

Late Metastatic Presentation of Ocular Melanoma

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Abstract Choroidal melanoma is the most common primary intraocular malignant tumor and the second most common type of primary malignant melanoma in the body. The liver is main site of metastasis in more than 80% cases. There is no consensus regarding follow up with patient having ocular melanoma to see any metastatic disease. We present a case admitted with right upper quadrant pain and diagnosed with metastatic melanoma due to right ocular lesion treated 20 years ago. After the diagnosis was made patient survived only for two weeks. That further signifies the unpredictable course of the disease.

Keywords: choroidal melanoma, follow up, liver metastasis

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1. Background

Choroidal melanoma represents 85 %, of all ocular melanomas and up to 50 % of patients develop metastatic disease [3]. Liver is the most common site of metastasis and its associated with a very poor prognosis. Uveal melanoma originates from melanocytes located anywhere in uveal tract. Choroid is involved in almost 85% -90% of cases, iris and ciliary body are involved in remaining cases. Despite the development of most effective therapeutic methods, 50 % of patients still develop metastatic disease [3]. Incidence of melanoma is increasing rapidly in both men and women. Cutaneous melanoma and ocular melanoma are considered different entities in both metastatic latency and metastatic diffusion. Liver is the principal target organ of ocular metastasis. While cutaneous melanoma spreads to lymph nodes and soft tissues with a minor incidence of hepatic diffusion [5].

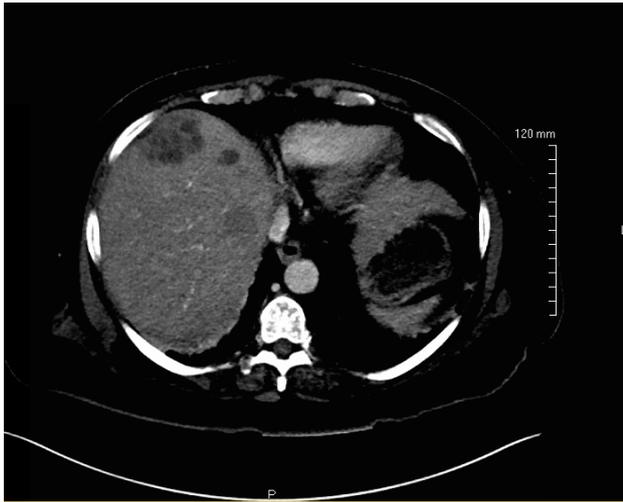
2. Case Presentation

61-year-old female was admitted with abdominal pain mainly in right upper quadrant of abdomen for last 4 weeks. Pain was constant, moderate and radiating to right upper flank with no known aggravating and relieving factors. Pain was associated with night sweats. According to patient she was trying to pull a chair and noticed pain. She did not seek medical attention thinking about muscle spasm but it did not get better. She has a history of right eye choroidal melanoma treated with enucleation in 7/1997. Since then patient was having regular follow up with an ophthalmologist and was negative for metastatic

diffusion or recurrence. Her past medical history was significant for basal cell carcinoma of forehead, squamous cell carcinoma of nose and diabetes mellitus. She was on oral hypoglycemic. Patient denied nausea, vomiting black color stools any recent changes in weight or appetite. Patient was feeling depressed due to recent death of her husband but denied any homicidal or suicidal thoughts. After initial treatment with analgesic she had CT of abdomen and pelvis that showed multiple lesion in liver suggestive of metastatic disease. Interventional radiologist consult was requested and patient has CT guided biopsy that came positive for malignant melanoma and there was no other lesion identified on physical examination suggestive of malignant melanoma. Patient has elevated AST and ALT but normal bilirubin level. Patient was discharged home to follow up with oncology.



CT scan showing multiple lesions in liver



One week later patient was brought into the emergency department with syncopal episode. Hypoglycemia and hyponatremia were present on labs. As part of trauma work up patient CT abdomen and pelvis was done which showed worsening of liver metastasis. Patient had worsening of LFTs and developed liver failure due to severe metastatic disease. MRCP abdomen was done that did not show any extrahepatic duct dilatation no intervention was performed. Hematology/oncology consult was requested. Patient was not started on any chemotherapy due to worsening liver failure and patient died within 2 weeks due to progressive liver failure.

3. Case Discussion

Malignant melanoma is the most common primary intraocular tumor with 40 % risk of metastasis to the liver within ten years of diagnosis. In this case, the patient is diagnosed with liver metastasis after 20 of enucleation that makes it unusual for its presentation. Hepatic metastasis occurs in 95% of patients which results in death in almost all the cases. Ocular melanoma that spreads to liver can be categorized into stage 1 (<50 um in diameter), stage 2 (51-500 um in diameter), or stage 3 (>500 um in diameter) metastasis [1]. Malignant melanoma can spread to any organ in the body but the most frequently involved sites are liver, bone and brain. Patients with metastatic melanoma generally has a poor prognosis. The site of metastasis is an important independent predictor of survival in patients with metastatic disease. Patients with metastasis to nonvisceral sites like skin, lymph nodes and subcutaneous tissues has median survival of 18 months. Those with lung metastasis had a median survival of 12 months and those with metastasis to visceral sites (such as liver, brain or bone) had a median survival of 7 months. Number of metastatic sites was the most significant prognostic factor in patients with distant metastasis [2]. Multiple factors are involved in determining the risk for metastasis which include tumor location, size and genetic profile. High risk patients can also be determined by genotypic profiling using multiplex ligation-dependent probe amplification method [3]. Ocular melanoma metastasis to the liver has well defined gene expression pattern that is remarkably different from other tumors.

Liver metastasis can be found many years after enucleation of the affected eye with negative screening for metastasis at the time of surgery. This fact suggest that micro metastases are present in many patients even before the time of diagnosis of disease [4]. So, to prolong the survival, efforts should be made to suppress the metastasis from the primary tumor rather than prevention of its recurrence [4]. Gene expression in ocular melanoma liver metastasis shows various similarities with other malignant tumors of other origins like leukemia and skin melanoma. It involves activation of common pathways in malignant tissues of different sites. For example, NFKB pathway is activated in many different malignancies like melanoma, leukemia and liver malignancies [4]. Curative treatment of liver metastasis from ocular melanoma is still debatable. Recent development of novel agents has shown greater efficacy than traditional ones. A monoclonal antibody Ipilimumab, directed to cytotoxic T lymphocyte antigen-4 (CTLA-4) has been shown to improve overall survival in metastatic melanoma patients. Likewise, (a selective B-Raf inhibitor) vemurafenib and trametinib (a selective inhibitor of MEK1/MEK2) were also noted to improve the survival among these patients. The other operative treatment options include hepatic resection, hepatic intra-arterial chemotherapy, chemoembolization and hepatic perfusions [5].

4. Conclusion

Any patient presenting with GIT symptoms after removal of ocular melanoma, should be investigated for liver metastasis. As liver is the most common site for metastasis in all cases. It can present several years after removal of the primary ocular tumor.

Abbreviation

LFTs- Liver function tests,
GIT- Gastrointestinal tract,
MRCP-Magnetic resonance cholangiopancreatography,
AST- Amino aspartate transferase,
ALT –Amino alanine transferase.

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