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Case Report

Successful Treatment of a Very Rare Angiosarcoma Involving the Lumbar Spine Via En-Bloc Resection and Radiotherapy: Case Report

Çok Nadir Bir Lomber Omurga Anjiosarkomunun En-Blok Rezeksiyon ve Radyoterapi ile Başarılı Tedavisi: Olgu Sunumu

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ABSTRACT

Angiosarcomas are rare malignant vascular tumors that comprise only approximately 2% of all soft tissue sarcomas. They are mainly located in the head and neck area and spinal involvement is particularly very uncommon, reported only in occasional case reports or as single cases as part of a clinical series. There is therefore limited data in the literature regarding the optimum treatment strategy. Due to the aggressive nature of these lesions total resection is challenging and the overall survival time is short. In this report the authors report the successful management of a 37-year-old male harbouring spinal angiosarcoma involving the L2 level via en-bloc resection and adjuvant radiotherapy. The patient is disease-free at the 4th year follow-up and the radiological investigations are without the evidence of local recurrence, metastasis or implant failure. En bloc resection of spinal angiosarcomas can significantly improve survival and the surgical treatment should aim for this whenever possible.

KEYWORDS: Angiosarcoma, En bloc spondylectomy, Lumbar spine, Radiotherapy, Surgery

ÖZ

Anjiosarkomlar tüm yumuşak doku tümörlerinin %2'sini oluşturan nadir, habis vasküler tümörlerdir ve özellikle baş-boyun bölgesi yerleşimlidir. Spinal yerleşimli hastalar çok nadirdir ve olgu sunumu veya klinik bir serinin parçası şeklinde bildirilmiştir. Bu nedenle en uygun tedavi stratejisi hakkında literatürde çok sınırlı veri bulunmaktadır. Bu lezyonların agresif doğası nedeniyle total çıkarımları çok zordur ve genel sağkalım süresi kısadır. Bu yazıda yazarlar L2 vertebra seviyesini tutan anjiosarkomu olan 37 yaşında bir erkek hastanın en-blok rezeksiyon ve adjuvan radyoterapi ile başarılı tedavisini sunmaktadır. Hasta 4. yıl kontrolünde sağlıklıdır ve radyolojik incelemelerde lokal nüks, metastaz veya implant başarısızlığı lehine bulgu tespit edilmemiştir. Spinal anjiosarkomların en-blok rezeksiyonu sağkalım süresini ciddi şekilde uzatmaktadır ve cerrahi tedavi mümkün olduğunca bunu hedeflemelidir.

ANAHTAR SÖZCÜKLER: Anjiosarkom, Cerrahi, En blok spondilektomi, Lomber omurga, Radyoterapi

INTRODUCTION

Angiosarcoma(AS)s are uncommon malignant vascular tumors that comprise only approximately 2% of all soft tissue sarcomas (9). A wide variety of of anatomical locations have been described for this malignancy. The most common site of involvement is the head and neck, accounting for 37-52% of cases, followed by the extremity and the breast (5). Primary AS of bone is exceedingly rare and accounts for less than 1% of all ASs (4, 6). Their rare occurrence leads to a paucity of data in the literature and experience regarding the therapeutic management.

In this report we present the successful management of a patient harbouring a rare primary AS of the second lumbar vertebra via total *en bloc* spondylectomy and adjuvant radiotherapy.

CASE REPORT

A 37-year-old male admitted to our clinic with a history of low back pain radiating down to his right leg for four months. He did not have any weakness, numbness, bowel or bladder dysfunction. The radiological investigations including contrasted Magnetic Resonance Imaging (MRI) and Computerized Tomography (CT) scans revealed a 3.4 x 4.7 x 4.1 cm, well defined lesion centered on the right pedicle of L2 with vertebral body lytic changes, extending into the epidural space medially, right psoas anteriorly and to the paraspinal muscles laterally (Figure 1A-F). Preoperative PET CT scan showed intense, hypermetabolic L2 vertebral body mass (SUV 13.4) with no evidence of a metastasis. He underwent a CT-guided biopsy that revealed cytologic and immunohistochemical findings that were consistent with an

