



Case Report

Adrenal Gland Hemangiosarcoma in a Patient with Chronic Myeloid Leukaemia

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Abstract

Hemangiosarcomas are rare tumours, predominantly affecting adult and elderly patients. Most frequently they involve the skin, although they can occur in visceral organs and other tissues. Hemangiosarcomas pursue an aggressive clinical course with high mortality rates. Primary adrenal hemangiosarcoma is extremely rare. We report a case of a 64-year-old male patient. He underwent ultrasound and computed tomography scan because of pain in his left lumbar area present over the previous 2 months. Tumor mass of the adrenal gland was found and he underwent left adrenalectomy. Macroscopically, cystic tumor that measured up to 9 cm in diameter was found. Histological diagnosis was hemangiosarcoma. The patient was being treated for chronic myeloid leukaemia for 7 years. During the time the adrenal tumor was diagnosed, he had been in remission. He died one and a half months after tumor resection because of profound bleeding in postoperative area. To our knowledge, this is the first case of a primary adrenal gland hemangiosarcoma in a patient treated for chronic myeloid leukaemia.

Keywords: Adrenal gland hemangiosarcoma, chronic myeloid leukaemia.

Introduction

Hemangiosarcomas are rare tumours, accounting for only 1% of soft tissue sarcomas. They predominantly affect adult and elderly patients. Most frequently they involve the skin although they can occur in visceral organs and other tissues. Hemangiosarcomas pursue an aggressive clinical course with high mortality rates (Meis-Kindblom and Kindblom, 1998; Deyrup et al., 2009). Primary adrenal hemangiosarcoma (PAA) is extremely rare. Here we report, to the best of our knowledge, the first case of a PAA in a patient treated for chronic myeloid leukaemia (CML).

Case Report

A 64-year-old male patient presented with pain in the left lumbar area lasting for previous 2 months. Abdominal ultrasound and computed tomography scan revealed tumour

mass of the left adrenal gland, measuring 6.5 cm in highest diameter. The tumor appeared well vascularized, dominantly solid with subcapsular necrotic areas. Laboratory tests showed no hormonal activity.

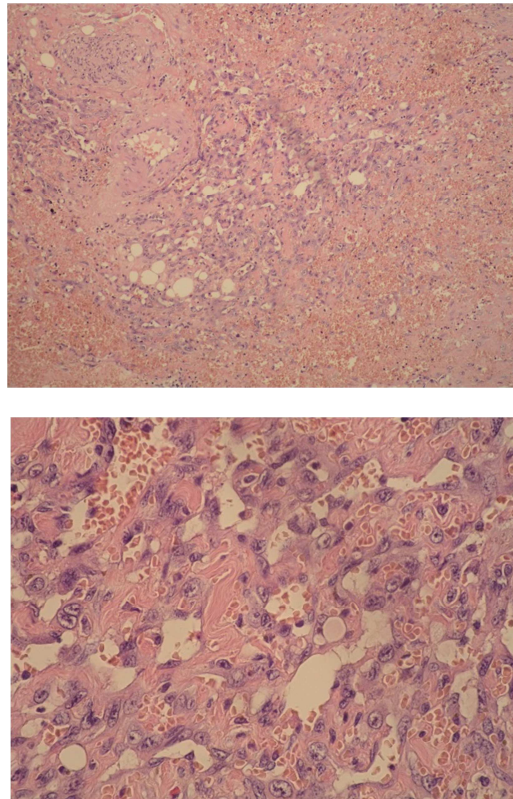
For 7 years the patient was being treated with Gleevec (Imatinib) for CML. During the time the adrenal tumor was diagnosed, he had been in cytogenetic and molecular remission (Bcr-Abl negative). He had been also treated for arterial hypertension for several years.

The patient underwent left adrenalectomy. During laparotomy 1000 ml of hemorrhagic fluid was evacuated from the tumor. There was no evidence of tumour spreading beyond the adrenal gland. The gland was removed with tumour and periadrenal fat tissue. Macroscopically, the tumour measured up to 9 cm in diameter and was cystic, filled with hemorrhagic content. The residual adrenal gland was displaced laterally (Fig. 1).



