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Vulval cancer in pregnancy: Two case reports

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ABSTRACT

Vulval cancer is rare in women of reproductive age. We report two cases of vulval squamous cell carcinoma (VSCC) in pregnancy. They presented with a solitary labial mass, at 20 and 21 weeks of gestation, diagnosed as stage 1B VSCC based on clinical examination and cross-sectional imaging. In the first case, the patient underwent close clinical surveillance whilst pregnant and had an elective caesarean section at 39 weeks of gestation. Two months post-partum she underwent a radical anterior vulvectomy and bilateral groin sentinel lymph node biopsy. In the second case, the patient underwent an anterior vulvectomy at 33 weeks of gestation followed by a vaginal delivery at 37 weeks of gestation. Six weeks post-natally she had bilateral groin sentinel lymph node biopsies. We conclude that surgical resection is safe during pregnancy under spinal anaesthesia but it can be deferred until the post-partum period if the cancer presents at early stage.

1. Introduction

Vulval squamous cell carcinoma (VSCC) is a rare disease, accounting for just 6% of all gynaecological malignancies in the UK [1]. It typically affects the elderly population, with three-quarters of cases occurring among women over the age of 60 years and just 10% diagnosed in women of child-bearing age [1,2]. VSCC pathogenetic risk factors primarily include vulval intraepithelial neoplasia (VIN), the known precursor to VSCC. Differentiated VIN (dVIN) occurs more commonly in older women and is associated with p53 mutations and lichen sclerosis (LS), a chronic inflammatory dermatosis. The classical or usual VIN (uVIN) subtype is more prevalent among younger women and is related to smoking and human papilloma virus (HPV) infection [3]. As such, the incidence of VSCC in young women is most likely due to the increased risk of HPV-associated VIN. In addition, early-onset LS predisposes women to VSCC development in their twenties and thirties [3–7].

Surgical resection is the gold-standard treatment for localised VSCC. Depending on the size and location of the lesion, either a radical local excision or vulvectomy aims to completely remove the primary tumour along with disease-free margins [3]. As VSCC initially metastasizes to the groin lymphatics, and up to a third of women with locally limited VSCC are found to have nodal involvement [8], inguinal lymph node treatment has significant prognostic implications [9,10]. Thus, inguinal node staging is required when the primary tumour size is ≥2 cm or invasion depth > 1 mm (International Federation of Gynecology and Obstetrics (FIGO) stage 1B) [3,11]. This consists of sentinel lymph node dissection (SLND) or inguinal lymphadenectomy depending on tumour size, location and radiological suspicions of lymph node involvement [3].

Due to the clinicopathological factors associated with VSCC, diagnosis in pregnancy is rare [12], and therefore management is unclear, with no definitive guidelines [13]. Here we report two cases of VSCC diagnosed in pregnancy at our tertiary gynaecological cancer centre.

2. Case 1

A 32-year-old woman, with a chronic history of early-onset LS, presented at 20 weeks of gestation during her second pregnancy with a one-centimetre mass on her right labia minora. There was no clinical or radiological suspicion of groin node involvement. A punch biopsy diagnosed well differentiated (grade 1), multifocal, FIGO stage 1B VSCC alongside dVIN. Upon review by the multidisciplinary team, it was decided that surgical intervention should be undertaken in the postnatal period. Antenatal surveillance by the gynaecological oncology team detected no signs of disease progression and, despite having previously had a normal vaginal delivery, an elective caesarean section was performed at 39 weeks of gestation to avoid the risk of perineal tears that could potentially complicate the planned tumour resection.

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Two months post-partum, she underwent radical anterior hemivulvectomy with right inguinal sentinel lymph node biopsy. Histological examination confirmed that the tumour had been completely resected with no residual disease and the sentinel lymph node biopsy did not show any metastasis. She was followed up regularly, at least three times a year, and her LS was treated with short courses of potent topical steroids whenever the condition flared.

Unfortunately, she developed a recurrence at a different site to the original tumour, with a biopsy confirming moderately differentiated (grade 2) VSCC with dVIN and a depth of invasion >1 mm. She underwent a radical anterior vulvectomy with bilateral groin lymphadenectomies. The cancer was completely resected and there was no metastasis detected in both her inguinal lymphatics. Subsequently, she underwent a modified Fenton's vestibulectomy with perineoplasty as part of reconstruction surgery to improve sexual function and was started on twice-weekly maintenance topical steroid, 0.05% clobetasol proprionate, for her residual LS.

