

Choroidal Melanoma Associated to Pregnancy: Case Report

Mohamed Ait Erraisse^{1, *}, Fatima Zahra Abboud¹, Badr Alami²,
Touria Bouhafa¹, Khalid Hassouni¹

¹Department of Radiation Oncology, University Hospital Hassan II, Fez, Morocco

²Department of Radiology, University Hospital Hassan II, Fez, Morocco

Abstract

This is a case of malignant melanoma of the choroid that occurred during pregnancy. This is a 32-year-old female mother of a daughter, and who is at 28 weeks of pregnancy with the diagnosis of malignant melanoma of the choroid on the decreasing of visual acuity and clinical and imaging findings. Given the diffuse involvement, an enucleation is performed with placement of an ocular prosthesis. Pathological examination confirmed the diagnosis of choroidal melanoma with positive posterior margin resection. Radiotherapy was then indicated but after delivery since no proton therapy is available. Intensity modulated radiation therapy (IMRT) was performed in a hypofractionated schedule. Reporting this observation is to discuss the difficulties of management in a pregnant woman and also the possible alternatives to the lack of material resources like proton therapy.

Keywords

Melanoma, Choroid, Pregnancy, IMRT

Received: June 30, 2018 / Accepted: August 20, 2018 / Published online: March 5, 2019

@ 2018 The Authors. Published by American Institute of Science. This Open Access article is under the CC BY license.

<http://creativecommons.org/licenses/by/4.0/>

1. Introduction

Melanoma of the choroid is a malignant melanic tumor. It accounts for 1.2 to 6.6% of malignant melanomas in the uvea [1]. The growth of melanomas of the choroid during pregnancy is described and the influence of hormones is suggested. Its positive diagnosis is based mainly on an increase in size documented by photographs, and its differential diagnosis is essentially with the benign naevus. The role of pregnancy in the acceleration of cutaneous melanomas is known, the growth of melanomas of the choroid during pregnancy is described and the hormonal influence is suggested. Surgery and or radiation therapy are the main treatment options. Conservative surgery is not always possible due to delay in diagnosis in developing countries. High technique radiation therapy (like protons) is the best radiotherapy in this case. But in the absence of this technique,

3D conformal radiotherapy or IMRT could be good alternatives.

2. The Case

This is a 32-year-old female patient who is married, has a daughter, and who is 28 weeks pregnant.

She had a pterygium removed 5 years ago. She has no other medical history events.

The symptoms date back to a year ago by a decrease in visual acuity of the left eye without any other associated signs. The patient consulted a general practitioner who advised her to see a specialist but did not for social reasons (no access to such care in a small village, lack of resources to travel to the city, appointment delay etc...). Then the symptomatology was followed by the appearance of a strabismus of the left eye

* Corresponding author

E-mail address: aiterraissemohamed@gmail.com (M. A. Erraisse), abboud@gmail.com (F. Z. Abboud), bouhafa@gmail.com (T. Bouhafa), hassouni@gmail.com (K. Hassouni)

which motivated the patient to consult an ophthalmologist.

The ophthalmological examination found a decrease in visual acuity to 2/10 and a diffuse left pigmented intra-ocular mass. The right eye was without abnormalities. The diagnosis of a choroidal melanoma was suggested.

For the local extension assessment, an orbito-cerebral MRI was performed at the university hospital and showed an evocative aspect of a choroidal melanoma because of its hyper intense signal in T1 weighted sequence and hypo intense in T2, its hyper-vascular activity on the Doppler. The tumor exhibits extraocular extension, particularly at the level of the insertion of the optic nerve. It involves the posterior segment of the eye developed in the vitreous, invading the posterior wall of the left eyeball, encroaches on the insertion of the optic nerve at the posterior wall of the eyeball. There is no extension the the contralateral orbit nor a second localization (Figures 1, 2, 3).



Figure 1. Axial MRI T1 slice showing high density left posterior intra-ocular mass.



Figure 2. Axial MRI T2 weighted showing involvement of the posterior segment.

