EPITHELOID HEMANGIOENDOTHELIOMA PRESENTING AS VULVA WARTS: A CASE REPORT

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Onafowokan O, Akaba G, Ekele B, Oluwole O, Abimiku B. Epithelioid Hemangioendothelioma presenting as vulva warts: A case report. Case Study and Case Report 2015; 5(2): xxxx.

ABSTRACT

Epithelioid haemangioendothelioma (EHE) is a rare vascular tumour that has been reported in several organs especially the liver and the lungs. There are no reports available on its occurrence in the vulva or oesophagus. The diagnosis is mainly histological and there are no specific treatment guidelines yet. It is said to be poorly responsive to chemotherapy and radiotherapy with surgery are the main treatment options. We report a chronically ill middle-aged HIV positive woman with duodenal nodules and vulvar warts who had a histological diagnosis of EHE. She responded well to chemotherapy while still on her antiretroviral drugs. She later had hysterectomy for persistent high grade squamous intra-epithelial lesion of the cervix. She has remained asymptomatic12 months after chemotherapy.

Keywords: Vulva warts, epithelioid haemangioendothelioma, chemotherapy, antiretroviral.

INTRODUCTION

Epithelioid haemangioendotheliomas are rare tumours that originate from the endothelial cells, most commonly in soft tissues. They present diagnostic dilemma and management challenges with relatively high case fatality rates. Treatment outcome is determined predominantly by the extent of surgical excision while response to chemotherapy and radiotherapy is said to be poor. We present a 35 years old HIV positive woman referred to the gynaecological clinic for vulva warts, diagnosed by histology and treated successfully with chemotherapy.

CASE STUDY

Miss. D.F was 35 years old Para 1^{+1} single woman whose delivery was in 1996. She presented at the Medical Out-patient department on 26/08/2011 with an 8 months history of recurrent abdominal pains, progressive weight loss, dyspepsia, dysphagia and anorexia. She also had non-projectile vomiting but no diarrhoea or symptoms of gastrointestinal bleeding. She was diagnosed as Human Immuno-deficiency Virus (HIV) positive 6 months earlier with a CD4 count of 9 cells/dL. She had been commenced on antiretroviral treatment (Nevirapine, Trurala and Efavirenz).

She had noticed a small growth hanging from her vulva 8 weeks prior to presentation. The growth was painless and non-itchy but bled easily on contact. There had been no significant increase in size.

The gastroenterologist evaluated her and performed an upper gastrointestinal (GI) endoscopy 01/10/11 based on the suspicion of gastroesophageal reflux disease. The endoscopy revealed nodular masses mostly in the stomach and duodenum which were biopsied. There were no signs of Gastro-oesophageal reflux disease. She was managed as a case of suspected gastrointestinal lymphoma and her medications included: fluconazole, cotrimoxazole, omeprazole, amitryptilline, cefuroxine, clavulinate and amoxicillin. She was then referred to the Gynaecological clinic for the vulva growth.

She had an exploratory laparotomy and salpingectomy for ruptured ectopic pregnancy in 2008 during which she was transfused with 2 units of screened whole blood. There were no complications following the salpingectomy and blood transfusion.

On physical examination, she was a middle-aged woman with sparse fluffy hair, mildly pale, afebrile, anicteric, acyanosed and not dehydrated. There were hyperpigmented macules on the left lower limb. She had no significant peripheral lymphadenopathy and no pedal oedema. She weighed 63kg and she was 1.57 meters tall (her body mass index - BMI was 25.5 kg/m^2).

Her pulse rate was 104 beats/minute, B/P was 110/70 mmHg, both heart sounds were normal and there were no murmurs. Her respiratory rate was 18 cycles/minute and her chest was clinically clear. The abdomen was full and moved with respiration. She had a well healed transverse lower abdominal scar. There was mild epigastric tenderness and the liver span was 12cm. The spleen and kidneys were not enlarged and there were no masses palpable. There was no ascites. Other systems were grossly normal.

Vaginal examination revealed a pedunculated growth on the left labia minora measuring about 4x4cm. It was non-tender but had a necrotic surface. There were similar but smaller growths on the right labia minora and the vaginal mucosa. The cervix appeared grossly normal with a parous os. A Pap smear was done. The uterus was normal sized, anteverted and mobile. The digital rectal examination was also unremarkable and the rectal mucosa was free.