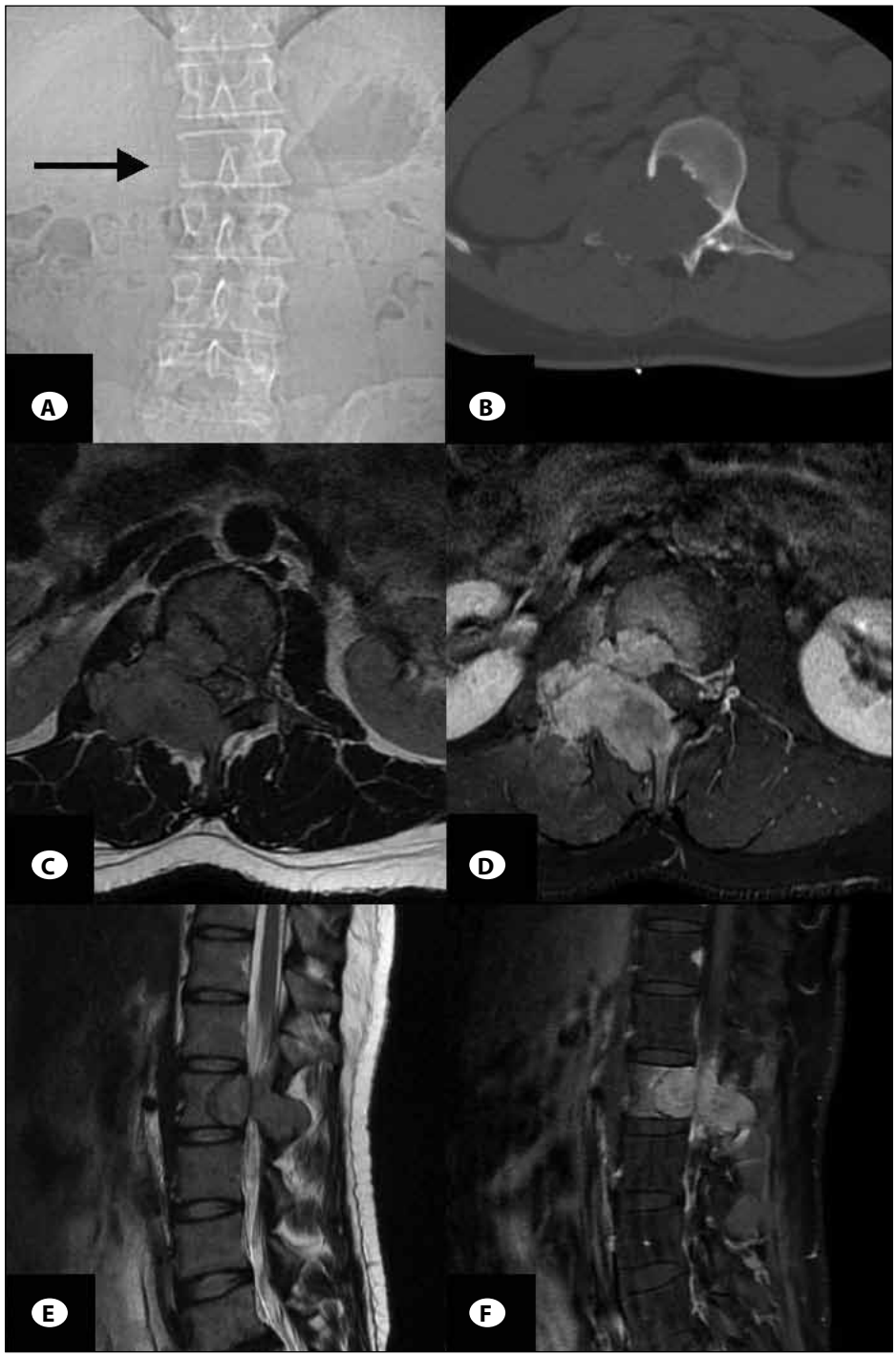

Figure 1: Preoperative **A)** AP lumbar X-ray and **B)** axial lumbar CT section showing L2 right pedicle and body lytic changes.; The axial and sagittal lumbar MRI sections with **(C** and **D**) and without gadolinium (**E** and **F**) showing a 3.4 x4.7 x 4.1 cm well defined lesion centered on the right pedicle of L2, which extends into the epidural space medially, right psoas anteriorly and to the paraspinal muscles laterally.

