Letter to the Editor

rare tumors

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Letter re: Uveal melanoma metastasis to the liver: Unveiling effective strategies with HEPZATO KIT

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Uveal melanoma, also called choroidal or ocular melanoma, is a collective term for melanomas of the choroid, ciliary body, and iris. It is the most common primary intraocular malignancy. The usual clinical presentation includes metamorphopsia (painless loss or distortion of vision). If the tumor is large, it may also be associated with a serous retinal detachment causing flashing or flickering of light (photopsia). Risk factors that lead to the development of uveal melanoma are Caucasian ethnicity, exposure to welding, light eye color, dysplastic nevus syndrome, ocular melanocytosis, and inheritance of BRCA1-associated protein 1 (BAP1) mutations.[1] Copy number profile (e.g. monosomy 3, chr 8q gain) and/or a class 2 gene expression profile determines whether the tumor will metastasize or not.[2]

The treatment depends upon whether the tumor is localized in the eye or has undergone metastasis. If it is a primary tumor, the patient can be kept under observation if there are no typical findings of melanoma. Surgical interventions include enucleation and selective excision of the tumor. But if metastasis is detected, systemic chemotherapy, chemoimmunotherapy, and molecular-targeted therapies can be used.[3,4]

In uveal melanoma, choroid most commonly spreads to distant sites. Approximately 50% of patients develop metastasis of uveal melanoma. Uveal melanoma metastasis mostly takes place in the liver (95%), followed by lungs (24%), bone (16%) and skin (11%). However, disease progression in the liver determines the clinical course of these patients.[2] Since the liver is the first site of metastasis via the hematogenous route because the eye does not contain lymphatic vessels, liver-directed therapies have shown promising results.[3,2] Over the years, various therapies have been used, like surgical resection, hepatic artery embolization, hepatic arterial infusion of chemotherapy, and radiofrequency ablation; with each treatment option associated with different sets of limitations. The disease has been affiliated with a discouraging prognosis over the years, and novel treatments are still being developed and explored.[3]

One such treatment option in liver-directed therapy, HEPZATO KIT (melphalan for Injection/Hepatic Delivery System) has recently been approved by the FDA in the United States after its evaluation in the FOCUS study, a single-arm, multicenter, open-label trial by the mechanism of Percutaneous hepatic perfusion (PHP), which is a minimally invasive technique that effectively delivers antineoplastic drugs precisely to liver tumors.[5]

Melphalan is a non-cycle specific DNA alkylating agent that adheres to guanine causing cross-link of DNA which ultimately disrupts DNA. The purpose of HEPZATO KIT is to improve the survival of patients who have unresectable liver metastases by reducing the size of the tumor and protecting liver functions. The target population of this study is adult patients with uveal melanoma with unresectable hepatic metastases (<50% of liver involved), or extrahepatic disease limited to an organ that is amenable to resection or radiation. This study reported encouraging results, 36.3% of patients showed reduction or disappearance of tumor, median duration of response was 14 months,

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disease control rate was 73.6% with 7.7% complete responses and 28% partial responses.[6]

The treatment of liver metastasis disease of uveal melanoma has a significant impact as it is the common cause of death in patients with metastatic uveal melanoma (mUM). The interventions of systemic chemotherapy, chemoimmunotherapy, immunotherapy, and molecular-targeted therapies are either ineffective or have serious side effects. But HEPZATO KIT is closing the gap and bringing us closer to more effective and targeted treatment therapies.

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