

A new approach to vulvar squamous cell carcinoma: two-year follow-up of a case report

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Summary

Background: Vulvar carcinoma is relatively rare gynaecologic malignancy. The most prevalent vulvar cancer is squamous cell carcinoma. It is not uncommon for patients to delay seeking medical attention or for physicians to delay diagnosing the condition. This delay results in many cases being diagnosed in advanced stage. The sentinel lymph node "concept" is attractive in vulvar cancer because it has the potential to avoid a radical vulvectomy associated with uni- or bilateral inguinofemoral lymphadenectomy and, thus, to avoid the morbidity associated with formal groin dissection.

Case report: A case of an 88-year-old woman with advanced local vulvar cancer is presented. A study of the inguinal-femoral lymph nodes was also conducted with intraoperative vital blue dye peritumoral injection and as the sentinel node was found to be negative for malignant metastasis, a radical vulvectomy without bilateral inguinofemoral lymphadenectomy and without additional treatment (chemotherapy and/or radiotherapy) was performed. Follow-up was performed at one, three, six, nine, 12, 18 and 24 months. No local recurrence or distant metastasis was found.

Conclusion: The sentinel lymph node procedure allows a less aggressive treatment to be carried out in patients with invasive vulvar cancer thus reducing the complications and morbidity of treatment. Moreover, reducing the operative stress can change the overall survival and reduce the mortality linked to complications and postoperative stress.

Key words: Vulvar squamous cell carcinoma; Sentinel nodes.

Introduction

Vulvar carcinoma is a relatively rare gynecologic malignancy. The most prevalent vulvar cancer is squamous cell carcinoma with vulvar melanoma being the second most common [1]. Squamous cell carcinomas account for 90% of vulvar cancers. It is not uncommon for patients to delay seeking medical attention and thus for physicians to delay diagnosing the condition [1]. This delay results in many cases being diagnosed in advanced stage. In the literature two biologically different types of squamous carcinoma are described: related and unrelated to human papillomavirus infection [2]. Squamous cell carcinoma seems to be the most frequent among major malignant complications associated with lichen sclerosus (LS) [3]. There is no direct association between LS and vulvar carcinoma but an increase in vulvar squamous cell carcinoma cases has been demonstrated in 4-5% of patients affected by lichen sclerosus [4-6]. This association seems more significant in squamous cell carcinoma not associated to HPV (32% of cases) vs the HPV-associated cases [4]. The main mode of spread is lymphogenic to the inguinofemoral lymph nodes; therefore, elective uni- or bilateral inguinofemoral lymphadenectomy is part of the standard treatment in combination with radical (wide) local excision of the vulvar tumour [7, 8]. The status of regional lymph nodes is a powerful predictor of survival in patients with early cancers of the vulva, cervix, and uterus. If there is associated VIN or lichen sclerosus, these areas may be superficially excised

to control symptoms and to exclude other areas of superficial invasion (level of evidence-B) [9]. Radical resection of vulvar and cervix cancers along with extensive lymphadenectomy remains the standard of care for these cancers. Intraoperative lymphatic mapping and sentinel node identification have the potential to improve the treatment of patients with gynaecologic cancers with improved detection of lymph node metastases and reduced morbidity [10]. In recent years there has been an increasing interest among gynaecologic oncologists to implement the sentinel lymph node (SLN) procedure in vulvar cancer patients in clinical practice [11].

Several techniques are performed to detect lymph node metastases. Sentinel nodes are labeled preoperatively with lymphoscintigraphy and intraoperatively with blue injection dye and/or a handheld gamma probe. The aim of these methods is to reduce the use of lymphadenectomy with a consequent reduction in mortality and postoperative morbidity. The follow-up at 24 months of a case of a large vulvar squamous cell carcinoma in a woman suffering from lichen sclerosus treated with a radical vulvectomy without bilateral inguinofemoral lymphadenectomy is described.

Case Report

An 88-year-old woman came to our attention in July 2004 suffering from lichen sclerosus with a large vulvar esophitic neof ormation the size of a large cabbage (Figure 1). The staging was performed in accordance with FIGO guidelines. No metastases nor inguinal lymph node (LN) involvement at clinical examination or at preoperative lymphoscintigraphy with technetium-99m (Tc-99m) were found.

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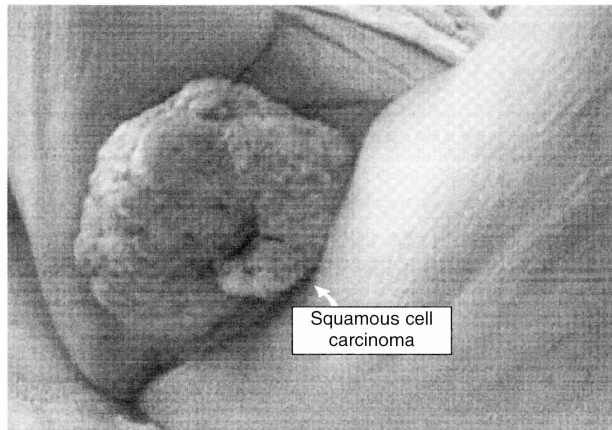


Figure 1. — Vulvar squamous cell carcinoma FIGO Stage II (T2 N0 M0).

