Proximal-Type Epithelioid Sarcoma of the Vulva – Case Report

J Wee, LK Kwek, KL Chuah, YK Lim

ABSTRACT

Epithelioid sarcoma, a rare type of mesenchyme tumour and the subtype of the proximal-type epithelioid sarcoma was only described in 1997. Histological features of this tumour include a large cell size, prominent epithelioid cell component, frequent occurrence of rhabdoid features, marked cytonuclear atypia, and the absence of a granuloma-like pattern.

We report a case of proximal-type epithelioid sarcoma of the vulva in a 30 year old primiparous Malay woman. Clinical examination showed a slow growing painless mass in the right vulva that subsequently underwent excision biopsy. Histological features were typical of proximal-type epithelioid sarcoma. Immunohistochemical staining was done with EMA stained positive.

Based on our literature review, there are currently less than 30 published cases of vulvar epithelioid sarcomas in the English literature. We noted the absence of a consensus regarding the management protocol of this tumour, including on adequacy of margins and roles of lymph node dissection, radiotherapy and chemotherapy. Our patient opted for conservative therapy and declined the offer (in view of potentially inadequate margins based on the management protocol for extra-genital epithelioid sarcoma) to have a second excision of the area. In contrast, a previously reported case from KK Women's and Children's Hospital (KKH), Singapore in 2012 opted for surgery with lymph node dissection. It is important to note that long term outcome for various combinations of management options of this tumour is still uncertain at the moment and management of such rare tumours is difficult as such.

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Mr Lee Koon KWEK
Medical Student
Yong Loo Lin School of Medicine
National University of Singapore

Dr Khoon Leong CHUAH
MBBS, FRCPA, FAMS
Senior Consultant
Department of Pathology
Tan Tock Seng Hospital, Singapore

Dr Yong Kuei LIM
MBBS, MRCOG, FAMS
Senior Consultant
Department of Gynaecological Oncology
KK Women's and Children's Hospital, Singapore

Corresponding Author:
Dr Jonathan Yeow Sherng WEE
MBBS, MRCOG, M.Med
Associate Consultant
Department of Obstetrics and Gynaecology
KK Women's and Children's Hospital, Singapore
Email: jonthan@singnet.com.sg
Telephone: +65-9756 1182, +65-6293 4044, +65-8123 0994

INTRODUCTION

Epithelioid sarcoma, a rare type of mesenchymal tumour, was first established as a distinct entity by Enzinger[1] in 1970 but it was not until 1972 when the first case of vulvar epithelioid sarcoma was reported by Piver et al[2]. It was only in 1997 that the term "proximal-type" epithelioid sarcoma was coined by Guillou et al[3]. There are currently less than 30 published cases of vulvar epithelioid sarcomas in the English literature. In this report, we describe a case of proximal-type epithelioid sarcoma of the vulva seen in our hospital, and review the current literature on the subject with particular emphasis on the diagnosis and management of this tumour.

CASE REPORT

A 30 year old para 1 Malay lady with a past medical history of type 2 diabetes mellitus, as well as 1 previous lower segment caesarean section (LSCS), first presented to a polyclinic in September 2010 with a painless mass in the right vaginal wall which she noticed almost 2 years ago.

On clinical examination, a 2 cm well-circumscribed, non-tender mass was felt in the right vulva with no discharge was noted. She was referred to KKH for a gynaecological review. She then presented to our institution 2 months later with the enlarging but painless mass. Physical examination showed a smooth cystic mass of 8 cm in diameter. It was regarded as a vaginal wall cyst and plans for excision were made for 3 weeks later in the Same Day Admission (SDA). The operation was subsequently postponed as the patient was found to be pregnant.

She was then seen in the clinics 11 months later and a 10 cm smooth, non-tender right vulvar tumour around the 7 o'clock to 11 o'clock position was noted. It was not closely adherent to the underlying soft tissue. No other abnormalities were detected during physical examination. The impression was then that of a lipoma and excision biopsy of the lump was performed in November 2012.

A well-encapsulated multi-lobulated yellowish white mass was seen intra-operatively, resembling the appearance of a lipoma. It was not very vascular or erythematous and haemostasis was achieved fairly easily. The specimen was sent for evaluation in neutral buffered formalin. Gross examination revealed a 8 cm by 7 cm by 4.3 cm lobulated fatty tissue and a separate sliver of skin 10 cm by 3 cm by 1.4 cm thick. There is no haemorrhage, fibrous and myxoid area in the fatty tissue.

