneal mass with calcification has a wide range of differential diagnoses, including several benign and malignant conditions. Among the non-tumoral benign conditions, myositis ossifications represents the most difficult differential diagnosis, also because a malignant transformation of myositis ossifications into ESOS has been reported[32,33]. However, the histological examination shows the presence in ESOS of the so called "reverse zoning phenomenon", that is a central deposition of osteoid material and a typical spindle cell proliferation in the periphery, unlike in myositis ossifications where the most mature portion is located in the periphery ("zoning phenomenon")[27]. The benign neoplasms of the retroperitoneum which may calcify include ganglioneuroma, Schwannoma, paraganglioma, hemangioma and mature teratoma, that are commonly heterogeneous, while ESOS is characterized by a typical uniform sarcomatous pattern[34,35,36]. Furthermore, the highly malignant behavior shown in our case and the histological features of malignity definitely excluded such benign conditions from differential diagnosis. There are also other malignant retroperitoneal tumors which may undergo calcification, such as malignant fibrous histiocytoma, malignant mesenchymoma, dedifferentiated liposarcoma and extraskeletal mesenchymal chondrosarcoma[29,37,38,39]. Even in these cases the typical finding of a uniform sarcomatous pattern and massive calcification, along with the other clinical, radiological, histopathological and immunohistochemical findings, properly addresses the diagnosis of ESOS (Table I). The treatment of choice for ESOS consists in the amputation or in a wide surgical resection of the tumor for local control and in order to prevent a possible recurrence. Chemotherapy and radiation therapy can be combined to surgery although their role in the neoadjuvant or adjuvant therapy has not been clearly defined yet[1,2,9,10,52]. Nevertheless, classical, high-grade ESOS still remains a very aggressive rare tumor with a poor prognosis[5,9,53,54]. In our case the surgical excision of the tumor invading the left iliac fossa was merely intended to allow a functional recovery of the ipsilateral kidney, otherwise compromised by the tumor compression exerted on the ureter. Indeed, the presence of a lesion infiltrating the iliac vessels and the right ureter had brought to a serious kidney failure that certainly aggravated the prognosis, already made poor by the presence of pulmonary metastases. The surgical intervention led to the rehabilitation of the renal function with normalization of creatinine and BUN values, thus it spared the patient to undergo subsequent dialysis. Our case report is

Table I. Differential diagnosis among calcified retroperitoneal soft tissue sarcomas.

Calcified retroperitoneal mlignant soft tissue sarcoma	Diagnostic criteria
Extraskeletal osteosarcoma (ESOS)	The increase of alkaline phosphatase (ALP) is a common finding[26]. It appears as a large soft tissue mass with focal or massive central areas of calcification, with no osseous involvement[5,9]. Uniform morphological pattern of sarcomatous tissue producing osteoid, bone or cartilage matrix, identical to that one produced by skeletal osteosarcoma (OS)[2].
Malignant fibrous histiocytoma (MFH) (termed undifferentiated pleomorphic sarcoma in the current nomenclature[40])	The definition of undifferentiated pleomorfic sarcoma/MFH is very controversial; MFH would not represents a distinct clinical entity, but rather a common "morphologic pattern" shared by many neoplasms, irrespective of their differentiation[41]. Areas of necrosis, hypervascularization, hemorrage, myxomatous tissue or cystic degeneration tissue areas are within a heterogeneous mass[42,43]. The most common subtype, the storiform-pleomorphic MFH, is typically characterized by spindle cells mixed to polygonal or rounded cells, arranged in a storiform pattern[44]. It can exhibit metaplastic calcifications which are characteristically located at the periphery of the tumor[37]. MFH tumor cells typically show immunoreaction only for vimentin[41]. The diagnosis of MFH is of exclusion, it is restricted to those cases when there is not a specific line of differentiation in a pleomorfic sarcoma[40].
Dedifferentiated liposarcoma	Liposarcomas are seen as poorly demarcated infiltrative lesions that typically contain mixtures of fat and soft tissue components[45]. The feature of dedifferentiated liposarcoma is the histological coexistence of well to poorly differentiated liposarcoma and non-lipomatous differentiated areas[46]. Hyperexpression and amplification of genes MDM2 and CDK4[47].
Malignant mesenchymoma	Soft tissue tumor of mesenchymal origin composed of two or more cellular types any of which, if taken by itself, might be considered a primary malignant neoplasm, in addition to undifferentiated or fibrosarcomatous elements[48]. Each of the two or more tissue elements has to be sufficiently differentiated[49]. Malignant mesenchymoma presents as a heterogeneous mass, with various radiologic and histological features which include wide areas of calcification corresponding to an osteosarcomatous component[29].
Extraskeletal mesenchymal chondrosarcoma	It often presents a well-defined granular calcification, showing a two-component configuration composed of calcified and uncalcified tissues with comparably clear demarcation[39]. Characteristic bimorphic pattern: coexistence of nests of well-defined cartilaginous tissue and calcification within a cellular poorly differentiated small round blue cell component[50,51].