Histologically, the tumour was dominantly necrotic and hemorrhagic with areas composed of atypical, polymorphic, polygonal cells with vesicular nuclei and prominent nucleoli. Tumour cells surrounded irregular vascular spaces filled with erythrocytes (Fig. 2, 3). Up to 10 mitoses per 10 high power fields were found. Tumour cells showed

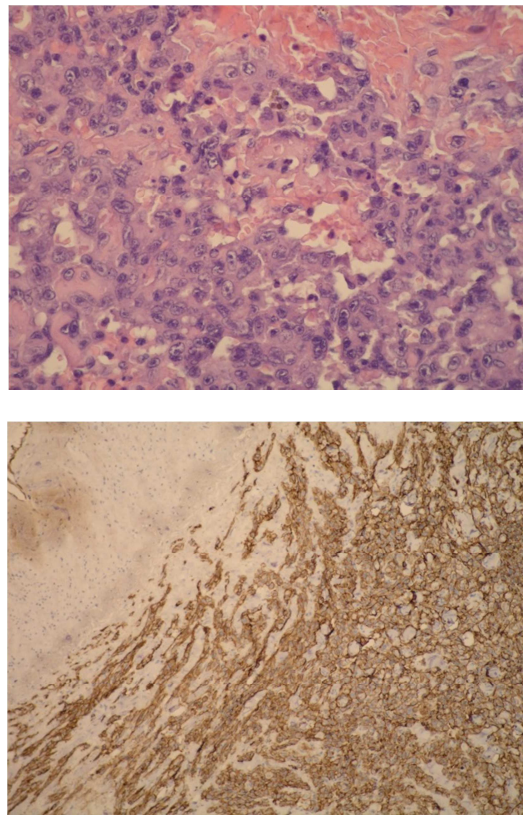
weakly positive immunohistochemical reaction for chromogranin and focal positivity for S100 and synaptophysin with negative reactions for cytokeratin, inhibin, CD31 and CD34. The rest of the adrenal gland cortex appeared normal. The tumour was suspected to be PAA.



The patient was released from the hospital but was submitted after 8 days because of pain in the postoperative field. Ultrasound and CT scan revealed left retroperitoneal hematoma. Cutaneous incision with hematoma drainage was performed. Because the bleeding didn't stop, angiography was performed with embolisation of the superior branch of the left renal artery. The patient was stable and was released for home care.

Four days later, the patient was again submitted to the hospital because of fatigue, shortness of breath, pain, anemia and hemorrhage in the postoperative area. He was treated with blood transfusions, substitution of factor XII along with supportive therapy. CT scan revealed spreading hematoma in the left retroperitoneum. Explorative laparotomy was

performed during which 2 liters of liquid blood were evacuated from the area. Upper pole of the left kidney was necrotic and there were foci of hemorrhage and organized hematomas on the omentum. Left-sided nephrectomy and omentectomy with evacuation of hematoma were performed. Macroscopically, attached to the upper pole of the kidney there was a brown, soft tumour tissue measuring up to 4 cm. Histologically, it was a residual tumour tissue as described previously but was less necrotic, forming blood vessels of different size (Fig. 4). Immunohistochemically, tumour cells were CD31 and CD34 positive (Fig. 5). Kidney was partially necrotic, without tumour infiltration. Omentum had foci of hemorrhage and necrosis with few foci of preserved tumor. Diagnosis of hemangiosarcoma was made.



The patient developed severe anemia, bilateral lung edema and hydrothorax along with hemorrhage from the postoperative wound. He was treated with supportive therapy and blood transfusions but with no response to therapy. He died 19 days after nephrectomy that was three and a half months after primary diagnosis of the adrenal tumour.

Literature Review, Discussion and Conclusion

In the studies performed by Meis-Kindblom and Kindblom (1998) and Deyrup et al. (2009), it was shown that except in the skin, hemangiosarcoma can occur in the mediastinum, breast, mesentery, deep soft tissue of upper extremity and visceral organs, usually liver. They usually present as multinodular hemorrhagic masses that range in size from a few millimeters to several centimeters in diameter. Extensive

hemorrhage is a characteristic feature of most tumours and it can mimic chronic hematoma. Although most cases are sporadic, important predisposing conditions include chronic lymphedema, exposure to toxins (e.g. vinyl chloride), and foreign bodies (e.g. arteriovenous fistulas). Association with radiation therapy was described in female patients treated for breast carcinoma (Yap et al., 2002).

According to Rosen et al. (1988), Meis-Kindblom and Kindblom (1998) and Deyrup et al. (2009), most hemangiosarcomas have a poor outcome, regardless of grade. After surgery, local recurrences develop in about one fifth of patients and one half may be expected to die within the first year after diagnosis. Older age, retroperitoneal location, large size and high Ki-67 values correlate with poor outcome. Systemic chemotherapy is usually administered in locally recurrent or metastatic disease or with less invasive

surgical approach in young patients. No optimal adjuvant chemotherapy has yet been identified.