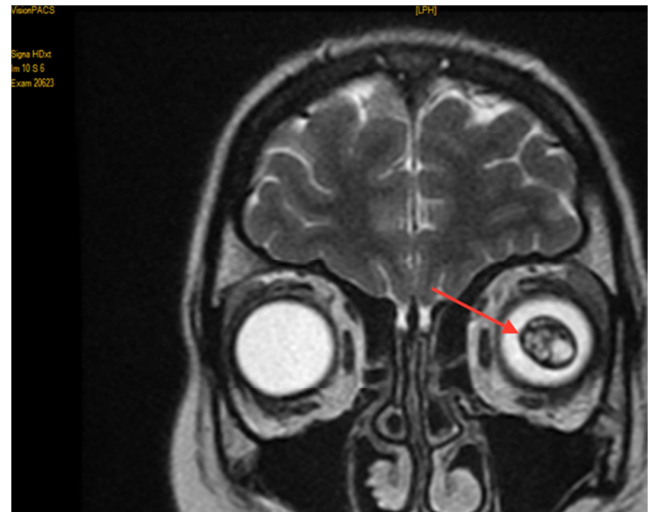


Figure 3. Coronal MRI slice with low density left intraocular image.

For the distance assessment, a cervico-thoracic CT-scan was performed and showed pulmonary parenchymal micronodules to be monitored in the context.

A liver ultrasound was without abnormalities.

Given this locally advanced aspect of melanoma, eye preservation was impossible. The stage and diagnosis were discussed with the patient and the prognosis was explained. After thinking, she accepted the radical surgery.

The patient was prepared physically and psychologically for herself and for her foetus. A left enucleation was performed with placement of an ocular prosthesis. The postoperative follow up was normal. The obstetrical ultrasound was also good.

Anatomopathological examination finds an epitheloid-type ocular melanoma of 1.3 cm x 1.3 cm, with infiltration of the sclera and periorbital soft tissues. absence of vascular emboli. The optic nerve margin was negative. The posterior resection limit of the soft tissues in retro-orbital areas was positive (R1). The tumor was classified pT4cR1 according to the AJCC.

Adjuvant radiotherapy was indicated on the histological R1 posteriorly.

Not having a proton therapy unit at the institution and given the risk of radiation to the foetus and after discussion with the surgeon, it was decided to delay radiotherapy until after delivery. The patient understood the risks and accepted the treatment rationale. She gave birth to a young healthy boy.

After that, an intensity-modulated radiotherapy (IMRT) was delivered at a dose of 24 Gy to the orbit at 6 Gy per fraction and two fractions per week for a total of 3 weeks. 6X energy photon beams were used given the superficial orbital region. The contouring was performed using an MRI / CT fusion. The IMRT technique helped to respect the dose constraints to the optic chiasm, right optic nerve, right retina and other organs at

risk such as brainstem and spinal cord. At the same time, the prescribed dose was confined to the planning target volume (PTV) (Figures 5, 6). She was seen in radiotherapy consultation every week until the end of treatment. She was breastfeeding.

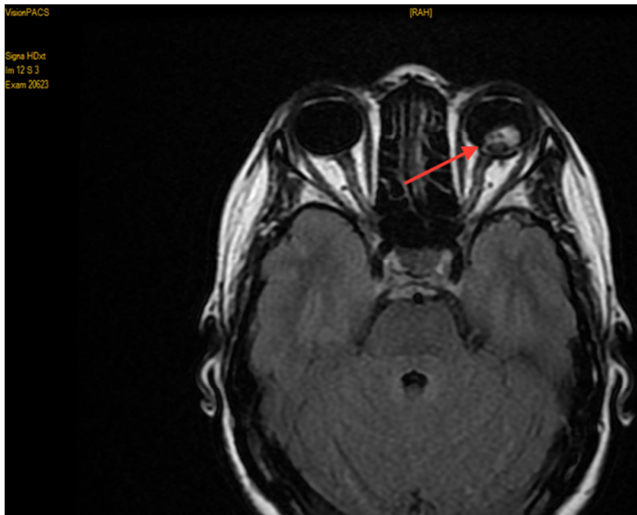


Figure 4. Axial MRI T2 FLAIR with left intraocular low density mass.

