CASE REPORT

Vulvar cancer in HIV-positive young women – a treatment challenge

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Vulvar carcinoma is rare in the premenopausal age group. Depressed immunity has now been implicated as a predisposing factor in the development of vulvar cancer in young patients, particularly for the progression of VIN to invasive cancer. In the past decade an increasing incidence of vulvar cancer in young immunosuppressed women has been observed. It is important to screen for and detect the disease in the early stages.

A 24-year-old woman presented at our oncology clinic with a 1-year history of a fast-growing vulvar lesion involving the labia majora, labia minora, clitoris, anal mucosa and urethra and extending to the left buttock. Bilateral mobile 2 cm lymph nodes were palpable. Histological examination showed the tumour to be an invasive squamous cell carcinoma. The disease was staged as T4N2M0. Owing to low CD4 counts of 218 cells/μl and her poor general condition, palliative radiation therapy according to departmental treatment protocol was offered. The patient was followed up 6, 16 and 28 weeks after radiation therapy, and 70% tumour reduction was observed at 6 weeks, 90% at 16 weeks and complete response at 28 weeks.

Vulvar carcinoma related to HIV seems to be sensitive to larger than conventional daily doses of radiation therapy, as we observed in this case. Appropriate treatment guidelines are required, as invasive vulvar cancer related to immune suppression due to AIDS is common in African countries.

Invasive squamous cell carcinoma of the vulva is an uncommon disease, accounting for 3 - 5% of cancers of the female genital tract. It is most common in women in their 7th or 8th decade of life. Invasive cervical cancer related to AIDS has been confirmed since 1993. Interestingly, an increased risk was demonstrated in Europe[1] but not in the USA, Africa or Australia.[2] HIV-infected women are at increased risk of developing vulvar cancer.[3] According to Kuhn *et al.*[4] this cancer is more common in immunosuppressed patients than in immonocompetent controls.

Vulvar squamous cell carcinomas can be divided into two general groups with two different pathogenetic mechanisms.[5] Older women (55 - 85 years) develop a keratinising type of invasive squamous cell carcinoma associated with lichen sclerosis, squamous hyperplasia, differentiated vulvar intraepithelial neoplasia (VIN) and P53 mutation. These tumours are not related to human papillomavirus (HPV) infection. Tumours in the younger age group (25 - 50 years) are basaloid or warty, usually less invasive, and associated with high-risk HPV. The associated VIN in these patients is often warty or basaloid, high grade, and shows increased staining with proliferation marker MIB-1[6] with a high risk of squamous neoplasia elsewhere in the lower genital tract, particularly the cervix.

An increased number of cases of vulvar carcinoma have been seen in the younger age group in the past 2 decades. The percentage of tumours in young women increased from 1% for the period 1975 - 1980 to 7.7% for 1993 - 1998.[7] The choice of appropriate treatment in HIV-positive patients with vulvar carcinoma, who commonly present with low CD4 counts and locally advanced disease, is extremely important.

We report a case of carcinoma of the vulva treated palliatively with excellent local results.

Case report

A 24-year-old woman presented at Pietersburg Oncology Centre with a 1-year history of a vulvar lesion. The lesion was of the warty type, and she had received local podophylline applications during the year at a local clinic. The tumour involved the labia majora, labia minora and clitoris. It had extended to the left buttock and anal canal and urethra, and was staged as T4 N2 M0 (Fig. 1). Bilateral mobile inguinal nodes measured up to 2 cm in size. The tumour was bleeding and the patient experienced severe pain and discomfort. Histological examination showed it to be an invasive moderately differentiated squamous cell carcinoma. Urea and electrolyte levels and a full blood count were

Fig. 1. The tumour at presentation.

normal, and the haemoglobin concentration was 11.7 g/dl. An ultrasound scan of the liver and an intravenous pyelogram were normal. A chest radiograph showed no lung metastases.

The patient was HIV positive with a CD4 count of 218 cells/µl. She was not receiving antiretroviral medication. Surgery was not possible owing to the enormous size and fixity of the tumour. Radical chemoradiation was not an option because of her low CD4 count and poor general condition. She was treated with palliative radiation 4 Gy per fraction daily to a total of 20 Gy with a 15 MV photon beam encompassing the entire vulva, perineum and inguinofemoral nodes according to departmental protocol. She was reviewed 6, 16 and 28 weeks after completion of this treatment. At 6 weeks a 70% reduction in tumour size was observed (Fig. 2). The bleeding had stopped completely and the patient was feeling much better.

Sixteen weeks after treatment excellent results were observed with almost 90% tumour reduction and complete pain control (Fig. 3). Complete response was observed at 7 months (28 weeks) after radiation (Fig. 4). The CD4 count had dropped to 68 cells/µl 7 months after treatment.