particularly intended to point out that ESOS may be one of the differential diagnoses to consider in the case of calcified masses arising in retroperitoneal space.

References

1) Bane BL, Evans HL, Ro JY, Carrasco CH, Grignon DJ, Benjamin RS, Ayala AG. Extraskeletal osteosarcoma. A clinicopathologic review of 26 cases. Cancer 1990; 65: 2762-2770.
2) Allan CJ, Soule EH. Osteogenic sarcoma of the somatic soft tissues. Clinicopathologic study of 26 cases and review of literature. Cancer 1971; 27: 1121-1133.
3) Hayden JB, Hoang BH. Osteosarcoma: basic science and clinical implications. Orthop Clin North Am 2006; 37: 1-7.
4) Lidang Jensen M, Schumacher B, Myhre Jensen O, Steen Nielsen O, Keller J. Extraskeletal osteosarcomas: a clinicopathologic study of 25 cases. Am J Surg Pathol 1998;22: 588-594.
5) Sordillo PP, Hajdu SI, Magill GB, Golbey RB. Extraosseous osteogenic sarcoma. A review of 48 patients. Cancer 1983; 51: 727-734.
6) Nagano A, Ohno T, Nishimoto Y, Yamada K, Shimizu K. Extraskeletal osteosarcoma of the thigh: an autopsy case report. Sarcoma 2009; 2009: 186565.
7) Heukamp LC, Knoblich A, Rausch E, Friedrichs N, Schildhaus HU, Kahl P, Tismer R, Schneider B, Büttner R, Houshdaran F. Extraosseous osteosarco-

ma arising from the small intestinal mesentery. Pathol Res Pract 2007; 203: 473-477.

8) Choudur HN, Munk PL, Nielson TO, Ryan AG. Primary mesenteric extraskeletal osteosarcoma in the pelvic cavity. Skeletal Radiol 2005; 34: 649-652.

9) Lee JS, Fetsch JF, Wasdhal DA, Lee BP, Pritchard DJ, Nascimento AG. A review of 40 patients with extraskeletal osteosarcoma. Cancer 1995; 76: 2253-2259.

10) Chung EB, Enzinger FM. Extraskeletal osteosarcoma. Cancer 1987; 60: 1132-1142.

11) Greenwood SM, Meschter SC. Extraskeletal osteogenic sarcoma of the mediastinum. Arch Pathol Lab Med 1989; 113: 430-433.

12) Cook PA, Murphy MS, Innis PC, Yu JS. Extraskeletal osteosarcoma of the hand. A case report. J Bone Joint Surg Am 1998; 80: 725-729.

13) Cannon TC, Bane BL, Kistler D, Schoenhals GW, Hahn M, Leech RW, Brumback RA. Primary intracerebellar osteosarcoma arising within an epidermoid cyst. Arch Pathol Lab Med 1998; 122: 737-739.

14) Schneiderman H, Fordham EW, Goren CC, McCall AR, Rosenberg MS, Rozek S. Primary cardiac osteosarcoma: multidisciplinary aspects applicable to extraskeletal osteosarcoma generally. CA Cancer J Clin 1984; 34: 110-117.

15) Riddle ND, Bowers JW, Bui MM, Morgan MB. Primary cutaneous osteoblastic osteosarcoma: a case report and review of the current literature. Clin Exp Dermatol 2009; 34: e879-880.

16) Sabloff B, Munden RF, Melhem AI, El-Naggar AK, Putnam JB Jr. Radiologic-pathologic conferences of the University of Texas M. D. Anderson Cancer Center: Extraskeletal osteosarcoma of the pleura. AJR Am J Roentgenol 2003; 180: 972.

17) Sanaat Z, Mohammady G, Esmaili H, Emrani M, Dolatkhah R. Osteosarcoma of the larynx. Arch Iran Med 2009; 12: 499-502.

