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Metastatic Cutaneous Malignant Melanoma to the Orbit: A Case Report

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Case Summary

Melanoma is a malignancy of melanocytes and can present anywhere in the body where there are melanocytic cells. Cutaneous melanoma is the third cutaneous cancer, but it is the most fatal. Cutaneous melanoma metastasizes widely; the commonest sites of metastasis are the lungs, skin, subcutaneous tissue, liver, brain, and bone. Rarely, metastasis can involve the orbit, and even more rarely, it can be the first presentation of widespread systemic metastasis. Orbital metastases from cutaneous melanoma typically occur at a late stage of the disease, where it carries a poor survival rate.

We report a 68-year-old woman, who presented with a 3-month history of right eye protrusion accompanied by vision loss. She reports having a non-healing black swelling on her left big toe, for which she underwent amputation a year ago. The amputated toe was not taken for histopathology examination. On ocular examination, a brownish-pigmented protruding mass that appeared to originate from both superior and inferior conjunctival fornices, pushing the eyeball laterally, with tortuous feeder vessels and an opaque cornea, was seen. Hyperpigmented skin nodules on the left foot and an ulcer on the anteromedial aspect of the left leg were seen. A histopathology examination of the skin nodule revealed a cutaneous melanoma (Clarks level VI) with positive margins. The patient underwent orbital exenteration, and the biopsy was conclusive for a metastatic malignant melanoma of the orbit.

Unfortunately, skin melanomas can mimic other benign skin lesions, making it easy to miss or delay diagnosis, which can lead to a poor survival outcome. The patient missed an opportunity for an early diagnosis of skin melanoma due to a lack of histopathological examination of the amputated toe, probably due to a low index of suspicion. To avoid delays in treatment, efforts should be made to do histopathology studies for every excised lesion, even in low-resource settings.

Keywords: *Orbital melanoma, Malignant cutaneous melanoma, Case report.*

Introduction

Orbital melanomas are the malignancy of melanocytes, which can present as a primary or secondary disease. Primary orbital melanoma (POM) is an extremely rare condition, representing less than 1% of all orbital tumours (1-3). Secondary orbital melanomas are more common than POM, contributing to 5-20% of all orbital metastases (4). Secondary orbital melanoma develops from local spread from the uvea, ocular surface, and sinuses or from distant metastases from the skin and leptomeningeal melanoma (1-2, 4-5). Although metastatic melanoma of the orbit always occurs in patients with a known primary site, in some cases the primary site is unknown (4, 6).

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Cutaneous melanoma metastasizes widely but rarely involves the orbit. The commonest site of metastasis is the lungs, skin, subcutaneous tissue, liver, brain, and bone (5). Metastatic cutaneous melanoma to the eye and orbit is very rare and accounts for less than 5% of all metastases in this region (7). Metastases to the eye are more common than to the orbit (7). In metastatic cutaneous melanoma to the orbit and eye, the most common primary tumour location is the trunk, upper and lower extremities, and the least common from the head and neck (7). Although uncommon, few cases of synchronous ocular and cutaneous melanoma have been observed, which give a clue these could be different diseases occurring simultaneously (8).

Orbital metastases from cutaneous melanoma typically occur at a late stage of the disease as part of a wide-spread systemic metastasis, where they carry a poor survival rate ranging from 5.7 to 19.7 months (5, 9). In a few cases, orbital metastasis can present as the first sign of cutaneous metastasis (5,7). The orbital metastasis commonly presents with double vision and restricted ocular motility. These symptoms occur due to the extraocular muscle infiltration by the tumour since these muscles are a preferred location of metastases from melanoma primaries. Proptosis is the most frequent clinical sign (5, 10). Despite recent advances in the management of metastatic melanoma, treatment is usually palliative.

Herein, we present a rare case of secondary orbital melanoma, as a first presentation of systemic metastasis from the skin of the lower limb. A patient with missed opportunity of early diagnosis from the amputated toe due to lack of histopathology examination. The patient's course of illness and outcome highlights the need to remind clinicians to perform histopathology examination to every suspicious lesion to improve care, reduce risk of metastasis and increase chances of survival to patients.