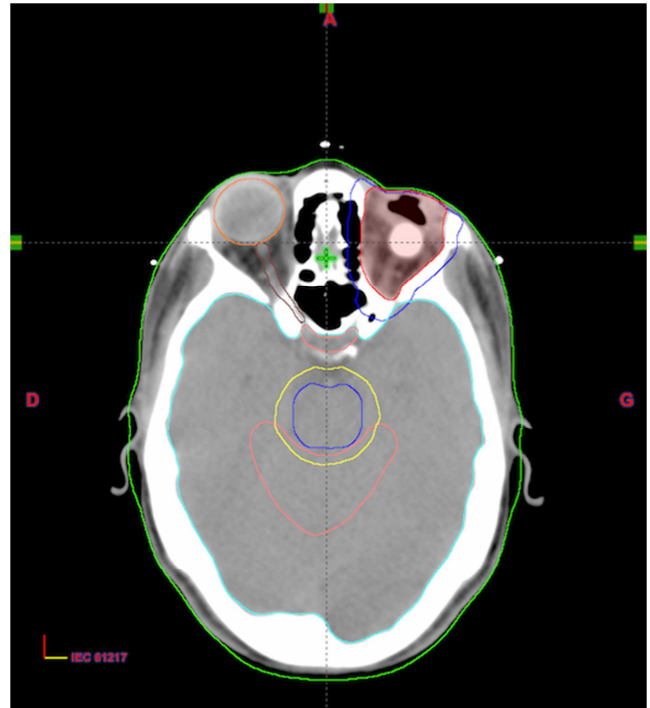


Figure 5. Axial CT slice showing countouring of different structures.

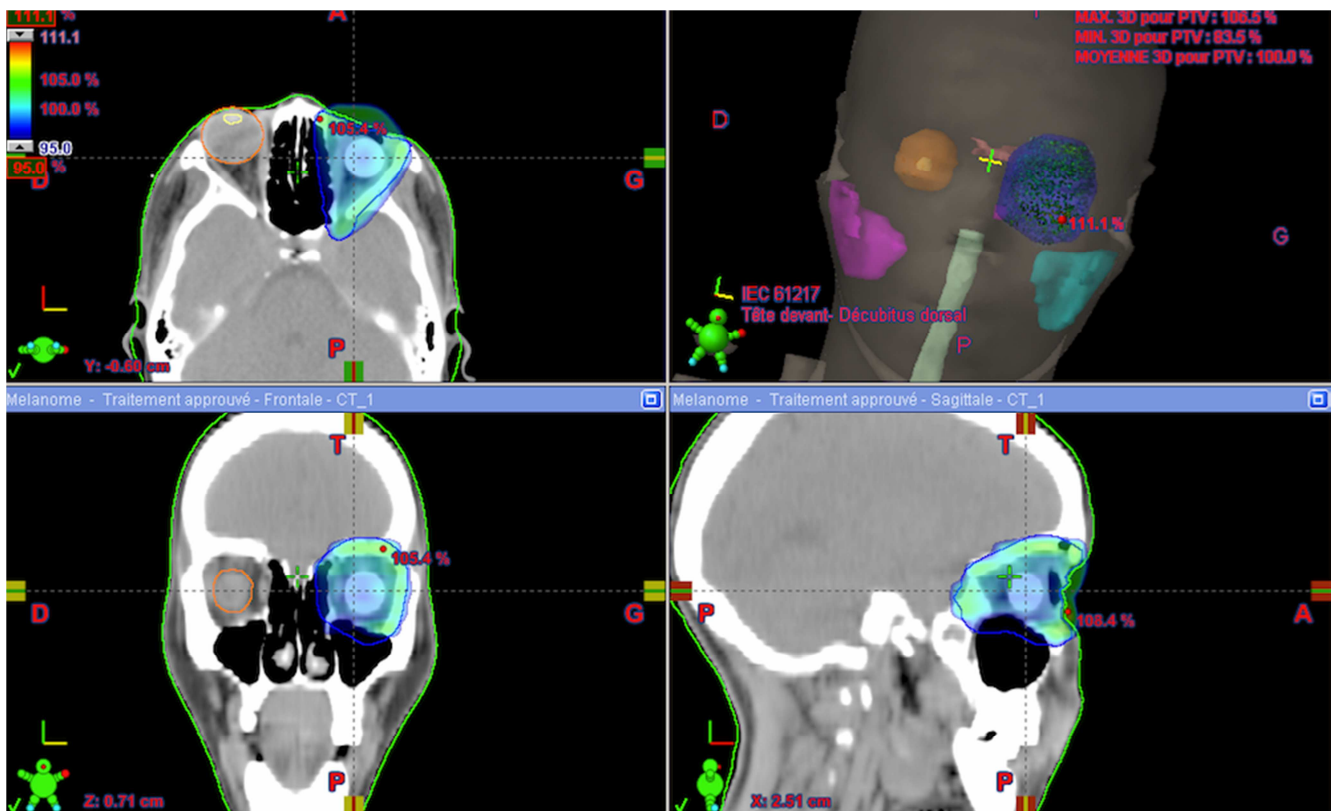


Figure 6. Dosimetric view showing the confinement of the prescribed dose to the target volume (in blue).

