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Case Report

Post-Transplant Epithelioid Angiosarcoma Arising in an Arterio-venous Fistula

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Abstract

Transplant recipients are at an increased risk of developing malignancies, which are an important cause of mortality. Many risk factors are linked to the increased incidence of malignancies after transplantation including type, intensity, and duration of immunosuppression, viral infections and sun exposure. The occurrence of angiosarcoma in the Arterio-venous Fistula (AVF) site in a post-transplant patient is a rare phenomenon. It is an aggressive tumor with a high rate of local recurrence and systemic metastasis. There are no specific guidelines for the treatment. They are treated with a multimodality approach of surgery, chemotherapy and radiotherapy. We present a case of Epithelioid Angiosarcoma developed at AVF site in a patient with dual Pancreas-Renal Transplant who also had lung metastasis at the time of histologic diagnosis. The presenting symptoms were very non-specific and careful evaluation with histopathological assessment and imaging findings helped in early diagnosis and management.

Keywords: Post-transplant, Angiosarcoma, Arterio-venous Fistula.

INTRODUCTION

Post-transplant malignancies are important cause of mortality in Solid organ transplantation. Lymphoproliferative disorders, melanoma, non-melanoma skin cancers and breast cancer are few common malignancies observed after Pancreas- Kidney transplant (PKT) [1],[2]. Though rare, angiosarcomas arising from arteriovenous fistulas (AVFs) are described in renal transplant recipients with 31 cases reported so far [3]. In English literature we have come across a single case of angiosarcoma in a Pancreas and Kidney transplant recipient [4]. We discuss an interesting case of rare cutaneous presentation of Epithelioid angiosarcoma confined within an arteriovenous fistula used for haemodialysis in a dual transplant patient.

CASE PRESENTATION

A 37-year-old Juvenile diabetic lady, who had undergone pancreas and kidney transplant one month back, presented with complaints of swelling over the left cubital non-functional AV fistula site, which was used previously for dialysis. Excision of fistula was performed.

We received an encapsulated cystic nodule measuring 8 x 4 x 2.5 cm. Cut section was haemorrhagic, fleshy grey brown along with some tan grey nodules with cystic spaces and lamellated blood clots (Figure 1, a). Multiple sections had been taken and subjected for microscopic examination. Those revealed a distinct vascular tumor with large areas of haemorrhagic necrosis with cystic spaces showing blood clots (Figure 1, b). The tumour was composed of abundantly vascularized, solid alveolar pattern with areas of neovascularization and blood-filled channels (Figure 1, c). The cells were large, cuboidal, epithelioid, pleomorphic and showed occasional bizarre nuclear forms (Figure 1, d). The cytoplasm was eosinophilic and myoid. Few vacuolated "blister" cells were also seen.