Case Presentation

We report a 68-year-old woman, a retired nurse officer presented with 3 months history of right eye protrusion accompanied with loss of vision and pain. The patient reported that prior to this presentation she had a non-healing black swelling on her left big toe for about nine months. She went to the nearby hospital where the amputation of the affected toe was done a year ago. The amputated toe was not taken for histopathology examination. Six months later the dark coloured raised swelling recurred again on the anterior aspect of her left leg closer to the amputated toe. However, this time the patient did not seek treatment because the swelling was not painful and post amputation she was not told if there was any risk of having a cancer. Review of other systems showed that the patient had significant weight loss. This was

determined by asking the patient about the current weight compared to previous weight and attire fittings.

Generally, she was fully conscious with Glasgow coma scale of 15, severely wasted with body mass index of 16kg/m2, mild pale with stable vital signs. The preauricular, submandibular and cervical lymph nodes were not palpable.

Ocular examination; RE Visual acuity was no light perception. The eyelid skin was hyperpigmented with incomplete mechanical ptosis. There was a brownish pigmented protruding mass which appeared to originate from both superior and inferior conjunctival fornices, pushing the eyeball laterally, with tortuous feeder vessels and an opaque cornea (figure 1). Ocular motility was restricted in all directions of gaze. The left eye revealed normal findings with visual acuity of 6/9.

Figure 1

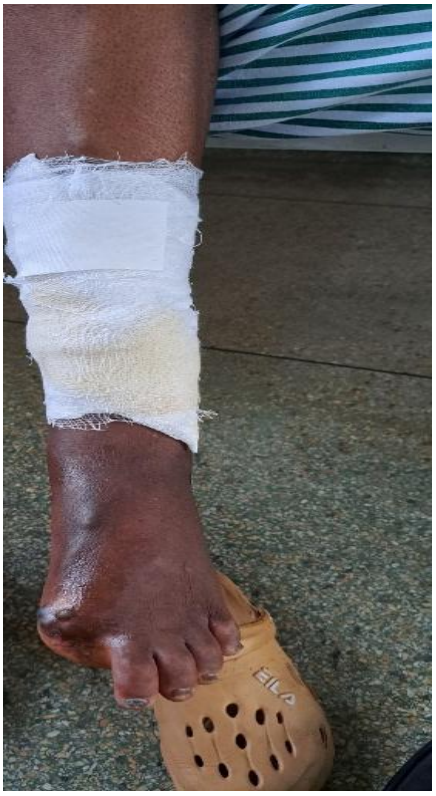

Figure 2

Figure 1. Image of hyperpigmented conjunctival mass originating from fornices of the Right eye.

Figure 2. Image of the left leg showing the amputated big toe and the hyperpigmented nodules on the stump and on mid foot. The gauze covers the recurrent wound on Left leg.

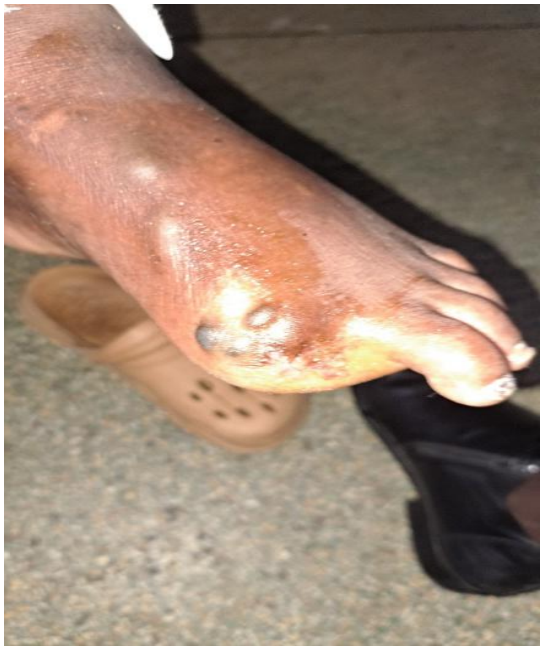

Figure 3. Image of the left leg showing the amputated big toe and the hyperpigmented nodules on the stump and on the dorsum of foot.