3. Case 2

A 42-year-old woman presented with discomfort and erythema to the upper right labia majora at 21 weeks of gestation in her eighth pregnancy. After seven previous normal vaginal deliveries, she had no medical comorbidities and no history of vulval disease. A biopsy diagnosed FIGO stage 1B VSCC on a background of LS and dVIN. A magnetic resonance imagining (MRI) scan of her pelvis and groin detected a 1.6 cm focus within the right vulva, but no evidence of tumour invasion into the adjacent bony pelvis or musculature and no enlarged pelvic or groin lymph nodes.

Following discussion by the multidisciplinary team, excision of the lesion was scheduled for 33 weeks of gestation, followed by groin node excision in the post-natal period. The operating team liaised with obstetricians and neonatologists to ensure a suitable plan was in place: surgery would be performed with a midwife and neonatal resuscitaire present in case of spontaneous pre-term labour, and cardiotocography would be undertaken prior to and following the operation. Despite being offered antenatal steroid protection, the patient declined due to the relatively small risk of pre-term delivery caused by the surgical intervention.

An uncomplicated anterior vulvectomy was performed under spinal anaesthesia, with incisions away from the vaginal opening and urethral meatus. Histopathological inspection confirmed well differentiated (grade 1) FIGO stage 1B VSCC; surgical margins were clear of disease and there was no evidence of lymphovascular space invasion. Despite initially suffering with wound breakdown, which was managed with oral antibiotics, the vulval wound healed well and the patient had a successful vaginal delivery at 37 weeks of gestation.

A computer tomography (CT) scan performed eight weeks after delivery showed no inguinal lymphadenopathy. Bilateral sentinel lymph node biopsies were undertaken two weeks later and found no metastatic disease within the nodes. Unfortunately, the left groin wound dehisced, requiring packing and vacuum-assisted closure (VAC), but the patient otherwise recovered well, with no sign of disease recurrence during her follow-up. She is now on maintenance topical corticosteroid twice weekly for her LS.

4. Discussion

These two reports of localised VSCC demonstrate differing management options when VSCC occurs in pregnancy. Both patients developed VSCC as a result of early-onset chronic LS. Due to its rarity and the small number of previously reported cases, there are no definitive guidelines available [12,14], and, as such, these women are managed on an individual basis depending on gestation, disease stage, tumour site and patient choice [15]. Following VSCC diagnosis from biopsy specimens, it is essential that specialised gynaecological oncology multidisciplinary teams carefully consider the timing and type of management, including the imaging, vulval resection and groin node treatment undertaken.

Upon diagnosis, specifically where tumour invasion depth is greater than 1 mm (FIGO stage 1B), groin node involvement can be assessed both clinically and radiologically with ultrasound, CT or MRI [3]. While CT is currently the preferred modality for groin node imaging [16], we and others have recently debated its reliability and value in preoperative evaluation of localised disease [17,18]. In addition, non-ionising methods (ultrasound and MRI) are preferable during pregnancy to avoid significant radiation risks to the fetus [12,19–21]; however, such modalities have been found to have variable accuracy [22]. In our practice, we have opted for MRI as our imaging modality of choice for two main reasons: firstly, it is safe for the mother and fetus; and secondly, it allows us to assess for potential inguinal and pelvic lymphadenopathy which will guide timing and modality of treatment.

Surgical excision of the primary vulval tumour, whether that be radical local excision or vulvectomy, can be performed either antenatally for symptom control and prevention of disease progression or post-partum. While antenatal surgery requires spinal anaesthesia to avoid the risks associated with general anaesthesia [23–25], Matsuo et al. [22] reported that vulval surgery performed during pregnancy does not increase the risk of preterm delivery or intrauterine death. Nevertheless, the timing of antenatal surgical intervention requires consideration. Routinely, we would advocate resection of primary tumours after 28 weeks of gestation to ensure adequate fetal maturation and better neonatal outcomes if delivery was necessary intra- or post-operatively [26]. However, resection of the primary tumour before 36 weeks of gestation allows adequate recovery post-operatively and avoids possible interference with delivery. Although half of patients deliver via caesarean section, often recommended to prevent wound dehiscence following antenatal vulval surgery, a normal vaginal delivery may be possible if the vulval incision is away from the introitus, has had adequate time to heal and is acceptable to the patient [12,22,27].