18) Pillay P, Simango S, Govender D. Extraskeletal osteosarcoma of the scalp. Pathology 2000; 32: 154-157.

19) Loyzaga JM, Fernandez Machin P, Sala J. Osteogenic sarcoma of the tongue. Case report and review of the literature. Pathol Res Pract 1996; 192: 75-78; discussion 79-80.

20) Sacker AR, Oyama KK, Kessler S. Primary osteosarcoma of the penis. Am J Dermatopathol 1994; 16: 285-287.

21) Olgyai G, Horváth V, Banga P, Kocsis J, Buza N, Oláh A. Extraskeletal osteosarcoma located to the gallbladder. HPB (Oxford) 2006; 8: 65-66.

22) Murakami S, Isozaki H, Shou T, Sakai K, Yamamoto Y, Oomori M, Toyoda H. Primary osteosarcoma of the breast. Pathol Int 2009; 59: 111-115.

23) Fang Z, Matsumoto S, Ae K, Kawaguchi N, Yoshikawa H, Ueda T, Ishii T, Araki N, Kito M. Postradiation soft tissue sarcoma: a multiinstitutional analysis of 14 cases in Japan. J Orthop Sci 2004; 9: 242-246.

24) Silver SA, Tavassoli FA. Primary osteogenic sarcoma of the breast: a clinicopathologic analysis of 50 cases. Am J Surg Pathol 1998; 22: 925-933.

25) Wurlitzer F, Ayala L, Romsdahl M. Extraosseous osteogenic sarcoma. Arch Surg 1972; 105: 691-695.

26) Narayanan S. Alkaline phosphatase as tumor marker. Ann Clin Lab Sci 1983; 13: 133-136.

27) Weiss SW, Goldblum JR. Extraskeletal osteosarcoma. In: Weiss SW, Goldblum JR, eds. Enzinger and Weiss's soft-tissue tumors, 4th ed. St. Louis: Mosby; 2001.

28) Varma DG, Ayala AG, Guo SQ, Moulopoulos LA, Kim EE, Charnsangavej C. MRI of extraskeletal osteosarcoma. J Comput Assist Tomogr 1993; 17: 414-417.

29) Choi JE, Chung HJ, Yoo WJ, Chung MH, Sung MS, Lee HG, Park IY, Kim J. Retroperitoneal malignant mesenchymoma: a case of mesenchymal mixed tumor with osteosarcoma, leiomyosarcoma, liposarcoma and fibrosarcoma. Korean J Radiol 2002; 3: 264-266.

30) Yamamoto Y, Ojima H, Shimada K, Onaya H, Hiraoka N, Mizuguchi Y, Kosuge T, Kanai Y. Long-term recurrence-free survival in a patient with primary hepatic carcinosarcoma: case report with a literature review. Jpn J Clin Oncol 2010; 40: 166-173.

31) Rosenberg AE, Heim S. Extraskeletal osteosarcoma. In: Fletcher CDM, Unni KK, Mertens F, eds. Pathology & genetics of tumors of soft tissue and bone. Lyon: IARCPress; 2002.

32) Ackerman LV. Extra-osseous localized non-neoplastic bone and cartilage formation (so-called myositis ossificans): clinical and pathological confusion with malignant neoplasms. J Bone Joint Surg Am 1958; 40-A: 279-298.

33) Wilson JD, Montague CJ, Salcuni P, Bordi C, Rosai J. Heterotopic mesenteric ossification ("intraabdominal myositis ossificans"): report of five cases. Am J Surg Pathol 1999; 23: 1464-1470.

34) Nishimura H, Zhang Y, Ohkuma K, Uchida M, Hayabuchi N, Sun S. MR imaging of soft-tissue masses of the extraperitoneal spaces. Radiographics 2001; 21: 1141-1154.

35) Rha SE, Byun JY, Jung SE, Chun HJ, Lee HG, Lee JM. Neurogenic tumors in the abdomen: tumor types and imaging characteristics. Radiographics 2003; 23: 29-43.

36) Secil M, Mungan U, Yorukoglu K, Dicle O. Case 89: Retroperitoneal extraskeletal osteosarcoma. Radiology 2005; 237: 880-883.

37) Ko SF, Wan YL, Lee TY, Ng SH, Lin JW, Chen WJ. CT features of calcifications in abdominal malignant fibrous histiocytoma. Clin Imaging 1998; 22: 408-413.