A clinical diagnosis of vulva warts in an immune-compromised patient was made. The labial wart was excised and sent for histology. The Pap smear report was consistent with High grade squamous intra-epithelial lesion (HGSIL)/ Cervical Intra-epithelial Neoplasm (CIN) III that was confirmed by a colposcopy and she had a loop excision of the transformation zone. The excised loop was also reported histologically as HGSIL. Other baseline investigations done were within normal limits.

The vulva histopathology report was that of a vascular tumour of intermediate malignancy. The tumor was growing around blood vessels; it was composed of cords and small nests of round to ovoid hyperchromatic to vesicular nuclei with prominent nucleoli and scanty eosinophilic cytoplasm. The tumor cells had intra-cytoplasmic vacuoles representing small vascular lumina, and which resembled mucin. Occasional osteoclast-like multinucleated giant cells were scattered within the tumour cells while minimal mitotic figures and necrosis were noted. A diagnosis of epithelioid haemangioendothelioma (EHE) with osteoclast-like giant cells was made (see Figure 1).

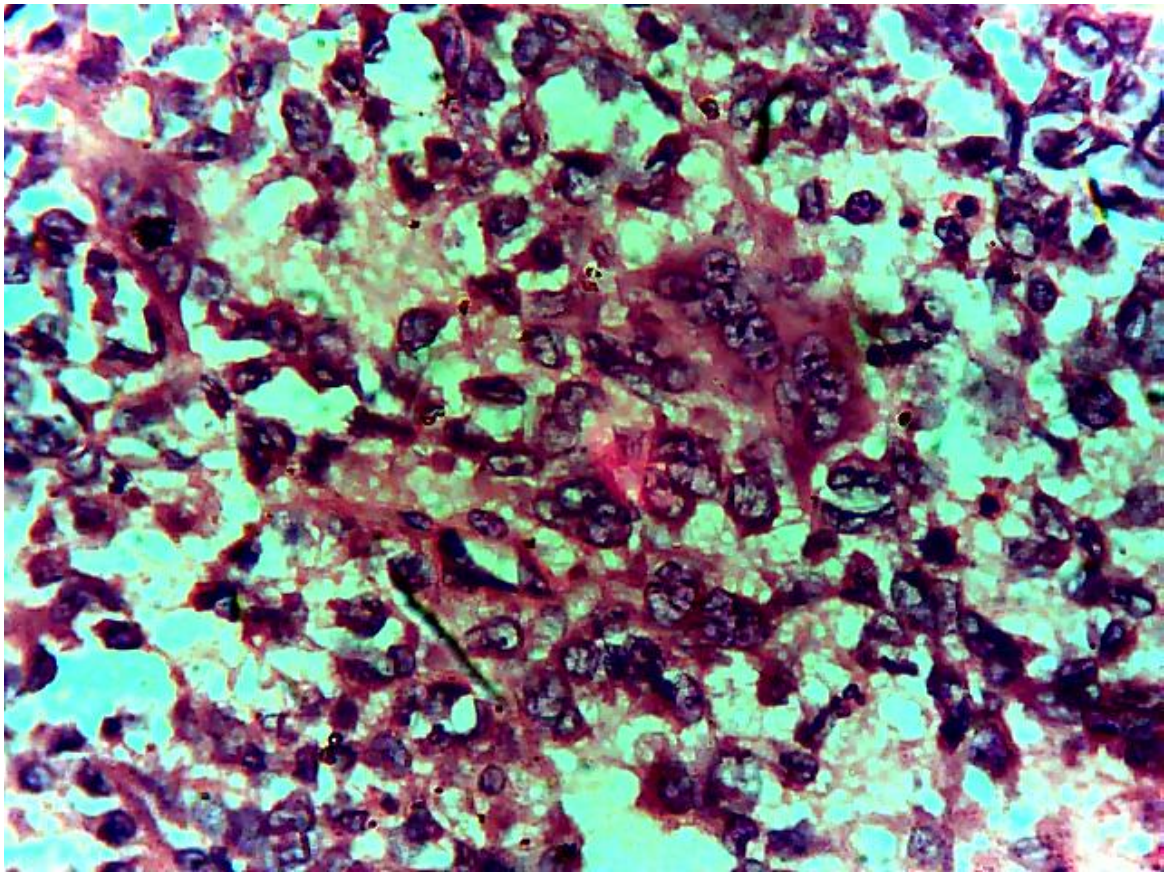

Figure 1. Histologic Section showing tumour cells having moderately pleomorphic hyperchromatic to vesicular nuclei and scanty cytoplasm. Osteoclast-like giant cell is also noted within the tumour cells.