Microscopic features included that of proliferation of epithelioid cells with moderate nuclear atypia. Focally, rhabdoid like cells and multinucleate giant cells were seen. The lesion appeared generally well circumscribed. However, focal nodules outside the main confines of the main nodule were seen. Necrosis was not a feature and there was less than 1 mitotic figure per 10 high power fields (hpf) in most areas. The tumour had extended to the margins but not to the skin. An initial diagnosis of atypical epithelioid tumour of the vulva was made in view of the microscopic appearance, but was subsequently reviewed in lieu of further microscopic and immunohistochemical evaluation. The specimen appeared to have sheet like proliferation of cytological atypical epithelioid cells with eosinophillic cytoplasm and plump vesicular nuclei. There were focally admixed osteoclastic giant cells as well as foamy histiocytes (Figure 1).

Immunohistochemical stains were performed on the specimen. The epithelioid component showed extensive positivity for EMA and demonstrated negativity for INI-1. Stains for keratin, CD34, SMA and desmin were negative. A diagnosis of proximal-type epithelioid sarcoma of the vulva was made (Figure 2).

Due to inadequate resection margins, the patient was referred to the gynaecologic oncology unit for further treatment. Clinical examination then showed no clinically palpable inguinal lymph node and only scar dimple seen on the vulva surface.

Computed tomography (CT) of the abdomen and pelvis done post operatively showed thickening of the skin of the right vulva. Bilateral small volume inguinal lymph nodes were seen, measuring up to 1.0 cm in short axis on the right. In view of the inadequate resection margins and potential bilateral inguinal lymph nodes involvement, she was counseled for wide local excision of the vulva and bilateral lymph node dissection which she refused. A second CT scan on the abdomen and pelvis was done 5 months later in view of the patient's request for conservative treatment, and this showed no evidence of recurrence of disease or distal metastases. Patient has opted for conservative treatment, and the plan was to follow-up with the patient in 3 months' time.

DISCUSSION

Epithelioid sarcoma was first described by Enzinger[1] in 1970 after the analysis of 62 cases of tumours occurring in the extremities, except for two that grew on the scalp. It was first noted that this tumour occurs mainly in young adults (median age 23 years), grows in a nodular

or multinodular manner along fascial structures and tendons, and follows a slow chronic course. Due to its slow-growing nature, and seemingly benign appearance, it can masquerade as benign lesions, such as infectious granuloma, Bartholin cyst, fibroma, lipoma or teratoma[4]. These misdiagnoses commonly lead to a delay in implementation of treatment.

There are 2 types of epithelioid sarcoma described in the literature. The "distal-type" epithelioid sarcoma is the commonest, and occurs in the limbs, particularly hands and wrists[5]. The "proximal-type" epithelioid sarcoma (PES) is an aggressive subtype of epithelioid sarcomas first described by Guillou et al[3] in 1997 as a deep-seated soft-tissue mass growing in proximal body sites (pelvis, perineum, genitals) with distinct histological characteristics. PES behaves more aggressively, has the propensity to metastasize earlier and has a much worse prognosis than the distal-type[6]. In this case, we note that the tumour grew from 2 cm to 10 cm within a year and indeed displayed aggressive characteristics.

The macroscopic appearance of PES has been varied, but generally describing that of a firm white nodule, with or without multiple satellite nodules, with or without a necrotic, haemorrhagic focus. In both our cases, the tumour appeared as a firm whitish lump without haemorrhagic or necrotic features.

PES is described to have histological characteristics such as a large cell size, prominent epithelioid cell component, frequent occurrence of rhabdoid features, marked cytonuclear atypia, and the absence of a granuloma-like pattern[3]. However, these histological features can be easily confused with that of many other tumours, namely conventional epithelioid sarcoma, primary/metastatic poorly differentiated carcinoma, malignant extrarenal rhabdoid tumour (MERT)[7], malignant melanoma, synovial sarcoma, rhabdoyosarcoma and malignant mesothelioma[8]. Immunohistochemical studies may play a role in differentiating these tumours.

This is the second clinic case of PES of the vulva in KKH. The previous case report published by Ong et al[8] in 2012 described a patient who presented with a 1 cm painless vulva mass of 1 year duration that underwent excisional biopsy. Microscopic examination showed a nodular growth pattern with cohesive looking sheets, nests and cords of epithelioid-looking tumour cells, with pleomorphic vesicular nuclei, prominent nucleoli and eosinophilic cytoplasm.