38) Okuda I, Ubara Y, Okuda C, Fujii T, Suwabe T, Kokubo T, Nakajima Y, Hashimoto M. A large calcified retroperitoneal mass in a patient with chronic renal failure: liposarcoma with ossification. Clin Exp Nephrol 2010; 14: 185-189.

39) Hashimoto N, Ueda T, Joyama S, Araki N, Beppu Y, Tatezaki S, Matsumoto S, Nakanishi K, Tomita Y, Yoshikawa H. Extraskeletal mesenchymal chondrosarcoma: an imaging review of ten new patients. Skeletal Radiol 2005; 34: 785-792.

40) Fletcher CD. The evolving classification of soft tissue tumours: an update based on the new WHO classification. Histopathology 2006; 48: 3-12.

41) Al-Agha OM, Igbokwe AA. Malignant fibrous histiocytoma: between the past and the present. Arch Pathol Lab Med 2008; 132: 1030-1035.

42) Ros PR, Viamonte M Jr, Rywlin AM. Malignant fibrous histiocytoma: mesenchymal tumor of ubiquitous origin. AJR Am J Roentgenol 1984; 142: 753-759.

43) Kitajima K, Kaji Y, Morita M, Okuda Y, Sugimura K. Malignant fibrous histiocytoma arising from the renal capsule. Magn Reson Med Sci 2003; 2: 199-202.

44) Matushansky I, Charytonowicz E, Mills J, Siddiqi S, Hricik T, Cordon-Cardo C. MFH classification: differentiating undifferentiated pleomorphic sarcoma in the 21st Century. Expert Rev Anticancer Ther 2009; 9: 1135-1144.

45) Henricks WH, Chu YC, Goldblum JR, Weiss SW. Dedifferentiated liposarcoma: a clinicopathological analysis of 155 cases with a proposal for an expanded definition of dedifferentiation. Am J Surg Pathol 1997; 21: 271-281.

46) Tateishi U, Hasegawa T, Beppu Y, Satake M, Moriyama N. Primary dedifferentiated liposarcoma of the retroperitoneum. Prognostic significance of computed tomography and magnetic resonance imaging features. J Comput Assist Tomogr 2003; 27: 799-804.

47) Kind M, Stock N, Coindre JM. Histology and imaging of soft tissue sarcomas. Eur J Radiol 2009; 72: 6-15.

48) Stout AP. Mesenchymoma, the mixed tumor of mesenchymal derivatives. Ann Surg 1948; 127: 278-290.

49) Enzinger FM, Weiss SW. Malignant soft tissue tumors of uncertain type. In: Enzinger FM, Weiss SW, eds. Soft tissue tumors, 3rd ed. St. Louis: Mosby; 1995.

50) González-Cámpora R, Otal Salaverri C, Gomez Pascual A, Hevia Vazquez A, Galera Davidson H. Mesenchymal chondrosarcoma of the retroperitoneum. Report of a case diagnosed by fine needle aspiration biopsy with immunohistochemical, electron microscopic demonstration of S-100 protein in undifferentiated cells. Acta Cytol 1995; 39: 1237-1243.

51) Wehrli BM, Huang W, De Crombrugghe B, Ayala AG, Czerniak B. Sox9, a master regulator of chondrogenesis, distinguishes mesenchymal chondrosarcoma from other small blue round cell tumors. Hum Pathol 2003; 34: 263-269.

52) Patel SR, Benjamin RS. Primary extraskeletal osteosarcoma–experience with chemotherapy. J Natl Cancer Inst 1995; 87: 1331-1333.

53) Ahmad SA, Patel SR, Ballo MT, Baker TP, Yasko AW, Wang X, Feig BW, Hunt KK, Lin PP, Weber KL, Chen LL, Zagars GK, Pollock RE, Benjamin RS, Pisters PW. Extraosseous osteosarcoma: response to treatment and long-term outcome. J Clin Oncol 2002; 20: 521-527.

54) Goldstein-Jackson SY, Gosheger G, Delling G, Berdel WE, Exner GU, Jundt G, Machatschek JN, Zoubek A, Jürgens H, Bielack SS; Cooperative Osteosarcoma Study Group COSS. Extraskeletal osteosarcoma has a favourable prognosis when treated like conventional osteosarcoma. J Cancer Res Clin Oncol 2005; 131: 520-526.