AS. Considering the highly vascular nature of these lesions and to minimize the blood loss a preoperative angiography and embolization is performed. Subsequently the patient was taken to the operating room by a multidisciplinary team including the neurosurgery, orthopaedics as well as vascular surgery for exposure.

Surgical Procedure

A two-staged surgery is planned. The first stage included complete discectomies and osteotomies around the L2 vertebral body to release the anterior structures via anterolateral thoracoabdominal approach. After the exposure, L2 was completely released, which required discectomy and osteotomy at L1-L2 as well as L2-L3 levels. The vessels were separated off the spine completely, and a membrane was then placed between the spine and the great vessels for safety when completing the osteotomies from the back. In addition, L3-4 and T12-L1 discectomies were performed and appropriate sized bone substitute filled cages were placed in the disc spaces as interbody devices with buttress plates

for anterior column support. The second stage included posterior stabilization and *en bloc* resection of the tumor. In prone position the right and the left paraspinal muscles were completely transected all the way out laterally and deep, connecting into the prior transection from the anterior procedure. The fascia were excised approximately two inches lateral to the paraspinal muscles in order to keep the tumor as an *en bloc* resection. Next, pedicle screws were placed at T12 and L4 on both sides starting from the left. A laminectomy of L1 and L3 were performed with particular attention to stay out of the tumor. The facets were then osteotomized at L2-3 and L1-2 on both sides. The soft tissue dissection was then continued with Bovie cautery, staying outside the tumor completely and connecting fully into the anterior defect. At this point, a temporary rod was placed on the left side for stability. Next sagittal osteotomy was performed witha sharp osteotome medial to the contralateral pedicle down to the anterior cortex, allowing complete release of the specimen as en bloc. The specimen was then carefully dissected off of the dura. The contralateral L2 nerve was then ligated and clipped with a Weck clip, and then severed. At this point, the specimen was loose and was carefully delivered and rotated around the spinal canal and removed as a single piece. No violation of the tumor was identified grossly on the specimen. Then an expandable cage was then placed in position from L1-L3 for an anterior spinal fusion and rods and connectors were inserted, posterior elements are decorticated and bone substitutes are placed to complete posterior stabilization and fusion stage. There was significant dead space on the right side because of the paraspinal muscle resection and therefore the wound is closed via paraspinous muscle advancement flaps by the plastic surgery.

Postoperatively the patient was taken to the ICU in stable condition, where he slowly regained his strength. He was neurologically intact except for mild numbness in right thigh and minimally decreased right quadriceps strength. He did not have any further complications during the postoperative course. Early postoperative anterior-posterior and lateral X-ray films (Figure 2A,B) confirmed good placement of the implants and accurate localization. He underwent aggressive physical and occupational therapy, and by the time of discharge at postoperative 11th day he was ambulatory without assistance. The postoperative histopathological examination revealed a 3.7 cm high-grade AS with essentially negative margins (Figure 3A-D, 4A-F). Given the proximity of the spinal cord and cauda equina to the tumor bed, a focused radiation therapy with CyberKnife was planned. Therefore the patient received 2500 cGy in five fractions to the 42% isodose line. The gross tumor volume received 3000 cGy. The patient was followed up in three months interval in the first year and 6 months intervals thereafter. At the 4th year follow up he is healthy and there was no hardware failure on anterior-posterior and lateral X-ray films (Figure 2C,D). Control radiological investigations including PET CT scan, thorax and abdomen CT, lumbar CT and MRI so far showed no evidence of mass within the spinal canal or abnormal enhancement in the follow up period.