A study of the inguofemoral lymph nodes was also conducted with intraoperative vital blue dye peritumoral injection. As the sentinel node was found to be negative for malignant metastasis, a radical vulvectomy without bilateral inguofemoral lymphadenectomy was performed.

The surgical specimen was sent for histologic examination and possible detection of HPV DNA. Histologic examination was performed on 12/08/2004. The histologic analysis showed lichen sclerosus associated with a well differentiated squamous cell carcinoma deeply infiltrating the epidermis but HPV-negative (FIGO Stage II, T2 N0 M0 - G1, WHO). Assessment of HPV deoxyribonucleic acid was done by polymerase chain reaction amplification and in situ hybridisation. Expression of p53 and pRb by immunohistochemistry in vulvar cancer tissue was performed and compared with adjacent non neoplastic epidermal lesions. Overexpression of p53 was found in the tumoral tissue while non neoplastic lesions in the adjacent epidermis had p53-positive basal cells but neither had suprabasilar extension of p53-positive cells; however, the expression of p53 in the non neoplastic lesions was significantly lower. No alteration in expression of pRb was found and no additional treatment (chemotherapy and/or radiotherapy) was performed. Follow-up was performed at one, three, six, nine, 12-18 and 24 months. Up to now no local recurrence or distant metastasis has been found.

Discussion and Conclusion

Vulvar carcinoma is a relatively rare gynaecologic malignancy. The most prevalent vulvar cancer is squamous cell carcinoma (90%). It is not uncommon for patients to delay seeking medical attention and thus for physicians to delay diagnosing this condition [1]. Moreover the diagnosis is often difficult. In fact this tumor at the beginning is usually treated like other benign pathologies. Older age of patients and clinical stage negatively condition the prognosis.

In our case the use of pre/intraoperative lymphatic mapping and sentinel node identification permitted a conservative surgical approach. Moreover, this approach allows complications and postoperative morbidity to be reduced and thus it is particularly advantageous because the operative stress is reduced.

Sentinel lymph node detection using preoperative lymphoscintigraphy with technetium 99 and an intraoperative blue dye injection permits exclusion of the involvement of the inguofemoral lymph nodes with a negative predictive value, which in accordance with the recent literature, is 100% [11-17].

Nonetheless gynaecological-oncologists who use the sentinel lymph node procedure in vulvar cancer patients should perform this technique by following a strict protocol and within the protection of a clinical trial, carrying out an accurate patient selection and carefully evaluating the risk/benefit ratio for a less aggressive treatment. In fact, it is possible that micrometastases using lymphatic vessels can bypass the sentinel lymph node and thus the long-term prognosis of these patients may be worse [11, 18-20]. These considerations do not lessen the role of this technique, and the sentinel lymph node procedure represents real progress towards less aggressive treatment in patients with vulvar cancer [21-28].

This case showed no progression of disease over 24 months and the overall disease outcome has been excellent.

References

- [1] Ghurani G.B., Penalver M.A.: "An update on vulvar cancer". *Am. J. Obstet. Gynecol.*, 2001, 185, 294.
- [2] Fox H., Wells M.: "Recent advances in the pathology of the vulva". *Histopathology*, 2003, 42, 209.
- [3] Neill S.M., Tatanall F.M., Cox N.H.: "Guidelines for the management of lichen sclerosus". *Br. J. Dermatol.*, 2002, 147, 640.
- [4] Carli P., De Magnis A., Mannone F., Botti E., Taddei G., Cattaneo A.: "Vulvar carcinoma associated with lichen sclerosus. Experience at the Florence, Italy, Vulvar Clinic". *J. Reprod. Med.*, 2003, 48, 313.
- [5] Zarccone R., Cardone G., Voto R.I., Palumbo S., Cardone A.: "Vulvar dystrophies and intraepithelial neoplasms". *Minerva Ginecol.*, 1991, 43, 43.
- [6] Zarccone R., Mainini G., Carfora E., Cardone A.: "Current etiopathogenetic views in vulvar cancer". *Panminerva Med.*, 1997, 39, 30.
- [7] de Hullu J.A., van der Zee A.G.: "Groin surgery and the sentinel lymph node". *Best. Pract. Res. Clin. Obstet. Gynaecol.*, 2003, 17, 571.
- [8] Dhar K.K., Woolas R.P.: "Changes in the management of vulvar cancer". *Best. Pract. Res. Clin. Obstet. Gynaecol.*, 2003, 17, 529.
- [9] Benedet J.L., Bender H., Jones H. III, Ngan H.Y.S., Pecorelli S.: "Staging classifications and clinical practice guidelines of gynaecologic cancers". FIGO Committee on Gynecologic Oncology, September, 2000.
- [10] Levenback C.: "Intraoperative lymphatic mapping and sentinel node identification: gynecologic applications". *Recent Results Cancer Res.*, 2000, 157, 150.
- [11] de Hullu J.A., Oonk M.H., Ansink A.C., Hollema H., Jager P.L., van der Zee A.G.: "Pitfalls in the sentinel lymph node procedure in vulvar cancer". *Gynecol. Oncol.*, 2004, 94, 10.
- [12] Pitynski K., Basta A., Oplawski M., Przeszlakowski D., Hubalewska-Hola A., Krysztopowicz W.: "Lymph node mapping and sentinel node detection in carcinoma of the cervix, endometrium and vulva". *Ginekol. Pol.*, 2003, 74, 830.
- [13] de Hullu J.A., Hollema H., Piers D.A., Verheijen R.H., van Diest P.J., Mourits M.J. *et al.*: "Sentinel lymph node procedure is highly accurate in squamous cell carcinoma of the vulva". *J. Clin. Oncol.*, 2000, 18, 2811.
- [14] Sideri M., De Cicco C., Maggioni A., Colombo N., Bocciolone L., Trifiro G. *et al.*: "Detection of sentinel nodes by lymphoscintigraphy and gamma probe guided surgery in vulvar neoplasia". *Tumori*, 2000, 86, 359.