In both cases, the specimens stained positive for EMA, negative for INI-1. However, while the specimen in our case report had a negative CD34, the previously described case had a patchy positive CD34. They were also negative for desmin and other markers used in the testing. In a study of 20 cases done by Hasegawa et al[6], all 20 cases showed positive staining for vimentin and cytokeratin. EMA was present in 85% of the cases and CD34 in 50% of the cases. They are usually negative for S100 and CD31 stainings[3]. These features are useful in differentiating them from the other possible differentials.

The management protocol of vulvar epithelioid sarcoma is still unclear, but it is widely accepted that initial management should consist of surgical excision with a wide margin (>2 cm) based on the management of extra-genital epithelioid sarcoma[9]. Adequacy of margins is a factor affecting risk of local recurrence. Epithelioid sarcomas tend to be accompanied by satellite lesions at a large distance (centimetres) from the primary tumour[10]. It is also recommended that inguinal lymph nodes be resected if they are suspicious or enlarged although there is no evidence that this has any beneficial effect on local or distal recurrence rates[11].

The role of postoperative radiotherapy is also controversial. In a study done by Argenta et al[7], adjuvant radiation therapy is recommended for high grade tumours or those with inadequate surgical margins. In the study, there was a recurrence rate of 14% in patients who received adjuvant radiation after primary surgery compared to 71% for those who did not ($p = 0.01$). There was an improvement in mortality as well, with 29% death from disease in those with radiation therapy compared with 50% in those without. As literature review reveals a consistent finding of recurrence of disease associated with mortality from disease, the role of radiotherapy in reducing the risk of recurrence can thereby reduce the risk of mortality from disease. Argenta et al reported that three-quarters of those who relapsed ultimately died from the disease[7] while Ulbright et al reported that all patients with local recurrence ultimately died from distant metastasis[12].

The role of chemotherapy has not been defined. A variety of chemotherapy regimens are currently in use and comparison is difficult to achieve. Due to the rarity of the vulvar epithelioid sarcoma cases, it is difficult to draw conclusive evidence. However, of the 14 patients with non-genital epithelioid sarcoma who received chemotherapy in a study done by Bos et al[9], no effect was seen in 9 of them, 2 were subsequently disease free

and there were varying degrees of success with the 2 who subsequently died, and 1 who survived eventually. In a study done by Argenta et al[7], of the 7 patients who tried chemotherapy as a front-line treatment, 3 were disease free at 8, 11, 21 months, while the other 4 died of disseminated disease within 8 months of disease (median 6 months). When chemotherapy was used for recurrence, only 1 patient survived more than 1 year from initiation of chemotherapy (median 3 months).

Our patient was offered wide local excision in view of inadequate surgical margins (>2 cm), and bilateral lymph node dissection was offered due to the presence of bilateral small volume inguinal lymph nodes measuring 1.0 cm in diameter. Adjuvant treatment was not offered yet as there are no clinical evidence of distal metastases or clinical evident tumour at that point in time. The option of conservative therapy was chosen despite the potential for disease progression. In comparison with the previous described case in 2012[8], the previous patient opted for a subsequent hemivulvectomy and inguinal lymphectomy, and was reported to be well with no evidence of disease recurrence 8 months post-surgery.

The 5-year survival rate for distal-type epithelioid sarcoma has been reported to be between 50-80%[13] with a worse prognosis for proximal-type in some reports. There is poorer prognosis associated with certain features. Extrapolating from extra-genital epithelioid sarcoma, a more aggressive behavior of the tumour is seen with increase in size, depth, presence of haemorrhage, necrosis, vascular invasion or mitotic figures[13]. Tumours more than 3 cm in diameter, deeply located or have focal necrosis are also associated with a worse prognosis[9]. Distal metastasis occurs in about 60% of the cases of PES[6].

In conclusion, the clinical diagnosis of proximal-type vulva epithelioid sarcoma is challenging due to the seemingly benign appearance of the lesion. The management strategy of proximal-type vulva epithelioid sarcoma can range from conservative management with imaging surveillance to aggressive treatment with lymph node clearance. As evidenced by this case, alongside the previously described case in 2012, the long term outcomes of both extremes remain unknown. There remains a lack of evidence-based standardized treatment protocols to guide management of this rare condition. It is important then to look into long-term studies to monitor the current pool of patients and the eventual outcomes of various treatment protocols employed.