The results were discussed with her. She was counseled on the treatment options and she consented to chemotherapy. She subsequently had 6 courses of Paclitaxel 65mg/m^2 weekly for 3weeks every month and lysosomal Doxorubicin 40mg/m^2, monthly. The chemotherapy was well tolerated and the symptoms gradually disappeared. She regained her lost weight and the vulva warts disappeared after 4 months of chemotherapy. A repeat GI endoscopy 6 months after treatment showed that the intestinal masses earlier seen had also disappeared. Her CD4 count had improved remarkably and her viral load had dropped significantly.

However, subsequent repeat colposcopy done 6 monthly showed persistent HGSIL which were confirmed by histology. Eventually a repeat biopsy on18/03/2014 reported severe dysplasia of the lining squamous cells with a focal micro-invasion of the myofibrous stroma. She then opted for total abdominal hysterectomy, which was done on 28/03/2014. The histology confirmed micro-invasion but no involvement of the vagina. Subsequent vault smears have been negative for cervical and vaginal intra-epithelial neoplasia.

DISCUSSION

EHE is a rare vascular endothelial tumour which appears slightly commoner in females [1]. The cause is unknown but oral contraceptives, vinyl chloride and biliary cirrhosis may be associated with the hepatic form [1]. None of these associations were present in this patient. It is also referred to as low-grade epithelioid angiosarcoma and has been described as an intermediary between angiosarcoma and haemangioma both clinically and histologically. The malignant form occurs as endothelial cell sarcoma of blood vessels and can arise from any site in the body. The most common sites being the liver and the lungs [2]. Epithelioid haemangioendotheliomas have been reported to occur the vulva (clitoris and labia) and as cutaneous lesions [3 - 5]. It has also been reported in the intestines [6]. However, there are no available reports of its occurrence as vulva warts or as an association of intestinal and vulva lesions. Thus, making this patient's presentation unique and unusual.

The challenges in the management of this rare condition include its atypical form of presentation, thus requiring a high index of suspicion. In this case it was not even suspected. It was an accidental discovery from tissue histology. It was masquerading as a GI tumour and vulva warts. It is not certain in this case, if the association was a form of metastases or if the two locations were primary multi focal lesions.

Even with histology, it is difficult to diagnose and may resemble close differentials like carcinoma and other epithelioid vascular neoplasms [7]. Immunostaining was used to differentiate the tumour although Zarifa and Kemal did not find immunostaining that useful [5, 8].

Histologically, the tumour appears as irregular anastomosing vascular channels, lined by endothelial cells with mucin-like intraluminal vacuoles. Both the background stroma and the cells lining the vascular channels stain positive for reticulum. Two histological subtypes are described: the epithelioid subtype which has epithelial-like cells lining the vascular channels as was demonstrated in this patient, and the spindle cell subtype which has spindle cells separating the vessels. Various criteria are used to determine if it is benign or malignant. The number of mitotic cells, hyperchromatic nuclei, presence of pleomorphism and the increased nuclear-cytoplasmic ratio in the case presented were the hallmarks of diagnosis.

Unfortunately, advanced diagnostic aids such as PET scan, CT scan and MRI were not readily available at the time of her presentation. Hence, diagnosis was based on tissue histology while metastases to other organs were excluded by basic investigations like renal function test, liver function test and chest x-ray. The associated GI lesion may have been an unusual metastases but that could not be confirmed. Human Papilloma Virus (HPV) testing was also not available but she had a Pap smear to screen for premalignant cervical lesions that may be associated with the HIV infection.

Surgical resection is the predominant mode of treatment for most EHE lesions [1, 9 - 10]. The two vulvar cases reported in literature had vulvectomy and inguinal lymphadenectomy [3 - 4]. Medical treatment of this condition can also pose serious challenges as they have been reported to be poorly responsive to chemotherapy, radiotherapy and immunotherapy. Thus, there is no standard chemotherapy treatment guideline for EHE yet, but success with drugs such as Paclitaxel, Doxorubicin, Thalidomide and interferon have been reported [11 - 13].