- [15] Ansink A.C., Sie-Go D.M., van der Velden J., Sijmons E.A., de Barros Lopes A., Monaghan J.M. *et al.*: "Identification of sentinel lymph nodes in vulvar carcinoma patients with the aid of a patent blue V injection: a multicenter study". *Cancer*, 1999, 86, 652.
- [16] Terada K.Y., Coel M.N., Ko P., Wong J.H.: "Combined use of intraoperative lymphatic mapping and lymphoscintigraphy in the management of squamous cell cancer of the vulva". *Gynecol. Oncol.*, 1998, 70, 65.
- [17] Rodier J.F., Janser J.C., Routiot T., David E., Ott G., Schneegans O., Ghnassia J.P.: "Sentinel node biopsy in vulvar malignancies: a preliminary feasibility study". *Oncol. Rep.*, 1999, 6, 1249.
- [18] Hakam A., Nasir A., Raghuwanshi R., Smith P.V., Crawley S., Kaiser H.E., Grendys E., Fiorica J.F.: "Value of multilevel sectioning for improved detection of micrometastases in sentinel lymph nodes in invasive squamous cell carcinoma of the vulva". *Anticancer Res.*, 2004, 24, 1281.
- [19] Raspagliesi F., Ditto A., Fontanelli R., Maccauro M., Carcangiu M.L., Parazzini F., Bombardieri E.: "False-negative sentinel node in patients with vulvar cancer: a case study". *Int. J. Gynecol. Cancer*, 2003, 13, 361.
- [20] Fons G., ter Rahe B., Sloof G., de Hullu J., van der Velden J.: "Failure in the detection of the sentinel lymph node with a combined technique of radioactive tracer and blue dye in a patient with cancer of the vulva and a single positive lymph node". *Gynecol. Oncol.*, 2004, 92, 981.
- [21] de Hullu J.A., Oonk M.H., van der Zee A.G.: "Modern management of vulvar cancer". *Curr. Opin. Obstet. Gynecol.*, 2004, 16, 65.
- [22] Sliutz G., Reinthaller A., Lantzsch T., Mende T., Sinzinger H., Kainz C., Koelbl H.: "Lymphatic mapping of sentinel nodes in early vulvar cancer". *Gynecol. Oncol.*, 2002, 84, 449.
- [23] Molpus K.L., Kelley M.C., Johnson J.E., Martin W.H., Jones H.W. 3rd: "Sentinel lymph node detection and microstaging in vulvar carcinoma". *J. Reprod. Med.*, 2001, 46, 863.
- [24] Puig-Tintore L.M., Ordi J., Vidal-Sicart S., Lejarcegui J.A., Torne A., Pahisa J., Iglesias X.: "Further data on the usefulness of sentinel lymph node identification and ultrastaging in vulvar squamous cell carcinoma". *Gynecol. Oncol.*, 2003, 88, 29.
- [25] Oda T., Fujiwara K., Suzuki S., Kono I.: "Treatment of vulvar cancer-updated information". *Gan To Kagaku Ryoho*, 2002, 29, 1383.
- [26] Zambo K., Schmidt E., Hartmann T., Kornya L., Dehghani B., Tinneberg H.R., Bodis J.: "Preliminary experiences with sentinel lymph node detection in cases of vulvar malignancy". *Eur. J. Nucl. Med. Mol. Imaging*, 2002, 29, 1198.
- [27] Ramirez P.T., Levenback C.: "Sentinel nodes in gynecologic malignancies". *Curr. Opin. Oncol.*, 2001, 13, 403.
- [28] Levenback C., Coleman R.L., Burke T.W., Bodurka-Bevers D., Wolf J.K., Gershenson D.M.: "Intraoperative lymphatic mapping and sentinel node identification with blue dye in patients with vulvar cancer". *Gynecol. Oncol.*, 2001, 83, 276.

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