Figure 1. Medium power view disclosing a proliferation of malignant epithelioid cells in the vulva mass (hematoxylin and eosin stain)

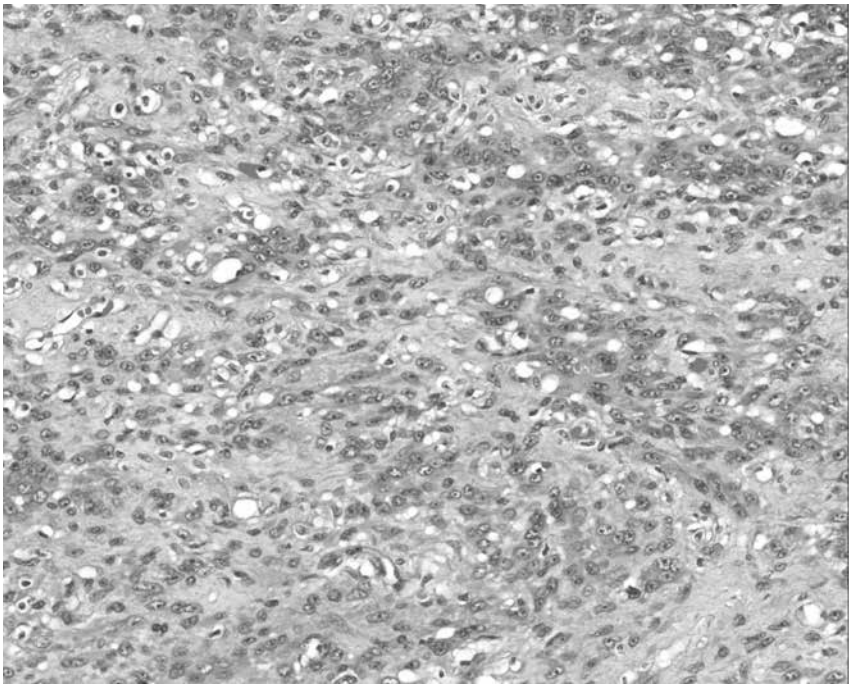
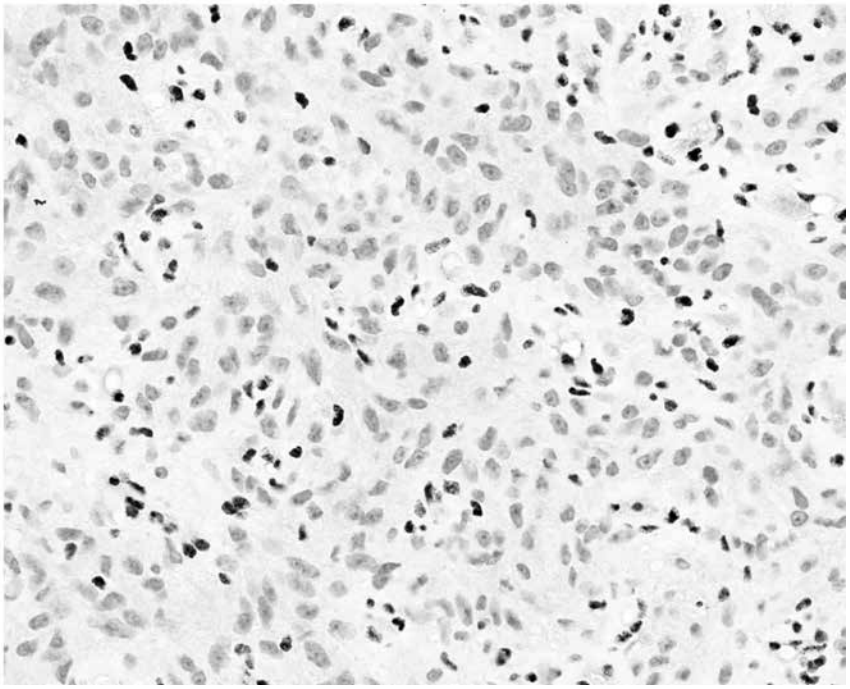


Figure 2. High power view of the immunohistochemistry stain for INI-1 showing loss of nuclear staining by tumour cells. Note the positive staining in the lymphocytes accompanying the tumour cells indicating that the stain was performing accordingly



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