DISCUSSION

AS of bone occurs slightly more frequently in males than females and the peak incidence is in 6th decade (2, 4). It has a tendency to involve the long tubular bones but almost any bone can be affected (4). ASs involving spine are extremely rare, reported only in occasional case reports (6, 7, 10, 12) or as single cases as part of a clinical series (2, 4, 11). Merimsky et al. have reported only 1 patient with AS located in the spine among more than 3,200 patients with bone or soft tissue sarcomas referred to their institution between 1980-1996 (11). Abraham et al. reported 82 patients with a confirmed pathological diagnosis of AS over a 26-year period between

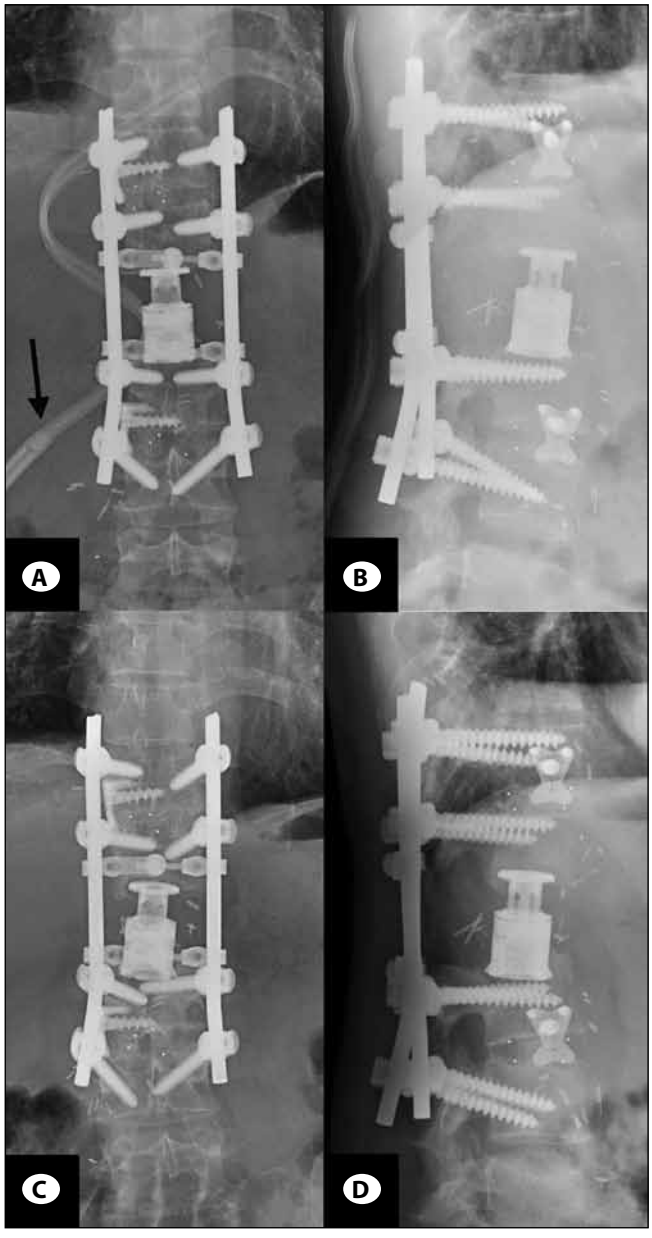

Figure 2: Early postoperative (**A** and **B)** and last follow up **(C** and **D)** AP and Lateral X-Ray films demonstrate accurate localization and appropriate hardware integrity.

