Melanoma Metastatic to Multiple Visceral Organs: Further Considerations

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By Nancy Lee, MD [1]

The case report by Magnuson and Halligan presents the palliative treatment of a patient with stage IV melanoma, distantly metastatic to several sites, including the lung, pulmonary vein, left atrium, and CNS. The article focuses on the external beam radiotherapy employed to treat the cardiac metastasis and includes a discussion of the role of radiotherapy in treating metastatic melanoma.

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Treatment Options

The diagnosis of metastatic melanoma portends a poor prognosis, and no treatment modality has yet demonstrated sufficient efficacy to claim a role as the standard of care. Systemic therapy is considered by some to be the mainstay of treatment, but even the most effective agents have modest results, and systemic therapy offers little benefit in patients with metastases to the central nervous system. The most active single chemotherapeutic agent is dacarbazine (DTIC), which has a response rate of approximately 15% to 20% and has not been shown to significantly improve survival.[1-3] Administration of high-dose interleukin-2 can result in durable responses in a small subset of patients but is associated with severe multiorgan toxicities.[4] Surgery is usually reserved for patients with solitary or oligometastases, in whom locoregional control has been achieved and complete resection of the metastasis is possible. Radiation therapy for metastatic melanoma is generally indicated in patients who stand to benefit from palliation of symptomatic lesions.

Prognostic Features

The patient presented in this case report had several tumor features associated with poor prognosis, including multiple metastases and visceral organ involvement. Literature data indicate median survival of 3 to 11 months for pulmonary metastasis, 1 to 5 months for brain metastasis, and 2 to 4 months for patients with multiple metastases.[5-7] Large metastases are also associated with lower response to treatment.[8] In addition to the pulmonary and brain metastases, this patient presented with a bulky extension of tumor into the pulmonary vein and left atrium. The expectation for medium- and long-term survival in this patient was low, and the primary goal of treatment was clearly to halt progression of the cardiac lesion. Although a complete response would be desirable, in the setting of multiple metastases prevention of tumor progression would be sufficient to achieve the goal of palliation. As the authors correctly note, minimization of severe acute toxicities such as tumor embolism and vessel rupture should be of high priority in this setting.

Cardiac Metastasis

Melanoma has the greatest propensity among all malignancies for metastatic spread to the heart, and tends to involve the endocardium and myocardium.[9] At autopsy, cardiac involvement is present in approximately 50% to 64% of patients.[9,10] Nevertheless, symptomatic cardiac metastases are uncommon, occurring in 2%-16% of patients with metastatic melanoma.[9,10] In this patient, tumor extended from a bulky pulmonary metastasis into the pulmonary vein and left atrium. This extension was at least 4-5 cm in length and occupied a large portion of the left atrium. This lesion presumably placed the patient at high-risk for outflow obstruction and/or valvular dysfunction.

Dose-Fractionation
Owing to a broad shoulder on the dose-response curve, hypofractionated radiation schedules have become widely adopted in the treatment of melanoma. Many retrospective series have found an advantage in response rates for radiotherapy regimens with higher doses per fraction.[11] RTOG 8305, however, found no difference between 32 Gy in 4 fractions vs 50 Gy in 20 fractions, with investigators recommending that the choice of fractionation regimen depend upon lesion location, life expectancy, convenience, and efficacy.[12] Because of the retrospective data suggesting a benefit from hypofractionation, many centers have adopted a treatment regimen of 5–6 Gy per fraction to a total dose of 30–36 Gy for dermal, subcutaneous, and lymph nodal metastases.[13] For visceral metastases, however, fractionation schemes such as 40 Gy in 10 fractions, or 50 Gy in 20 fractions have been commonly employed in order to reduce normal tissue complications. The treatment regimen in the patient in this case was 45 Gy in 20 fractions. The authors note that a unique hazard was the potential for tumor fragmentation with subsequent embolism to vital structures. To decrease the chance of acute sequelae resulting from embolism, a standard fractionation schedule was adopted. Given the goal of treatment in this case, this was an appropriate decision that minimized the chance of severe acute toxicity.

Final Thoughts

Despite advances in immunotherapy and biochemotherapy for stage IV melanoma, the prognosis for patients with visceral metastases continues to be dismal. Although a subset of patients with solitary metastases may be candidates for aggressive treatment, care must be taken to avoid severe sequelae related to therapy; this holds especially true in the treatment of patients with metastatic melanoma and multiple poor prognostic features.

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References:


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