Vulvar Epithelium Epithelioid Sarcoma In Pregnancy: A Case Report And Review Of Literature

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Abstract: Vulvar sarcoma is a rare neoplasm in female genital tract. We report a case of 27-year-old woman, 28-weeks pregnant presented with vulvar mass. Right hemivulvectomy with rotation flap was done during her pregnancy. Pathological diagnosis confirmed vulvar epithelium epithelioid sarcoma. No adjuvant treatment was given. She had no disease recurrence at seven years after primary surgery.

Key Words: Epithelioid sarcoma, Pregnancy tumour, Sarcoma, Vulvar

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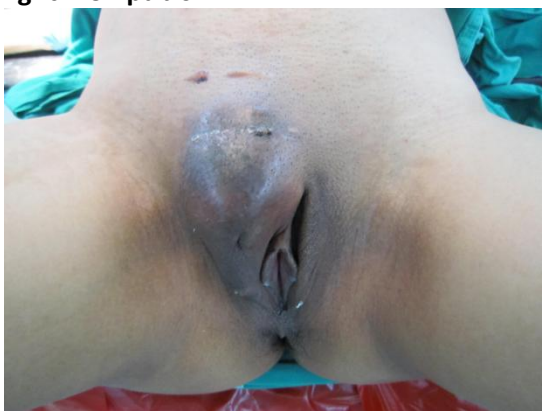
Introduction: Vulvar sarcoma is a rare neoplasm in female genital tract, which comprise approximately 1-3% of all vulvar cancers.[1] There are many different subtypes of vulvar sarcoma such as leiomyosarcomas, malignant fibrous histiocytoma, malignant rhabdoid tumour,angiosarcoma, rhabdomyosarcoma and epithelioid sarcoma. Vulvar sarcoma occurs most often in women of middle and older ages (range 20-68 years).[2] The clinical presentation are non-specific, including pain at vulvar area, vulvar mass, Bartholin's cyst or abscesses.[3]Here in, this report showed extremely rare subtype of vulvar sarcoma —epithelioid sarcoma—in pregnancy and reviewing the literature focusing on vulvar epithelioid sarcoma in pregnant women. In the past, about 20 cases have been reported as vulvar epithelioid sarcoma but only three cases reported in pregnant woman. Most of them were non-pregnant with poor prognosis. Only a few cases were totally cured. To date, there is no standard treatment guideline because the rarity of the disease [2]

Case presentation:A case of 27-year-old woman, 28-weeks pregnant presented with painless vulvar mass gradually enlarged in three months since January 2011. It located just above her right mon pubis. [Figure 1] She was referred to Division of Gynaecologic Oncology, King Chulalongkorn Memorial Hospital, Bangkok, Thailand on 15th March 2011. The obstetric ultrasound reported a single viable fetus without gross anomalies and all parameters were compatible with 28-week gestation. In addition, abdominal magnetic resonance imaging (MRI) showed a 5x6x6.6 centimetres (cm) well-defined multiloculated cystic lesion in subcutaneous layer at right mon pubis area. Excisional biopsy was performed and 5-gram of gray-white tissue was sampled. A sarcoma with epithelioid feature and smooth muscle differentiation was suspected then the immunohistochemical stains revealed positive for vimentin, SMA, MSA, EMA (focally) and negative for keratin, S100, CD31, CD34, desmin and calretinin. As this result, epithelioid leiomyosarcoma was diagnosed.

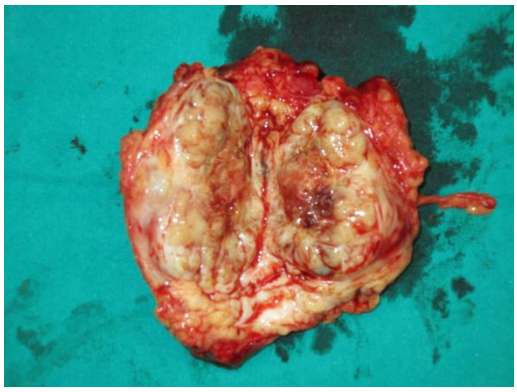
Figure 1: A 10x10 cm. slightly movable cystic mass at right mon pubis.



This case was thoroughly review of history, physical examination, and pathological report at institutional tumour board. The final consensus for definite management was radical surgery. Pre-operative chest radiography and abdominal MRI did not demonstrate distant metastasis and inguinal lymphadenopathy. The right hemivulvectomy, with rotation flap was done without perioperative complication at 33-week gestation on 19th April 2011. Total operative time was 150 minutes and estimated blood loss was 500 millilitres. Tumour was firm, well circumscribed, whirl-liked on its cut surface, measured 7x11 cm. The mass revealed heterogeneous appearance with area of haemorrhage and necrosis. [Figure 2] The tumour involved right distal vagina, right crus of clitoris and deeply invaded into inferior fascia of diaphragm. The

bilateral inguinal lymph node dissection was omitted due to absence of lymphadenopathy.

Figure 2: Gross specimen showed a 7x11 cm. firm, heterogeneous well-circumscribed tumour with whirl-liked and area of haemorrhage and necrosis on its cut surface.