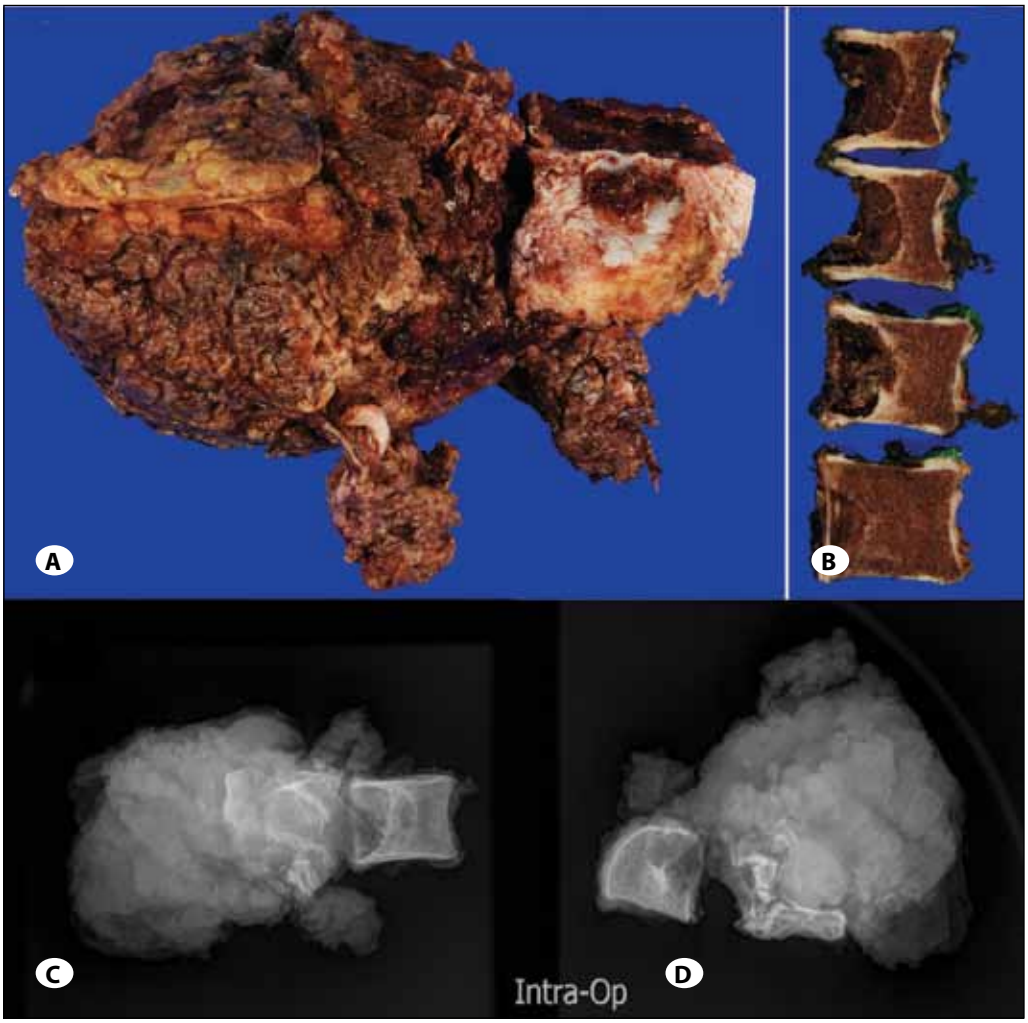

Figure 3:
A) Macroscopically the tumor was an irregular, poorly circumscribed, hemorrhagic mass with punctate fibrotic areas; **B)** The tumor had almost entirely replaced the pedicles and extended to the vertebral body in addition to the large soft tissue component; Intraoperative **C)** lateral and **D)** AP fluoroscopy images of the excised lesion.

1980 and 2006 and only 1 of them was located in the spine (2). Thus, the literature regarding the management of spinal AS is limited due to low incidence of these lesions.

The clinical features of spinal ASs relate to the anatomical sites involved and patient may present with radiculopathy, neurological deficits related to spinal cord compression or solely with dull aching pain over the affected region (4, 10). Radiological signs are not pathognomonic and share the common features of many other malignant tumors of the spine including local osteolysis and destruction, ill-defined margins, and erosion of the cortex with soft-tissue involvement. Although nondiagnostic a CT scan must be performed for evaluating the extent of bone destruction. MRI with gadolinium is mandatory for evaluating the relationship of the neural structures as well as the extent of soft tissue involvement. Preoperative angiography may be considered for showing the vascular nature of the lesion as well as for evaluating the chance of embolization that may minimize the blood loss as it was done in the present case. Nevertheless the definite diagnosis necessitates histopathological examination either after surgery or before by CT-guided biopsy. Because of multifocality and inapparent spread a CT examination of the chest, abdomen, and pelvis, bone scintigraphy and PET CT scan should be considered when the diagnosis is made (9, 10).