This treatment paradigm is applicable only to early-stage tumours that are small. Although there are no reported cases of locally advanced VSCC in pregnancy to our knowledge, if reconstructive surgery was required following the resection of a large tumour, we feel it would be best undertaken six to eight weeks post-natally. This is due to subcutaneous skin oedema and vulval hypertrophy, normal physiological changes in pregnancy, and impeding surgical wound healing. In addition, extensive surgical flap reconstruction also reduces mobility, hence, predisposes women to an increased risk of venous thrombosis. Furthermore, women who undergo antenatal reconstructive surgery may not be suitable for vaginal delivery.

For those patients whose vulval surgery is delayed until the post-natal period, again there is no definitive guidance regarding the timing of such surgery [12]. We describe a case of resection at two months post-partum, yet others have operated within four weeks of delivery [28,29]. While it is imperative that antenatal surveillance ensures no evidence of disease progression during pregnancy, radiological assessment of groin nodes and planning of surgical intervention are less challenging following delivery. Patients can then undergo one combined procedure of vulval and nodal surgery. As such, delaying vulval surgery until the post-natal period is a safe and viable option in selected cases, with no implications for overall disease outcome. In addition, there is no evidence to suggest that a vaginal birth before post-natal vulval surgery increases the risk of tumour cell dissemination and disease recurrence, giving these women the option of a normal delivery [19,22].

Inguinal lymphadenectomy is an integral part of VSCC surgical staging, as undiagnosed inguinal node metastases are often fatal [30,31]. During pregnancy, groin lymphadenectomy would likely result in severe and debilitating bilateral leg lymphoedema and inguinal seroma due to the poor venous return. As a result, the timing of such surgery is crucial and we believe should be delayed at least until six weeks post-natally unless there is clear evidence of inguinal node metastasis on clinical and cross-sectional imaging assessment. In such

cases, women should be offered the choice for the fetus to be delivered prematurely, probably through caesarean section, followed immediately by radical vulvectomy and bilateral inguinal lymphadenectomies. This will allow uninterrupted adjuvant treatment post-operatively if indicated.

SLND is increasingly becoming a gold standard surgical assessment for groin lymphatic metastasis as it has comparable accuracy to total inguinal lymphadenectomy but is associated with significantly lower short- and long-term surgical morbidities [32,33]. Inguinal SLND is believed to be safe in pregnancy [19,34], with the use of technitium-99 (Tc-99 m) deemed safe and acceptable when indicated in pregnancy for diagnostic purposes [35]. However, we believe that the risk of disease progression is low in early-stage cancer and, as such, have opted to delay undertaking inguinal nodal assessment until the early post-natal period. Our cases have demonstrated that it is safe to undertake early VSCC surgery as a two-stage procedure: resection of primary tumour during pregnancy and inguinal node staging after pregnancy. Nevertheless, antenatal inguinofemoral lymphadenectomy procedures have also been reported [15,22,34,36].

In conclusion, a consensus on the management of VSCC in pregnancy would assist gynaecological oncology specialists in guiding and counselling these women with regard to imaging, vulval tumour resection, groin node surgery and delivery. As early-stage VSCC is a relatively slow-growing tumour, with progression not accelerated in pregnancy, treatment can be safely deferred until after pregnancy, provided that the patient is under regular surveillance and there is no evidence of distant metastasis. Moreover, surgery to resect primary tumours for symptom control can also be safely undertaken under spinal anaesthesia after 28 weeks of gestation without adversely affecting the fetus or mother. In addition, second-stage surgery for inguinal node assessment is acceptable and can be undertaken in the post-natal period.

Contributors

Ellen Gaunt wrote the manuscript and obtained written consent from the patients.

Rachel Pounds conceived the idea for the case report and wrote the manuscript.

Jason Yap contributed to patient management, conceived the idea for the case report, edited the manuscript and obtained written consent from the patients.

All authors read and approved the final version of the manuscript.

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Conflict of interest statement

The authors declare that they have no conflict of interest regarding the publication of this case report.

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