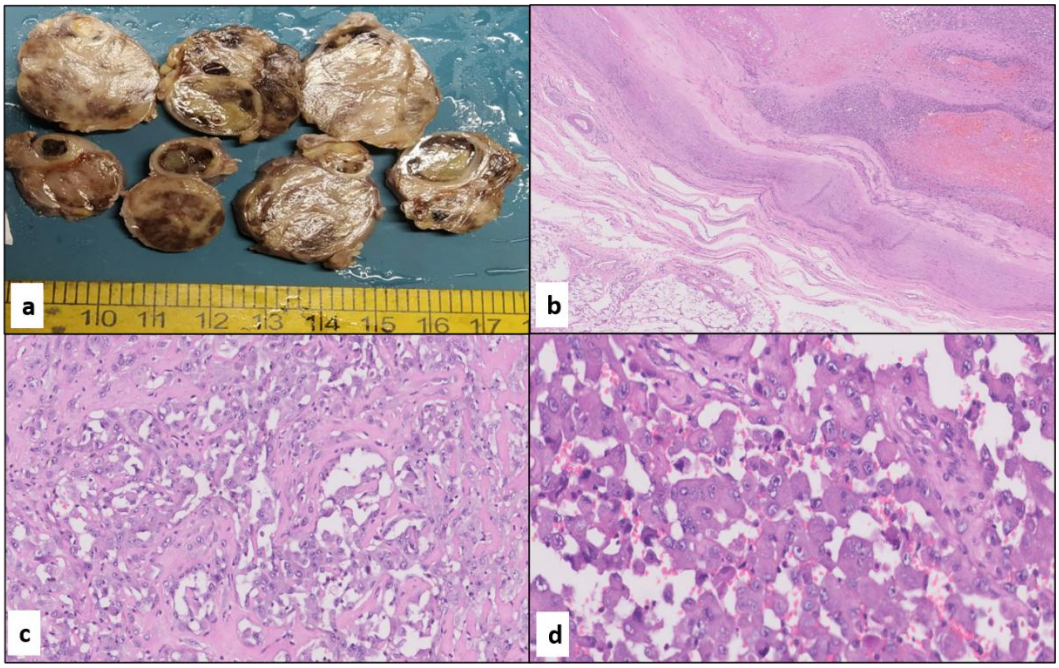

Fig-1: (a) Gross appearance of tumor with well circumscribed nodule and areas of hemorrhage and fleshy brown areas. (b) Tumor with areas of Fibrinoid necrosis (H and E × 4). (c) Solid alveolar growth pattern of tumor (H and E × 10). (d) Individual tumor cells with epithelioid morphology (H and E × 40)

Immunohistochemistry (IHC) was performed and it showed positivity for CD31, FLI1, and ERG along with high Ki67 index (Figure 2 a,b,d). CD34 and was focally positive. (Figure 2, c) Desmin, SMA, EMA and CK were Negative.

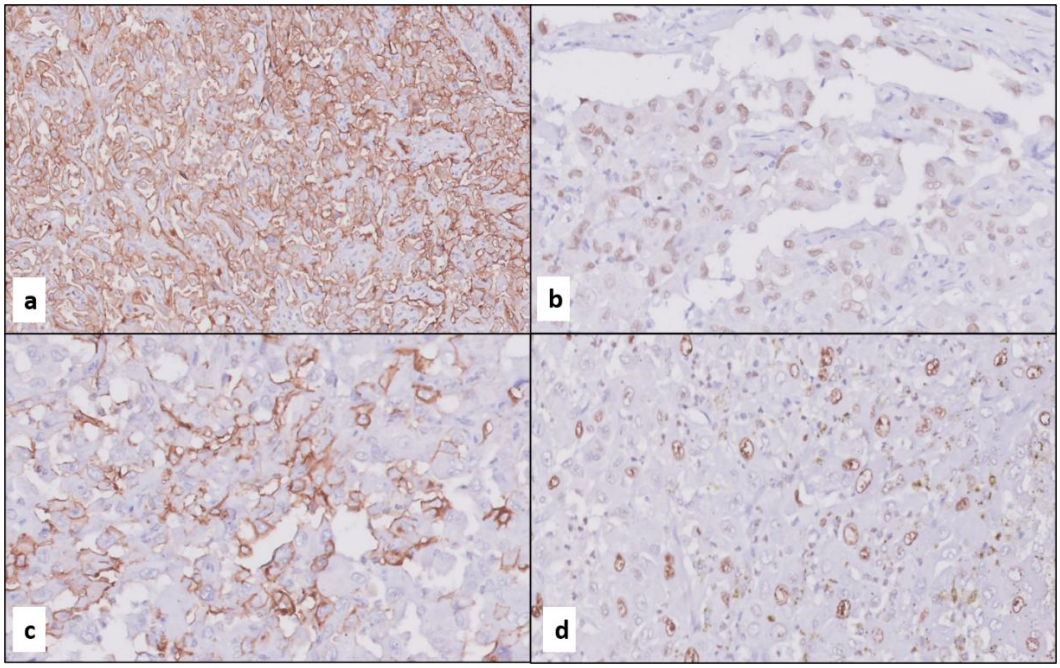

Fig-2: Immunohistochemistry (a) CD31 (x10), (b) ERG (× 40), (c) CD34 (× 40), (d) Ki67 index (× 40)

Based on the above a diagnosis of Epithelioid Angiosarcoma arising in an AV fistula site was offered, notably in a dual organ transplant case.

