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Case Report Open Access

Neoadjuvant Vemurafenib for Borderline Resectable Metastatic Melanoma to Liver: A Case Report

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Abstract

Vemurafenib is a selective inhibitor of mutated B-Raf protein, which is found in 60% of metastatic melanoma. Neoadjuvant Vemurafenib for patient with metastatic melanoma, to decrease tumor size prior to surgical resection has been reported in patients with metastatic melanoma to the brain and lymph nodes. We present a case of neoadjuvant Vemurafenib in a patient with large borderline resectable metastatic melanoma to the liver.

Keywords: Vemurafenib; Metastatic melanoma; Liver

Introduction

About 60% of metastatic melanoma tumors were found to have mutated B-Raf protein, which is a serine/threonine-protein kinase in the B-Raf/MEK/ERK pathway controlling cell division and differentiation [1]. The most common B-Raf mutation is at amino acid position 600, in which the normal valine is replaced by glutamic acid (B-Raf V600E mutation). The mutation causes the B-Raf gene to be constitutively activated to signal excessive cell growth [2]. Vemurafenib is a selective inhibitor of the active form of B-Raf [3]. Vemurafenib has been shown to cause programmed cell death in melanoma cell lines [4] and has been shown to improve survival in patients with metastatic melanoma with B-Raf V600E mutation [5].

Neoadjuvant Vemurafenib has been reported in patients with metastatic melanoma to the brain and lymph nodes [6]. We present a case of Vemurafenib neoadjuvant therapy prior to surgical resection in a patient with large borderline resectable metastatic melanoma to the liver and retroperitoneal lymph nodes.

Case Report

A 63 year old white male with history of posterior neck melanoma underwent wide excision and sentinel lymph node dissection 3 years prior to development of distant metastasis. The sentinel lymph node was negative and patient underwent expectant follow up. Patient presented with an episode of abdominal pain 5 months prior to surgery which prompted an evaluation with abdominal CT revealing a 10 cm tumor in the left lobe of the liver with adjacent retroperitoneal adenopathy (Figure 1). CT guided biopsy of the liver lesion showed metastatic melanoma, B-Raf mutated.

The patient was started on Vemurafenib (marketed as Zelboraf). Restaging CT scan 4 months after neoadjuvant Vemurafenib showed significant shrinkage of the liver lesion from 10.8 X 9.9 cm to 3.9 X 3.0 cm as well as significant shrinkage of the adjacent retroperitoneal adenopathy (Figure 2). There was no additional site of disease. The patient subsequently underwent left hepatectomy, retroperitoneal lymph node dissection including periportal and celiac nodes.

Surgical pathology showed the liver metastasis measuring 4.5 X 4 X 2.6 cm. Histologically, the tumor showed extensive necrosis with less than of 10% viable cells (Figure 3). Tumor bed was replaced by melanin-pigment laden macrophages consistent with treatment effect of Vemurafenib (Figure 4). Periportal and celiac lymph nodes did not show viable tumor cells (Figure 5).

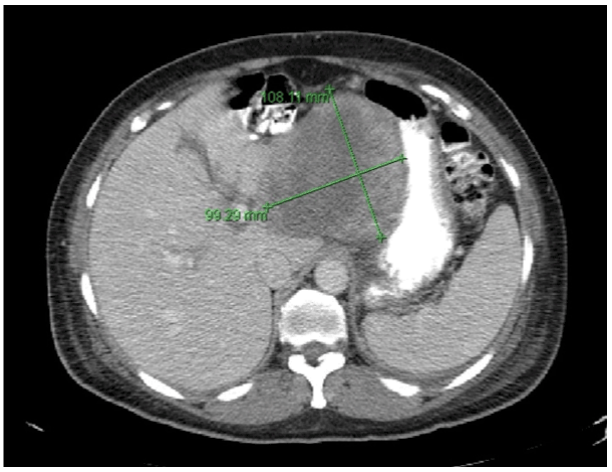

Figure 1: Liver lesion before treatment with Vemurafenib measuring 10.8 x 9.9 cm.

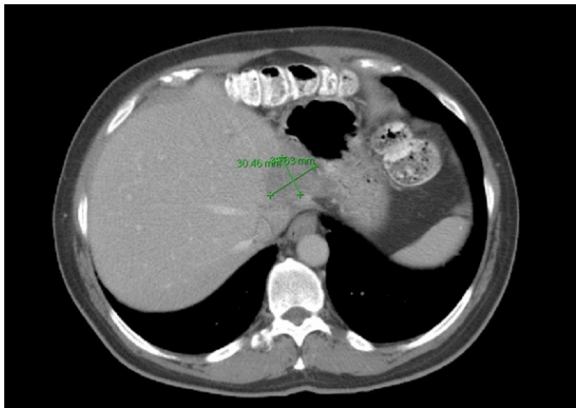

Figure 2: Liver lesion after treatment with Vemurafenib measuring 3.9 X 3.0 cm.