A provisional diagnosis of secondary orbital melanoma from cutaneous metastasis was made.

Investigations

Computed tomography scan of the orbit and brain with contrast revealed a homogenous hyperdense right intraorbital mass measuring 4.8x2.24cm with homogenous enhancement on post contrast. The mass was inseparable from the globe and the globe was deformed. The mass caused the expansion of right orbit without evidence of bone erosion (figure 5 and 6). The brain parenchyma and paranasal sinuses were normal. A chest x-ray revealed large, round, well circumscribed opacities suggestive of cannon ball metastasis (figure 4). Multiple well-defined hypoechoic lesions in the liver suggestive of liver metastasis were visible in the abdominal ultrasound. A histopathology examination of the skin nodule was done and it revealed a spindled cell neoplasm composed of intersecting fascicles of atypical spindle and epithelioid cells, with vesicular chromatin and many mitotic figures. The deep and lateral margins were involved by tumour. These features were conclusive for cutaneous melanoma Clarks level VI with positive margins.

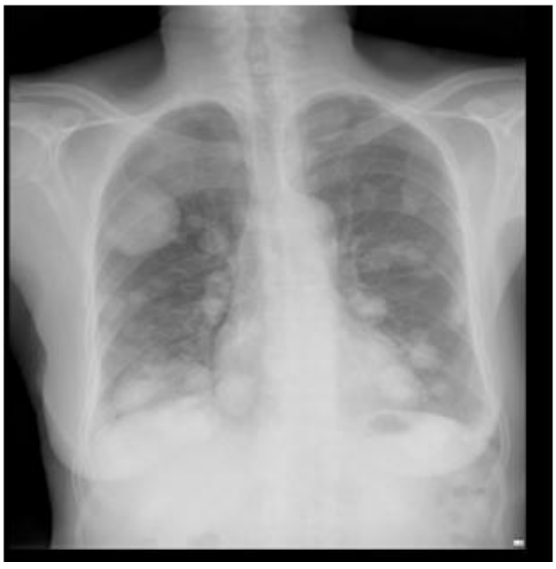

Figure 4. Posterior-Anterior view of Chest X-Ray showing cannon ball metastasis

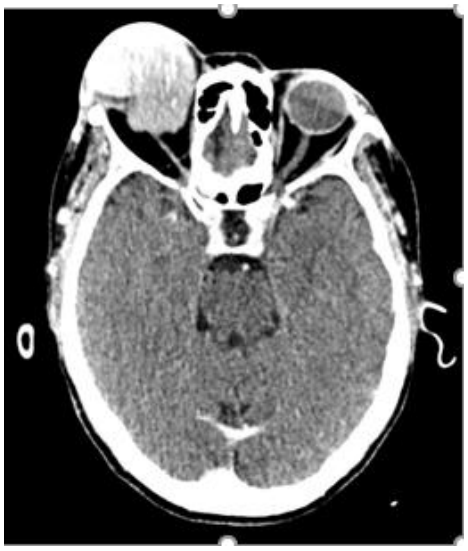

Figure 5

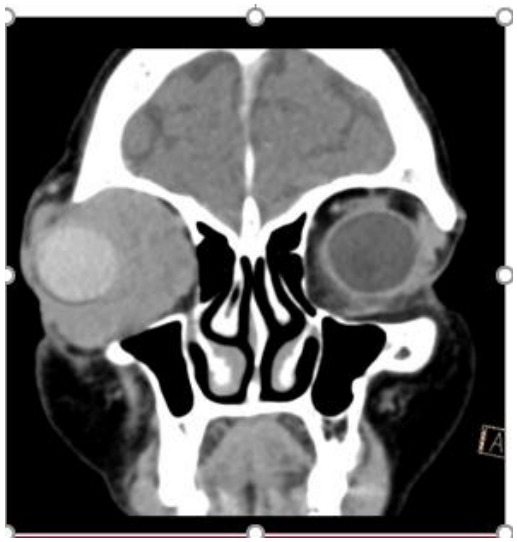

Figure 6

Figure 5/6 Axial and coronal CT scan view respectively showing the hyperdense intraorbital mass surrounding the deformed globe.