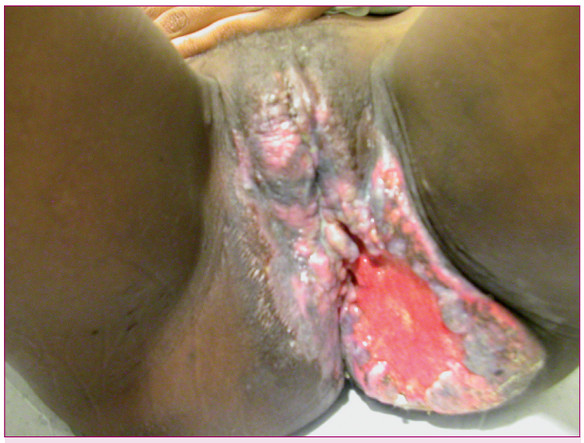

Fig. 2. The lesion 6 weeks after completion of radiation therapy.

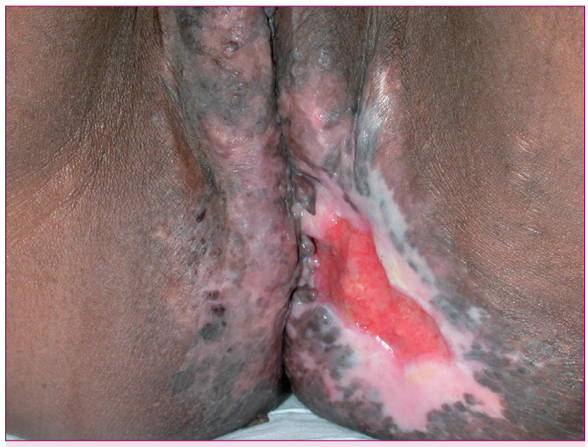

Fig. 3. The lesion 16 weeks after radiation therapy.

Fig. 4. Seven months after completion of radiation therapy.

Discussion

Over the past decade there has been a striking increase in the incidence of VIN and invasive vulvar squamous cell carcinoma in young women. This disease is associated with depressed immunity and HPV infection, as has been shown in various studies and case reports. There have been several reports of cancer associated with HIV-related immune suppression.[1-4]

Piura *et al.*[8] reported a case of a 25-year-old woman with systemic lupus erythematosus (SLE) who developed invasive squamous cell carcinoma of the vulva; she underwent radical vulvectomy and bilateral groin sentinel lymph node dissection and is alive without evidence of disease 1 year later. This patient had immunosuppression related to SLE and/or steroid therapy. Park *et al.*[9] reported a case of carcinoma of the vulva *in situ* in a CD4-positive, T-lymphocytopenic woman without HIV infection. Regan *et al.*[10] reported a case of vulvar carcinoma in pregnancy, which is also a state of decreased immune status. In their case report Ogunleye *et al.*[11] agree that the immunosuppressive state of pregnancy allowed HPV-infected areas of the vulva to progress to invasive carcinoma.

Immunodeficiency related to HIV is a major factor related to various cancers, including squamous carcinoma of the cervix, and now vulvar cancer in young women has been reported in various parts

of the world. In developing countries such as South Africa the incidences of cervical and vulvar cancer in young females has increased in the past decade. The dilemma is that most of our patients present in locally advanced stage of disease with massive tumour bulk, poor nutritional status and very low CD4 counts (usually < 200/µl). According to one South African survey[12] about 70% of patients first seek health care from traditional healers and only come to hospitals when the disease is at an advanced stage and the symptoms are unbearable. At this stage surgery is not possible and in certain cases radical chemotherapy and/or radiation cannot be offered owing to very low CD4 counts and poor general condition and performance status. In this situation palliative radiation can be delivered, encompassing the local disease with the palliative dose of 20 Gy in 5 fractions (4 Gy daily dose) or 30 Gy in 10 fractions (3 Gy daily). We have observed very good palliative results in locally advanced vulvar cancer in HIV-positive patients. This good response is probably due to clinicopathological differences in these cases and the relation to HPV with warty/basaloid features and lesser invasiveness.

The case reported here reinforces the importance of a very high suspicion of malignancy when warty vulvar lesions are seen in immunosuppressed patients. Such lesions should be biopsied and histological evaluation should be done to detect the cancer early so that radical treatment can be offered. Furthermore, there is a need to determine the most effective doses of radiation for this cohort of patients.

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CASE REPORT

Uterine artery embolisation in a Jehovah's Witness patient

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A 30-year-old nulliparous woman was referred with life-threatening massive vaginal bleeding and failed medical treatment. She was of the Jehovah's Witness faith and refused transfusion with any blood products. Uterine artery embolisation arrested the haemorrhage.

Presentation

The patient presented with a history of heavy vaginal bleeding with associated clots. This had necessitated the use of 20 sanitary towels per day with double padding, flooding and soiling. There was also associated dizziness, weakness and malaise. She was not sexually active, and was a devout Jehovah's Witness.