PAA is extremely rare. To our knowledge there are 20 cases of PAA described to date in the English literature (Kareti et al., 1988; Livaditou et al., 1991; Bosco et al., 1991; Wenig et al., 1994; Otal et al., 1999; Ben Izhak et al., 1999; Krüger et al., 2001; Croitoru et al., 2001; Invitti et al., 2001; Pasqual et al., 2002; Lepoutre-Lussey et al., 2012; Derlin et al., 2012).

The first case of PAA was reported by Kareti et al. in 1988. In their case, a 54-year-old man was found to have left adrenal mass on abdominal CT scan. The tumour was surgically removed. Diagnosis of adrenal hemangiosarcoma, supported by findings of immunoperoxidase and ultrastructural studies, was made.

The largest series with 9 cases of PAA was described by Wenig et al. in 1994. In their study, patient age range was 45-85 years with most occurring in sixth and seventh decades of life with no sex predilection. The size of the tumour ranged from 6 to 10 cm in greatest dimension. Mostly it presented as an isolated adrenal mass either asymptomatic or causing non-specific symptoms like pain in the adrenal area occupied by the tumour mass as in our case, or in patients presented with slight fever, anorexia and fatigue. Three patients were alive in the time of study, three died from lung metastases and 3 others died from unrelated causes.

The youngest patient diagnosed with PAA was a 34-year old that had overt Cushing's syndrome due to ACTH-secreting pituitary adenoma and PAA described by Invitti et al. in 2001. Some patients can have symptoms similar to paraneoplastic syndrome as was described by Bosco et al. (1994).

Although most described cases of PAA appear sporadically, chronic arsenical intoxication (especially of vineyard cultivators) may be an important causative factor in the pathogenesis

of the disease as was suggested by Livaditou et al. (1991).

According to Otal et al. (1999), the radiology workup may suggest only an indistinct malignancy, since radiological features of hemangiosarcoma are nonspecific.

Definitive diagnosis of PAA, as for hemangiosarcomas that arise in other sites is based on histology and immunohistochemistry. According to Meis-Kindblom and Kindblom (1998), light microscopy findings of various atypical cells forming rudimentary vascular channels should raise suspicion for hemangiosarcoma. Immunohistochemically hemangiosarcomas express CD31 and CD34, the fact that can be helpful in confirming the diagnosis.

PAA is highly infiltrative beyond its clinically apparent borders and is often multifocal. Local control has a high failure rate. Patients usually die of extensive haemorrhage or tissue infarctions as was described by Krüger et al. (2001). In their case a 70-year-old man with PAA died 3 weeks after tumour resection due to intestinal infarction and acute renal failure. There were no distant metastases.

As for hemangiosarcomas arising in other sites, initially extensive surgical procedure with removal of whole periadrenal tissue and locoregional lymph nodes is considered to be a treatment of choice for PAA as was argued by Pasqual et al. (2002).

More extensive initial surgery was considered in a case reported by Lepoutre-Lussey et al. in 2012. They presented a 35 year-old man with combined PAA and functioning adrenocortical adenoma. The right adrenalectomy was performed with removal of periadrenal fat tissue. After histological diagnosis, the patient was suggested for another more radical operation with ipsilateral nephrectomy and psoas removal along with omentectomy. Because there was no residual disease and the young age of the patient, a conservative strategy was preferred and the patient received 4 cycles of chemotherapy

(adriamycin/ifosfamide). After 2 years he had no signs of relapse.

Chugh et al. (2009) performed the phase II trial study in which they assessed Imatinib efficacy in treating 10 different subtypes of advanced sarcomas. Among different sarcoma types there were 16 patients with stage IV (proven metastatic or locally advanced disease) hemangiosarcomas. Imatinib did not prove as an efficient drug in advanced hemangiosarcoma. In our case the patient developed PAA while treated with Imatinib for CML, so indirectly our case support findings from the described trial.

From the information available at the website eHealthMe (accessed 13 February 2013), 19753 people have been reported to have side effects when taking Gleevec (Imatinib). Among them, 2 women (0, 01%), older then 60 had hemangiosarcoma. They were taking Gleevec between 6-12 months in the time hemangiosarcoma was diagnosed. We cannot say if there is a correlation between occurrence of hemangiosarcoma and Gleevec therapy in our patient.

Our patient was first treated with adrenalectomy and removal of periadrenal fat tissue, but eventually developed complications and underwent ipsilateral nephrectomy and omentectomy. A review of the literature underlines the poor clinical outcome of PAA with most patients dying because of hemorrhage and recurrence of disease as in our case.

Radiological findings are nonspecific so the diagnosis of PAA can be made only microscopically. Because of the small number of cases described in the literature, the question remains whether relaparotomy and more radical en bloc surgical procedure should be done after histological diagnosis of PAA or some other type of treatment should be applied.

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