The choice of Doxorubicin and Paclitaxel for this patient was based on their effects on angiosarcomas and HIV associated sarcomas [12 - 13]. The absence of hepatic and pulmonary lesions in this patient may also have contributed to the success of the chemotherapy [14]. The antiretroviral drugs were continued and did not seem to adversely affect her chemotherapy. This patient eventually had total hysterectomy for the persistent high grade squamous intra-epithelial lesion (HGSIL) which transformed to early stage cervical cancer despite local excision.

CONCLUSION

Epithelioid haemangioendothelioma is a rare tumour that affects many organs and it may masquerade as vulva warts. A high index of suspicion is necessary for early detection and chemotherapy was be a useful adjunct to surgical excision.

CONSENT

A signed informed consent for publication of this case report was obtained from the patient.

COMPETING INTERESTS

The author declares that there is no competing interest.

REFERENCES

1. Mehrabi A, Kashfi A, Fonouni H, Schemmer P, Schmied BM, Hallscheidt P, Schirmacher P, Weitz J, Friess H, Buchler, MW, Schmidt J. Primary malignant hepatic epithelioid hemangioendothelioma. Cancer. 2006; 107: 2108 – 21.
2. Yousaf N, Benson C, Al-muderis O, Fisher C, Judson IR. Hemagioendothelioma, ASCO Annual Meeting (Poster presentation). J Clin Oncol. 2013; 31.
3. da Silva BB, Lopes-Costa PV, Furtado-Veloso AM, Borges RS. Vulvar epithelioid hemangioendothelioma**.** Gynecol Oncol. 2007; 105: 539 - 41.
4. Strayer SA, Yum MN, Sutton GP. Epithelioid hemangioendothelioma of the clitoris: a case report with immunohistochemical and ultrastructural findings. Int J Gynecol Pathol. 1992; 11: 234 - 9.
5. Mentzel T, Beham A, Calonje E, Katenkamp D, Fletcher CD. Epithelioid hemangioendothelioma of skin and soft tissue: Clinicopathologic and immunohistochemical study of 30 cases. Am J Surg Pathol. 1997;21:363–74.

6. Alvarez Sánchez JA, Fernández Lobato R, Coba Ceballos J, Fradejas López JM, Marín Lucas J, Moreno Azcoita M. Epithelioid hemangioendothelioma localized in the small intestine. Gastroenterol Hepatol. 1995; 18: 464 – 7.
7. Rubin BP, Tanas MR. Towards a Proper Diagnosis and Understanding of the Pathogenesis of Epithelioid Hemangioendothelioma. Available online at http:// sarcomahelp.org/research/epithelioid-hemangioendothelioma.html. [cited 2015 3/31]
8. Zarifa Y, Kemal K. CAMTA immuno staining is not useful in differentiating Epithelioid Hemangioendothelioma from its potential Mimickers. Tjpath. 2014; 30: 159 - 65.
9. Bagan P, Hassan M, Le Pimpec Barthes F, Peyrard S, Souilamas R, Danel C, Riquet M. Prognostic factors and surgical indications of pulmonary epithelioid hemangioend othelioma: areview of the literature. Ann Thorac Surg. 2006; 82: 2010 - 3.
10. Grotz TE, Nagorney D, Donohue J, Que F, Kendrick M, Farnell M, Harmsen S, Mulligan D, Nguyen J, Rosen C, Reid-Lombardo KM. Hepatic epithelioid haemangioendothelioma: is transplantation the only treatment option? HPB (Oxford) 2010; 12: 546 - 53.
11. Raphael C, Hudson E, Williams L, Lester JF, Savage PM. Successful treatment of metastatic hepatic epithelioid hemangioendothelioma with thalidomide: a case report. J Med Case Rep. 2010; 4: 413.
12. Skubitz KM, Haddad PA. Paclitaxel and Pegylated-liposomal doxorubicin are both active in angiosarcoma. Cancer 2005.104:361–366.
13. Kelly H, O'Neil BH. Response of epithelioid haemangioendothelioma to liposomal doxorubicin. Lancet Oncol. 2005; 6: 813 – 5.
14. Lau K, Massad M, Pollak C, Rubin C, Yeh J, Wang J, Edelman G, Yeh J, Prasad S, Weinberg G. Clinical patterns and outcome in epithelioid hemangioendothelioma with or without pulmonary involvement: Insights from an internet registry in the study of a rare cancer. Chest. 2011; 140: 1312 – 8.