Multimodality Treatment in the Management of Anorectal Melanoma: A Case Report and Review of the Literature

Anorektal Malign Melanomada Multimodalite Tedavi; Bir Vaka Raporu ve Literatür Analizi

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Abstract

Anorectal melanoma represents approximately 0.2-1% of all malignant melanomas and has a poor prognosis, with a median survival of 8 to 23 months after the time of diagnosis. The typical treatment modalities include surgery, radiotherapy and chemotherapy. The particular approach taken depends on the patient's status and disease stage. Although there are different treatment options for this rare condition, there are not enough studies on multimodality treatment. Here, we present the case of a 54-year-old female with anorectal melanoma that had metastasized to an inguinal lymph node. She underwent local excision of the rectal mass and inguinal lymph-node dissection. Temozolomide treatment was started after radiotherapy and was given for 24 months. Follow-up revealed that the patient has been doing well with no signs of recurrence three years after the completion of treatment. We aim to discuss combined treatment modalities for ARM in light of the pertinent literature.

Key Words: Anorectal melanoma, Multimodality treatment, Temozolomide

Introduction

Anorectal melanoma (ARM) represents less than 1% of all malignant tumors of the anorectum and ~0.2–1% of all melanomas. Anorectal melanoma is associated with a poorer prognosis compared to cutaneous melanoma, and reports of clinical responses to systemic therapy have been anecdotal. The median survival of patients with ARM ranges from 8 months to 23 months from initial diagnosis, and the 5-year overall survival rate ranges from 3% to 22% [1, 2]. The treatment of ARM includes surgery, radiotherapy and chemotherapy, depending on the stage of the disease and patient status. Due to the rarity of the disease, it is difficult to assess the efficacy of each treatment modality in clinical trials. Emerging data suggest that multimodality treatment might be a better choice in the management of these patients. Here, we report the case of a patient with locally advanced malignant ARM who was treated with combined surgery, radiotherapy and chemotherapy without significant toxicity, resulting in long-term survival. We aim to discuss treatment options for ARM in light of the pertinent literature.

Case Report

A 54-year-old female patient presented with rectal fullness and inguinal swelling. She also had constipation and...
hematochezia. Physical examination revealed a right inguinal lymphadenopathy. On digital rectal examination, a 3x2 cm mass could be palpated in the anal canal. Complete blood count and serum biochemistry were within normal limits. Rectosigmoidoscopy showed an ulcerating black lobulated mass in the anal canal protruding to the rectum, biopsy of which was consistent with melanoma. Computed tomography (CT) scans of the thorax and abdomen detected no metastasis except for that involving the inguinal lymph node. The rectal mass was locally excised and the affected inguinal lymph node was dissected. Pathology was consistent with malignant melanoma and inguinal lymph node metastasis. The surgical margin was positive. Conventional radiotherapy was delivered postoperatively to the pelvic area (by opposed AP-PA fields up to 50 Gy in 2-Gy doses by 6 MV X-rays) and to the perineum (boost dose of 6 Gy supplied by an enface 6-MeV electron beam). A linear accelerator that utilized both electron and 6 MeV photon energy was used for radiation therapy. Systemic treatment with 200 mg/m² temozolomide (TMZ) for five consecutive days every 4 weeks was initiated after radiation therapy. The patient received 24 cycles of temozolomide without any significant toxicity. Follow-up examination showed that the patient was still doing well without any sign of recurrence three years after the completion of treatment.

Discussion

Most patients with ARM who have localized or locoregional disease are surgically treated with either abdominopereineal resection (APR) or local excision (LE). APR has traditionally been performed to reduce the risk of locoregional recurrence of primary anorectal melanoma and provides higher local control rates compared with LE. However, APR is functionally debilitating, results in urinary and sexual dysfunction and a stoma, and yields no clear improvement in overall survival compared to LE. A recent review by Droesch et al. [3] demonstrated similar stage-specific survival rates in patients with ARM treated with either APR or LE. Furthermore, adjuvant radiation after LE increases 5-year local control rates after LE by up to 74%, to levels at least equivalent to the local control rates previously obtained with APR. In this study, no patient had locoregional failure as the only failure site, and no patient required salvage APR for the palliation of local-regional disease recurrence [4]. A number of studies in patients with mucosal melanoma of the head and neck also suggest better outcomes with postoperative radiotherapy; this approach is currently recommended for invasive melanoma in patients with positive or close excision margins [5].

Regardless of the type of surgery, most patients die secondary to metastatic disease within 5 years. This highlights the need for effective adjuvant systemic treatment to eradicate micrometastasis after locoregional treatment. The limited efficacy of such systemic treatment underlies the lack of impact of local control rate on overall survival. More effective chemotherapeutic options may increase the prognostic importance of better local control in patients with ARM. Currently, dacarbazine (DTIC) remains the standard of care in metastatic cutaneous melanoma [6]. TMZ is an oral imidazotetrazinone methylating agent that has similar activity to DTIC in the treatment of melanoma [7]. TMZ is highly bio-available after oral administration and is spontaneously cleaved in vivo to monoethyl triazenoimidazole carboxamide (MTIC), a reactive DNA methylating species. Myelosuppression is the primary toxicity associated with TMZ, but it is non-cumulative and manageable in the majority of patients [8]. Other systemic treatment options include TMZ- or DTIC-based chemotherapy regimens and biochemotherapy with cytotoxic drugs in combination with biological agents, including interleukin-2 or interferon [6]. The results of adjuvant chemotherapy trials in cutaneous melanoma have been disappointing [9]; however, newer therapeutic options such as TMZ or biochemotherapy regimens that have shown substantial activity in metastatic disease may offer better outcomes in the adjuvant setting [7, 10]. Additionally, mucosal melanomas are more prone to systemic dissemination than their cutaneous counterparts, probably because of the rich vascular and lymphatic networks surrounding these lesions [1]. Therefore, mucosal tumors may benefit most from adjuvant therapy. Clearly, further research is needed to develop better systemic treatments.

Surgical resection continues to be the mainstay of primary therapy. Conservative surgery with local excision plus adjuvant local-regional radiation seems to be an acceptable treatment option and should be preferred to APR when technically feasible. It would be interesting to assess the efficacy of chemoradiation with TMZ for the treatment of ARM (as in the case of glioblastoma multiforme) in future clinical trials. However due to the rarity of the disease, it is nearly impossible to organize randomized trials to test the efficacy of adjuvant systemic treatment in ARM. In this context, indirect data from the metastatic setting can be used to guide the selection of adjuvant therapy. In our patient, adjuvant treatment with temozolomide was effective and well tolerated and demonstrated efficacy in the metastatic setting. It may therefore be advisable to use temozolomide in the adjuvant setting to reduce local and systemic recurrences.

In conclusion, we suggest multimodality treatment with surgery, radiotherapy and chemotherapy or biochemotherapy in patients with ARM confined to the pelvis. Our results may serve as an initial indication that adjuvant chemotherapy with TMZ in the context of multimodality therapy may help reduce the frequency of disease recurrence.
Conflict of interest statement: The authors declare that they have no conflict of interest to the publication of this article.

References

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