After that a PET-CT scan was performed which showed multiple metabolically active variably sized bronchocentric and discrete bilateral lung nodules (Left> right) with hilar lymph node enlargement and transplant kidney in left iliac fossa without any metabolically active lesion. The lung biopsy was also performed and subjected to histopathology and IHC which revealed similar tumor confirming radiologic impression of metastases. In view of unusual presentation and rarity, a second opinion was sought,

which was in agreement with our diagnosis of Epithelioid Angiosarcoma.

She was initially put on chemotherapy with Paclitaxel and within two months there was decrease and complete resolution of lung lesions; however there was increase in arm lesion, hilar nodes and new bone lesions in left humerus and hand. With this picture she was started on liposomal doxorubicin and bevacizumab.

The molecular analysis was performed which identified ERBB2 amplification, CDKN2A/B CDKN2A loss exon 1 and CDKN2B loss, alteration in KMT2C (MLL3), MLL2 and RPTOR amplification.

DISCUSSION

Post- transplant malignancy are topics of concern as studies have shown an overall two to four-fold elevated risk of cancer after the organ transplant [5]. Many risk factors are linked to the increased incidence of malignancies after transplantation such as type, intensity and duration of immunosuppression, oncogenic viral infections and sun exposure [6]. There are very few published studies available about post pancreas kidney transplant malignancies. The prevalence of malignancy in PKT has been reported as around 6 % and 8.4% in different parts of world [1]. Handful of malignancies after PKT are documented including lympho-proliferative disorders, breast cancers, melanoma, non- melanoma skin cancers, astrocytoma, prostate and bladder cancer, leiomyosarcoma, hepatocellular and small cell lung carcinoma [1, 2].

According to recent study the median time from PKT to development of denovo solid organ malignancy is 6.6 years with earliest presentation at 72 days after transplant [1]. In another study the time interval from PKT to development of malignancy has been mentioned as 1.5-73.0 months [2]. Our patient had presented with this malignancy within a month after transplant.

Occurrence of Post PKT angiosarcoma is a rare phenomenon. Angiosarcoma is an aggressive tumor with a high rate of both local recurrence and systemic metastasis, which leads to a poor prognosis [7]. The possible mechanisms for predilection for malignancy at the site of an AVF can be increased venous pressure at fistula site, oscillatory blood flow causing impaired local immune response, sheer stress at endothelium with upregulation of growth peptides and enhanced activity of DNA transcription regulators resulting in heightened proliferative response to allow vascular remodelling [8].

The most frequent symptoms in such cases were pain followed by growth of lesion, swelling or mass at the fistula site [3]. Our patient presented with pain and swelling at the fistula site. However, these symptoms are not specific and careful evaluation of them is important to get an early diagnosis.

The final and gold standard for diagnosis is histopathology and systemic imaging is important for the staging of the disease [9].

The recent review study has mentioned that nearly one half of the patients of post-transplant angiosarcoma presented with metastases at the time of diagnosis and 85% of the patients had experienced recurrence, with 7.75% in the bone and 76.95% in the lungs [4]. Our patient had lung metastasis at the time of diagnosis and then developed bone metastasis.

No specific guidelines are available for treatment of angiosarcoma. In localized angiosarcoma, radical surgery remains standard of care [10]. In high grade, deep seated and larger angiosarcomas Radiation therapy is a standard treatment [11]. The treatment of systemic disease includes supportive care, chemotherapy especially with paclitaxel and change of immunosuppressive regimen [3]. In metastasized disease chemotherapy is associated with overall reduced recurrence [12]. Our patient had undergone local excision of tumour and received a chemotherapy along with reduction of immunosuppressant doses.

In the molecular analysis, recently MYC gene amplification has been found in an angiosarcoma arising from clotted AV graft site [13].

Rarity does not exclude its presence and course. Careful consideration and evaluation of any symptoms after transplant is important for early diagnosis and treatment of such rare complications.

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