The terminology for malignant vascular tumors has been controversial, and it is difficult to interpret the literature. Especially the term "hemangioendothelioma" had used variably for benign, intermediate, and malignant lesions such as hemangioma, hemangioendothelioma, and AS, respectively (3). According to the latest World Health Organization classification scheme, AS is the most acceptable term for malignant vascular tumors, and the term "hemangioendothelioma" is mostly reserved for intermediate grade lesions except for epithelioid hemangioendothelioma (8). Currently accepted diagnoses for malignant vascular tumors show a range of findings from well formed to rudimentary vascular channels composed of epithelioid to spindle cells. Epithelioid hemangioendothelioma is composed of anastomosing cords and nests of bland epithelioid endothelial cells with vacuolated cytoplasm and intracytoplasmic lumina in a characteristic myxoid to hyalinized stroma. It has metastatic potential but seems to be less aggressive than conventional AS. AS is composed of complex anastomosing vessels lined by multilayered cells with slight atypia and nuclear hyperchromasia. With increasing anapla-

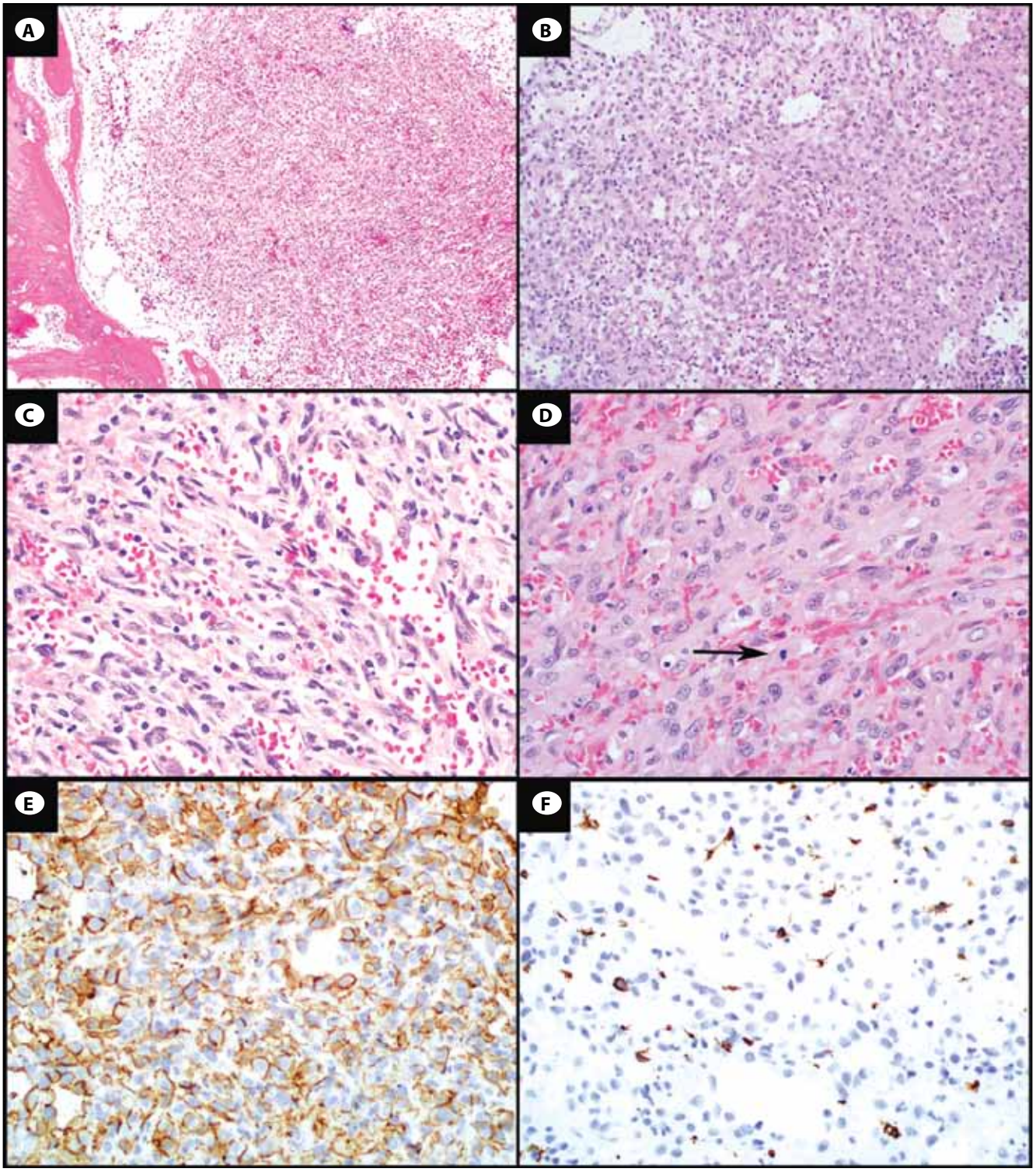

Figure 4: Histological evaluation of the biopsy and the subsequent resection revealed a malignant vascular neoplasm composed of irregular vascular channels lined by epithelioid- to spindle-shaped endothelial cells with moderate nuclear atypia. (Hematoxylin and Eosin **A)** x40, **B)** x200 and **C)** x400); **D)** There were areas of necrosis and scattered mitotic figures (arrow), (Hematoxylin and Eosin, x400); **E)** Immunohistochemical stains showed diffuse strong membranous positivity with antibodies against CD31 (x400); **F)** Rare, isolated positive tumor cells with the antibodies against CD34 (x400). Staining with epithelial, smooth muscle and neural markers were negative. The tumor showed an approximate proliferation index of 15% on Ki-67 (MIB-1) staining. Epithelioid hemangioendothelioma was excluded based on the lack of typical features such as intracellular lumina and myxohyaline stroma, and the presence of spindle cell areas. Thus the tumor was diagnosed as an angiosarcoma.

sia, tumor cells become more spindle-shaped with progressive loss of vascular channels and increased mitotic activity. Epithelioid AS is an aggressive variant of AS composed of predominantly solid areas of large rounded epithelioid cells with abundant eosinophilic cytoplasm and vesicular nuclei (8).

