Recurrent Vulvar Cancer

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Opinion statement

Recurrent vulvar cancer occurs in an average of 24% of cases after primary treatment after surgery with or without radiation. The relatively few primary vulvar cancers, combined with the low proportion of recurrences, has made it difficult to perform randomized studies to document the most appropriate therapeutic modalities. Most reports are small retrospective studies and anecdotal reviews that have emphasized the importance of surgery and have led to new approaches with respect to chemoradiation. Traditionally, the most accepted treatment of vulvar cancer has been and continues to be surgery. Recently, radiation and chemotherapy have been combined with very encouraging results. The therapeutic modality used depends on the location and extent of the recurrence. Most recurrences occur locally near the original resection margins or at the ipsilateral inguinal or pelvic lymph nodes. Lateralized local vulvar recurrences treated with a wide radical local excision with inguinal lymphadectomy results in an excellent cure rate of 70%. With a central pelvic recurrence with antecedent radiotherapy involving the urethra, upper vagina, and rectum, total pelvic exenteration is indicated in a select group of patients with curative intent. Radiotherapy or chemoradiation concomitantly with wide radical local excision of an advanced vulvar has proven successful in avoiding an exenteration, with improved survival and less morbidity. Prospective and retrospective studies have shown excellent results using radiation or chemoradiation with wide radical local excision in patients with locally advanced disease in whom adequate resection margins are difficult to achieve (with a central lesion requiring exenteration) or with debilitating medical conditions that preclude surgery. In these patients, chemoradiation has shown favorable results when used before a wide local resection. In patients with advanced local disease, external beam and interstitial radiation has been used for palliative and curative intent with encouraging results. Regional recurrences to the inguinal and pelvic lymph nodes have been shown to have a poor prognosis with a high mortality rate. We recommend that inguinal recurrences without prior radiation therapy undergo excision followed by radiotherapy with chemosensitization. In patients with previous radiation to the inguinal lymph nodes, we try to avoid any excisional procedures because of the high rate of complications. We offer these patients brachytherapy for palliation. With pelvic recurrences, we recommended chemoradiation as the treatment modality. In the subset of patients with distant metastasis, chemotherapy may be offered; however, few studies have been performed to advocate any single combination. The literature supports the use of 5-fluorouracil or cisplatin as single agents or in combination to have sensitivity against squamous cells. There are few studies revealing improvement in 5-year survival, thus these patients may benefit from recruitment into research protocols.
Introduction
Squamous cell carcinoma of the vulva accounts for 3% to 5% of female genital tract malignancies, with an estimated incidence of one to two per 100,000 persons [1]. The most common histology of vulvar cancer is squamous cell carcinoma. Many other malignant neoplasms can occur within the vulvar soft tissue and skin appendages, including basal cell carcinomas, malignant melanomas, adenocarcinomas arising from Bartholin's gland, Paget's disease, sarcomas, leiomyosarcomas, angiosarcomas, liposarcomas, and metastatic tumors from other organs. Much of the experience with the treatment of vulvar cancer is based on squamous cell carcinomas.

Although vulvar lesions are external and easily visible, most of these tumors are diagnosed at Stages II and III, with overall 5-year survival rate of 85% achieved using surgery and radiation (Fig. 1). Eleven percent to 37% of patients will have recurrence after initial treatment during the first 2 years, but other recurrences have been detected in the following 10 years (Table 1) [2,3,4,5]. The prognostic factors that correlate with survival and recurrence include initial staging, pattern of tumor invasion, depth of invasion, and lymph node status.

Surgical excision is the mainstay of treatment for recurrent carcinoma of the vulva. Over the years, the radical disfiguring surgical treatment for primary and recurrent vulvar cancer has been replaced by more conservative and localized approaches. The rarity of this disease limits the ability to perform randomized prospective studies, but multiple retrospective studies have confirmed the efficacy of radical wide local excision in the treatment of recurrences. This article focuses on the various surgical approaches for local and regional recurrences and the role of radiation and chemotherapy for more advanced disease.

Treatment
Diet and lifestyle

- Previously, reports linked vulvar cancer with multiple infections, including chronic granulomas, herpes simplex, syphilis, and human papilloma virus. Subsequent studies have not confirmed such associations. The presence of the human papilloma virus in 10% to 50% of invasive vulvar cancers has established the neoplastic potential of the intraepithelial infection. Lifestyle modifications that may decrease the incidence of vulvar carcinoma include safe sexual practice and smoking cessation because women who smoke and have genital warts have a combined 36-fold increase compared with low risk women.

Surgery

- The treatment of primary squamous cell carcinoma of the vulva is radical surgical excision of the lesion. The radicality of the operation has changed over the last 20 years with the understanding of the disease process and the mechanism of tumor spread via lymphatic drainage within the vulva and perineum. Previously, all patients with invasive vulvar cancer would undergo a radical vulvectomy and inguinal lymph node dissection through a single incision or an en bloc resection. The consequences were significant disfiguration of the external genitalia and a high incidence of wound infection (approximately 30%–50%). Most patients undergo a radical wide local excision alone for a lateral lesion or with an accompanying unilateral lymphadenectomy only if invasion is > 1 mm. If the lesion is centrally located (i.e., near the clitoris, introitus, and perineum), a radical vulvectomy and bilateral lymphadenectomy is performed through separate incisions.
- With respect to all stages of vulvar carcinoma, approximately 20% will fail primary treatment. During the first 2 years after initial treatment, 60% to 70% of all recurrences are clinically detected. Most of the recurrences occur locally on the vulva (57%), and then in the groin (22%), pelvis (14%), or distant sites (23%) (Table 2) [2,5]. The initial advanced stage at the time of...