Specimen section showed neoplastic cells arranged in sheets admixed with fibrocollagenous tissue. The neoplastic cells possessed oval to spindle cells, eosinophilic cytoplasm and vesicular nuclei with prominent nucleoli. Mitotic figures were frequently seen. These pathological findings confirmed epithelioid leiomyosarcoma with adequate lateral resected margin but inadequate deep-resected margin in several sections.

The pregnancy had been safely continued until gestational age of 39 weeks with spontaneous vaginal delivery. Due to the adjuvant treatments in this subtype of vulvar sarcoma is controversial, this patient decided to received no further treatment with closed follow up with pelvic examination and annual chest radiography. Five years later, she had another pregnancy and had successful vaginal delivery. Fortunately, the recurrent disease was not found at seven years after primary surgery.

Discussion: Epithelioid sarcoma is a rare malignant soft tissue tumour of mesenchymal origin.[1] It is one subtype of sarcoma, firstly reported by Enzinger F.M. in 1970.[4] Two years later, Piver et al. reported this disease in vulvar area.[5]Abnormal growth of aponeurotic structure and soft tissue spreading were main pathophysiology. [1]Molecular pathogenesis of this tumour is still incomplete understood.There are two classifications of epithelioid sarcoma, proximal type (trunk and pubic regions) and distal type (upper and lower extremities).[2]

From review literatures, the median age of patients were 36 years (range 23-80 years).[6]The most common manifestation is painless vulvar mass. Other benign conditions such as Bartholin cyst, lipoma, fibroma, dermoid cyst, and genital wart should be considered as differential diagnosis.[2]

The standard treatment guideline has been unclear. Nevertheless, an aggressive surgical management was generally recommended. Some experts strongly suggested that excision should include 2 cm from the tumour margin.[7] Moreover, a guideline of management bilateral inguinal lymph nodes was also undetermined. Kim et al. recommended that the lymph nodes dissection should be done if having lymphadenopathy on physical examination or imaging findings.[8] The macroscopic findings have various forms, shapes and colours. White-yellow discoloration were common. According to microscopic appearance, they are composed of plump spindle cells, large polygonal cells with deeply acidophilic cytoplasm.[9] Sometimes they are difficult to distinguished between epithelioid peripheral nerve sheath tumour, epithelioid leiomyosarcoma, epithelioidangiosarcoma, rhabdomyosarcoma, malignant melanoma and poorly differentiated squamous cell carcinoma. Immunohistochemical stains have a major role for determining the definite diagnosis.

In this reported case showed positive for vimentin, SMA, MSA, EMA which are muscle markers but negative for keratin, S100, CD31, CD34. Therefore, she should be diagnosed as epithelioid leiomyosarcoma. Eventhough, it is slow growing tumour, the poor prognosis was reported because pulmonary and inguinal lymph node metastasis were frequently found.[1] The recurrent risk was reported range between 42-77%. [1]Hasegawa et al. reviewed 20 cases of this tumour in 2001. They found that tumour-related mortality rate was up to 65% and proximal type of epithelioid sarcoma had worse prognosis than distal type. Interestingly, proximal type at vulvar regions may have better prognosis than other regions.

In pregnant cases, there have been only 4 cases reported since 1970 included our patient. [Table 1]

Table 1 Review of literatures of epithelioid leiomyosarcoma in pregnant women

Author	Moore et al, 2002[1]	Aydan et al, 2008[10]	Rai et al, 2009[7]	Panyavarananant et al, 2018
Age (years)	29	25	17	27
GA at diagnosis	36 weeks	6 weeks	8 weeks	28 weeks
Size of tumour	2.5x3.5 cm at vulvar Multiple bilateral lung nodule	NA	3 cm.at vulvar Multiple small nodules in bilateral lungs	7x11 cm at vulvar
GA at treatment	6 weeks - postpartum	Termination of pregnancy at 6-week gestation	8 week	33 week
Primary treatment	Radical hemivulvectomy, excision of deep vaginal fascia and the periosteal pubic rami	Clitoris-sparing wide local excision, left inguinal node dissection	Local excisional biopsy, bilateral groin lymph nodes dissection	Right hemivulvectomy with rotational flap
Adjuvant treatment	Doxorubicin (50mg/m^2)+ Ifosfamide (1.5g/m^2)	External beam radiotherapy, of 54 Gray in 30 fractions	Patient denied adjuvant treatment	No adjuvant treatment
Follow-up	6 ½ months, DOD	16 months, NED	2 months, NED	90 months, NED

GA, gestational age; NA, not available; DOD, dead of disease; NED, no evidence of disease

Although pregnant patients have significant changes in their hormonallevels and immunologic activities, the incidence of sarcoma were similarbetween pregnant and non-pregnant patients. Moore et al. illustrated that thistumour type neither express estrogen nor progesterone receptors.[1] As this result, pregnancy status does not change the outcome ofthis tumour. This reported case in pregnant womenshowed very excellent oncological outcomes with longest follow-up time. Despite of the largesttumour size and absence of adjuvant treatment, the treatment result has beenstill excellent. However, our report is the exceptionalcase. In the future, more research andexperiment that aim to study of pathophysiology and tumour progression may beclearly established.

Conclusion:

The epithelioid sarcoma of vulva is extremely rare disease. Pathological diagnosis and immunohistochemical stains confirmation are essential. Nowadays, the standard treatment is still unclear. The aggressive surgical treatment is strongly recommended. However, the adjuvant therapies have been widely debated.

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