Like in many other primary malignancies surgical resection is the only potentially curative approach for vertebral AS. Unfortunately, wide resection of vertebra tumors is not always possible to achieve because of the anatomical relations to the spinal cord, the major vessels, and the lung (15). Incomplete resection of vertebra tumors has a high incidence of local recurrence and reduced effectiveness of surgery (14). Total spondylectomy with piecemeal resection of the tumor can result in tumor cell contamination, massive bleeding that is difficult to control and incomplete resection (1, 14). On the other hand, e*n bloc* spondylectomy promotes more complete resection of the tumor than total spondylectomy, with good control of bleeding, decreased local recurrence and possibly improve survival (6, 15). In 2004 Kawashima et al. reported the first documented example of successful treatment of AS of the thoracic spine via *en bloc* spondylectomy and adjuvant chemotherapy (6). The patient was a 48-year-old man harbouring an AS of the T8 vertebra and after *en bloc* resection and three courses of adjuvant chemotherapy consisting of ifosfamide, etoposide, doxorubicin, and cyclophosphamide he was reported to be disease free at 5th year follow up (6). The present case to the best of our knowledge represent the first successful AS of lumbar spine treated via *en bloc* resection and adjuvant radiotherapy. We also acknowledge the Sybert et al reported *en bloc* resection of a "malignant hemangioendothelioma" involving the fifth lumbar vertebral body. However, it is unclear whether this tumor represented an intermediate grade lesion or an AS using today's terminology (13).

Given the aggressive nature of these lesions and high propensity for both local recurrence and distant metastasis the prognosis is poor. In 67 soft tissue AS treated over a period of 35 years the actuarial 2 and 5 year disease free survivals were reported to be 44% and 24% respectively (9). Results with surgery or chemotherapy or radiotherapy alone have been disappointing and surgery with adjuvant radiotherapy is reported to offer the best survival (2, 9). Chemotherapy with doxorubicin or paclitaxel have been used but, no direct evidence have been found that these treatments prolongs overall survival (2, 5). Since the reported spinal AS cases are extremely rare and follow-up periods have been too short, prognosis for these lesions is still not clear. Survival after subtotal resection with adjuvant chemotherapy (Adriamycin 75 mg/m2) has been reported as 20 months (11). However the survival can be as short as 7 weeks after palliative radiotherapy alone (4).

In conclusion, *en bloc* resection of vertebral AS significantly improved survival and should be attempted whenever possible. Radiotherapy as an adjuvant therapy after surgical excision may have prevented local recurrence. Although there may be a place for chemotherapy in the management of AS, precise indications and regimens have not yet been established. The patients should be closely monitored with frequent follow-up intervals due to the risk of local recurrence and distant metastasis.

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