The patient underwent subtotal right orbital exenteration. There was bone erosion involving the floor and medial orbital walls of the orbit. Histopathology of the orbital tumor showed large tumor cells, pleomorphic with abundant brownish pigments in the cytoplasm. The nuclei had open chromatin with prominent nucleoli (figure 7/8). The tumour was extraocular. A Conclusion of metastatic malignant melanoma to the orbit was reached. The patient was referred to the National Cancer treatment centre for palliative chemotherapy but she opted not to go and she was discharged for palliative care. However, the patient died four months later due to systemic metastases.

H&E stain

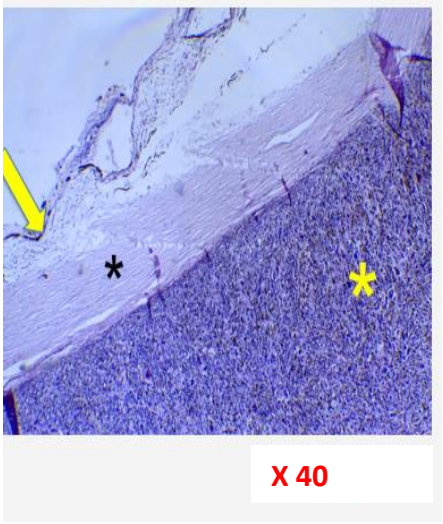

Figure 7

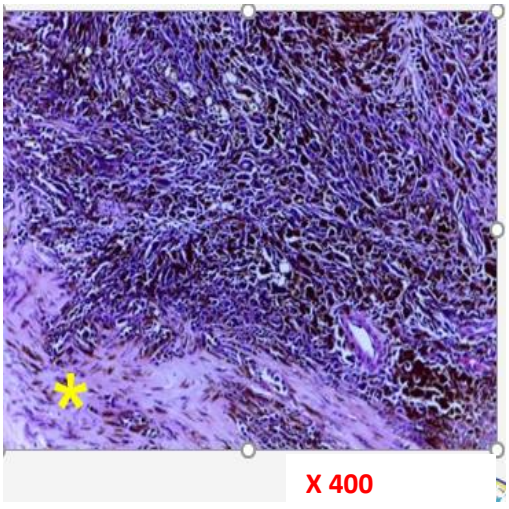

Figure 8

Haematoxylin and Eosin histopathology features of the exenterated orbital tumour. ***Figure 7.*** *Yellow asterisk, shows the circumscribed diffuse tumour abutting the extraocular surface, Note intact sclera (asterisk) and intraocular benign choroidal layer* ***Figure 8****. Shows the diffuse tumour with large pleomorphic cells having abundant intracytoplasmic melanin pigment. Note sclera disruption by the tumour (yellow asterisk).*

Discussion

The orbit is a rare site of distant metastases from cutaneous melanoma. The most common reported sites for cutaneous melanoma metastasis are the lungs, liver, skin, and brain (7). Orbital involvement is very rare and usually occurs in the late stage, however in few cases it can be the first presentation of the systemic metastasis (5-7, 9). Rosenberg et al. showed that the common primary site for skin melanoma metastasis to the orbit is from the lower extremities (5). This is similar to our case, where the patient presented with dark swelling on the left toe for more than a year before the occurrence of the orbital disease. The toe was amputated but the swelling recurred.

Metastatic orbital melanoma usually occurs late as part of a wide-spread metastasis, and in the majority, the primary source is known (5-6). Most patients present with a previous known history of a wide-spread metastasis or disseminated disease is found during the metastatic workup (4-5, 9). This is similar to the findings of our case; the patient had metastatic tumours in the other skin areas, inguinal lymph nodes, liver, and lungs, which were found during the metastatic workup. However, the orbital disease was the first presentation of the widespread metastasis of the cutaneous melanoma in this case.