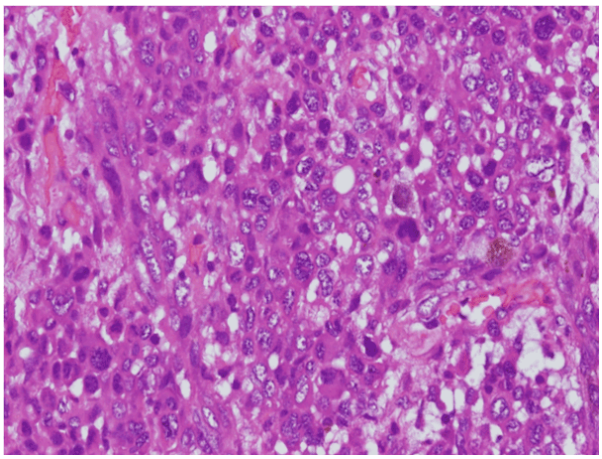

Figure 3: Focus of rare malignant melanoma cells from the liver lesion

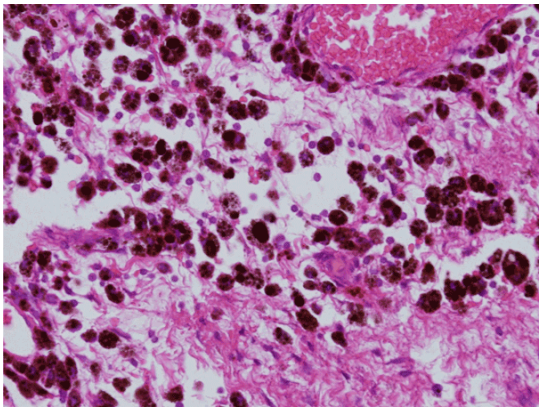

Figure 4: Pigmented macrophages in liver lesion.

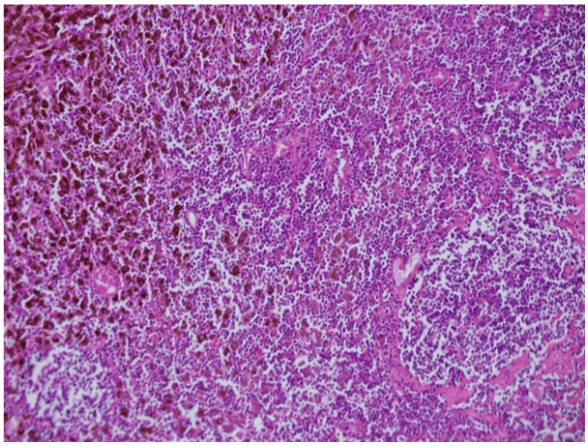

Figure 5: Lymph node with pigmented macrophages.

Discussion

Metastatic melanoma to the liver is an aggressive disease with median survival of 6 months [7]. Improved survival is associated with liver resection. However not all hepatic lesions are easily resectable.

Vemurafenib is a potent selective inhibitor of B-Raf protein with V600E mutation. It has been shown to improve patient survival in phase III clinical trial [5]. It is currently approved for the treatment of unresectable or metastatic melanoma. It has been shown in multiple cases to induce significant metastatic melanoma tumor shrinkage and often complete regression of the gross tumor [8]. However, the response was not durable with median response time of 6.7 months and most responding patient had progression of disease after initial clinical response [5,8]. Therefore, vemurafenib is proposed to be a promising neoadjuvant agent prior to surgical resection of otherwise unresectable or borderline resectable disease.

Review of literature revealed four reports of neoadjuvant Vemurafenib in the setting of borderline resectable metastatic melanoma. Fadaki et al. [9] first reported a case of melanoma involving the left axilla and neck treated with vemurafenib to achieve 50% reduction in tumor size enabling a modified radical neck and axillary dissection. Koers et al. [10] reported a case of axillary lymph node metastasis that was treated with 28-day cycle of vemurafenib to allow an axillary lymph node dissection. The third case [11] was a metastatic melaonoma to the brain, which due to its size precluded stereotactic radiosurgery. After treatment with vemurafenib, the patient received complete resection of the mass. The fourth case [6] was a patient with metastatic melanoma to the left axillary lymph node and brain. Pathology from the surgical resection after vemurafenib treatment showed complete tumor necrosis for both brain and axillary lymph node metastasis.

Our report is the first case of metastatic melanoma to the liver and retroperitoneal lymph node treated with neoadjuvant vemurafenib prior to surgery. Our patient was found to have more than 90% tumor cell reduction in his liver lesion as well as complete tumor necrosis in his periaortic and celiac lymph nodes upon histologic evaluation of his left hepatectomy and retroperitoneal lymphadenectomy specimens.

In conclusion, vemurafenib is a promising agent as neoadjuvant therapy in metastatic melanoma. This report supports further evaluation of the targeted therapy to reduce tumor burden in patients with otherwise unrespectable or borderline resectable metastatic melanoma.

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