On examination she was calm, co-operative and undistressed. She was obese (body mass index 30) with no signs of hirsutism, acne or acanthosis nigricans. Her blood pressure was 120/65 mmHg with an associated tachycardia of 102/min. The peripheral oxygen saturation was 98% and fingerprick haemoglobin 2 g/dl. Her temperature was 37.4°C and no abnormalities were detected on dipstick urinalysis. She had a normal

jugular venous pressure and precordium with normal heart sounds on auscultation. She was awake, alert, well orientated and responsive to questions.

The abdomen was obese with no surgical scars present. On palpation it was soft and non-tender, and no organomegaly was detected.

The vulva and vagina were normal with normal hair distribution. The cervix appeared normal on speculum examination. The uterus was of normal size, axial and mobile. Both adnexae were non-tender and no lesions were palpated on digital examination.

Over the following 24 hours management of the patient included the following medication:

- tranexamic acid (Cyclokapron) – 1 g intravenously 8-hourly
- ibuprofen – 400 mg orally 8-hourly
- medroxyprogesterone acetate (Depo-Provera) – 300 mg intramuscular injection
- norethisterone (Primolut N) – 10 mg orally 8-hourly
- conjugated oestrogen (Premarin) – 25 mg intravenously
- antibiotics – ampicillin and metronidazole intravenously.

The above treatment did not succeed in reducing the vaginal blood loss. Further investigation revealed negative serum beta-human chorionic gonadotrophin (β-hCG), a normal pelvic ultrasound scan, normal thyroid function and a normal haematological profile other than continuing anaemia. Over the following 36 hours the patient's condition deteriorated. Her blood loss continued, her haemoglobin continued to drop and she became shocked. Despite extensive counselling, she continued to decline blood transfusion.

She was transferred to Groote Schuur Hospital for uterine artery embolisation (UAE) since all other options to control her bleeding had failed. She was resuscitated with crystalloids (modified Ringer's lactate) and colloids (Haesteril). Bilateral uterine artery embolisation was undertaken by an interventional radiologist. The internal iliac artery was entered through the right groin area via a #5F sheath. Both uterine arteries were embolised using gelatin (Spongistan) pledgets.

After embolisation the vaginal bleeding ceased. Resuscitation continued with crystalloids and colloids. The patient was also given intravenous erythropoietin (10 000 U intravenously once daily) and oral haematinics (ferrous sulphate 200 mg orally twice daily and folic acid 5 mg orally daily), resulting in an increase in her haemoglobin concentration from 2.5 g/dl to a discharge level of 8.9 g/dl over a period of 26 days.

The prolonged period of hypovolaemia resulted in small cerebral infarcts. A CT scan revealed small infarcts including two small hypoechoic areas adjacent to the anterior horn of the left and right lateral ventricle. She was mobilised with parallel bars and was ultimately able to walk aided by a walking cane.

She was discharged 33 days after admission on the combined oral contraceptive levonorgestrel/oestrogen (Nordette) and haematinics. She continued to need a walking cane, and initially did not return to work and was cared for by relatives. At the time of writing she has resumed her previous position as a domestic worker and is in a stable relationship.

Discussion

UAE entails the occlusion of arterial uterine blood flow with embolisation material. It incorporates angiography to visualise the uterine arteries and is performed by an experienced interventional radiologist.

UAE been used successfully in the treatment of obstetric and gynaecological haemorrhage. It has been shown to be an effective alternative to surgical intervention in the treatment of uterine bleeding resulting from a variety of conditions, including postpartum haemorrhage, postoperative haemorrhage, cervical pregnancy, arteriovenous malformation and most recently uterine leiomyomas.[1-3]

UAE has had success rates of 86 - 90% in treatment of excessive menstrual blood loss, with symptomatic relief seen as early as the first menstrual cycle in the majority of patients.[1] In the above case, where medical management failed and surgical intervention was not a viable option, UAE proved successful in controlling blood loss. To date there have been no reports of this procedure being utilised to control haemorrhage in patients of the Jehovah's Witness faith.

After UAE, uterine viability is sustained due to a non-collateral arterial blood supply with contributions from the ovarian arteries.[4] Embolisation of uterine arteries has a distinct effect on leiomyomas as opposed to the myometrium, being able to stop the blood supply to leiomyomas while collateral circulation sustains the viability of the uterine tissue.[1,4] Embolisation involves the injection of one of three types of embolisation materials (polyvinyl alcohol micro particles/PVA, gelatin sponges or calibrated microspheres) through a catheter.[5] If the procedure is done electively, patients are discharged within 24 hours.[1,4]

Conclusion

Uterine artery embolisation is a novel technique that can be utilised in both obstetric and gynaecological settings as a minimally invasive procedure. There are no documented cases of UAE used in a Jehovah's Witness patient in the setting of life-threatening haemorrhage.

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