Majority of cutaneous melanoma cases are diagnosed over 65years, similar to our case (14). About 98.2% of cutaneous melanoma are reported amongst white-skinned individuals (13), and arises from a complex interaction between environmental and constitutional or phenotypic factors (13). The main environmental factor implicated in the development of cutaneous melanoma is ultraviolet radiation (13). Our patient was a nurse attendant of dark skin complexion, being a nurse with most works doing indoors probably had limited sun exposure. Fair pigmentation being the commonest phenotypical risk factor was absent in our patient. A mutation in BRCA-associated protein-1 (BAP1) has been identified in families with multiple members with cases of uveal and cutaneous melanomas (9). Perhaps this could account for quite a rare presentation with both ocular and cutaneous presentation in our case. However, patient had no family history of melanoma. Genetic testing was necessary to this case but due to lack of resources it was not done.

Metastatic cutaneous melanoma had a higher predilection to the extraocular muscles than other tumour primaries (10). In our case the orbital CT scan, showed a diffuse involvement of extraocular tissue and the extraocular muscles. The orbital disease was confirmed in the extraocular tissues, and the eye was not involved. This ruled out the possibility of the primary site of the orbital disease being the uvea, which is the commonest site of secondary orbital melanoma.

The treatment of orbital melanoma is controversial. The treatment options include local tumour resection, debulking, and subtotal or total orbital exenteration. Adjuvant radiotherapy, immunotherapy and chemotherapy can be given depending on the presence of other systemic metastases and the life expectancy (3-5). When a wide-spread metastatic disease is present or when both orbits and eyes are involved, the treatment is usually palliative (3, 5). Our patient presented with a disseminated disease in which she underwent subtotal right orbital exenteration as part of palliative care. A surgical intervention was done to relieve the disfiguring proptosis, pain and for a biopsy. It had no benefit in terms of long-term survival.

The survival rate of patients with orbital melanoma from cutaneous malignant melanoma is very low, ranging between 5.7 and 19.7 months. This is due to the fact that the orbital disease usually occurs late as part of a wide-spread metastasis (4-5, 9). This is similar to the observation seen in our patient, where the patient died four months after the diagnosis of the orbital disease. The patient had wide-spread metastasis at the time of the initial orbital diagnosis. Our patient missed the opportunity of early diagnosis and treatment simply because the affected toe was amputated but not sent for histopathology examination at the time of first presentation to the hospital. The patient's course of illness and outcome highlights the need to remind clinicians to perform histopathology examination to every suspicious lesion to improve care, reduce risks of metastasis and increase chances of survival to patients.

This case has some limitation, from our case its difficulty to be certainly sure that the primary source of the secondary orbital melanoma was from the skin or metastasis from other primary sites. Due to lack of enough resources, molecular studies were not carried out which would have helped us to know if we are dealing with the same cancer or different cancer. The fact that inguinal lymph node, lung and liver lesions were not biopsied, pose a challenge to tell exactly if this was the same melanoma from skin and not malignancy form other sites. Reports of ocular melanoma coexisting with second primary cancers have been reported (12). But also a personal history of cutaneous melanoma is also a known risk factor for further melanoma primaries (13).

Conclusion

Secondary orbital melanomas from cutaneous melanoma show a poor survival rate because they are usually the result of widespread metastases. A high index of suspicion is required for earlier identification and treatment of cutaneous melanoma. Histopathological examination and early referral are necessary for all patients with suspicious lesions to avoid missing the diagnosis.

Ethical considerations

The patient gave a written consent for using her information and pictures and this manuscript to be published, as long as patient details were anonymous.

Declarations

Acknowledgements

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Authors' contributions

HM and JS were responsible for clinical care for the patient, prepared and revised the manuscript. CM reviewed the manuscript and performed literature review. FS and HM finalized the manuscript and case writing coordination.

Competing interests:

The authors have no competing interests to declare

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