Radiation therapy was well tolerated with moderate skin reaction. Topic treatment was prescribed.

The patient was seen after two months of radiotherapy without any signs of progression. She was advised a long term follow

up given the risk of recurrence. Given her social situation, she couldn't have a PET CT at any time of her treatment course. She will have MRI or at least CT scans during follow up.

3. Discussion

Malignant melanomas of the uvea are frequented more often in the choroid and the ciliary body in comparison to the iris. It affects subjects quite young [1], as in this case where the patient is 32 years old. Melanomas are highly malignant epithelial cancers [2].

The clinical presentation of choroidal melanomas is highly variable. anterior choroidal melanomas have a delayed presentation because of slow growth. Usually, patients present with vision blur. When peripheral melanoma enlarges, patient may experience painless and progressive visual loss. Floaters are experienced in case of necrosis of tumour or haemorrhage. Severe pain may be observed with compression of tumour on ciliary nerves or due to acute angle closure glaucoma. Sometimes, the patient remains asymptomatic until the tumour has grown sufficiently to become necrotic and produce complications such as endophthalmitis, massive intraocular haemorrhage, and/or secondary glaucoma. The majority of the choroidal melanomas spread by haematogenous route mainly to the liver [3].

The role of pregnancy in the acceleration of cutaneous melanomas is known, the growth of nevi and melanomas of the choroid during pregnancy is described and the influence of hormones is suggested [4], [5], [6]. This could be the case in this patient where the symptoms started before pregnancy but increased during it.

Hyper-pigmentation, which reflects an increase in melanocyte activity, is induced by hormonal stimulation either during pregnancy, oral contraception or hormone therapy during menopause [7].

The most reliable sign is the existence of an increase in size documented by photographs [7], this tumor growth suggests the diagnosis of melanoma and imposes a therapeutic sanction. For this patient and given the lack of resources and access to care, patients consult with delay which compromise conservative treatment.

The modified Callender's classification of uveal melanomas has four categories [8]:

1. Spindle cell type tumours comprising 45% of all choroidal melanomas.
2. Pure epitheloid cell Melanomas 5% (rare occurrence).
3. Mixed cell melanoma 45% (comprising of spindle cell and epitheloid cell types).
4. Necrotic melanoma 5% (predominant cell type unrecognizable).

Differential diagnosis can be: Macroscopically: choroid nevus, disciform degeneration, peripheral disciform

degeneration, congenital hypertrophy of retinal pigment, choroidal haemangiomas [9] and microscopically: the spindle cell nevus, metastatic carcinoma and metastatic melanoma. Besides certain spindle cell variants (amelanotic types) may be difficult to distinguish from uveal neurobroma and schwannomas. Immunohistochemically, malignant melanomas are reactive for S-100 protein, HMB-45, and Mart-1 [10].

MRI signal characteristics will generally help differentiate melanoma from benign lesions and could be considered in cases where there is diagnostic uncertainty [11].

Localized tumors are treated by surgical excision.

Diffuse forms can only be treated by enucleation. The locally advanced involvement of the tumor for this patient could not spare the patient the enucleation, the only curative option at this stage.

Circumferential irradiation performed by brachytherapy or accelerated proton beam can be effective for local tumor control [12], but does not allow histopathological examination of the tumor! This irradiation can be used alone or in combination with surgery if there is an impairment of the optic nerve, or adjacent structures. [13]. In the context of developing countries, there is no brachytherapy eye plaques nor proton therapy. There is only 3D conformal and intensity-modulated radiation therapy which found its indication in this patient for the optic nerve positive margin.

Both normo-fractionated and hypo-fractionated radiotherapy protocols are valid in melanoma with some series in favor of hypo fractionation. A protocol of 24 Gy in 6 fractions and 2 fractions per week was chosen for its convenience both for the patient and for the department given the high demand on radiation therapy and the limited resources in the country. Prolonged follow up after treatment is necessary to detect possible recurrence, sometimes late [14].

Mortality remains very high at up to 50%. [15]

The risk factors found are the large initial tumor volume, the previous tumor site and the age of the patient. The extrascleral extension was cited by other authors [15].

4. Conclusion

Choroidal melanoma is a rare disease with variable prognosis. surgical resection with adjuvant radiotherapy is the main treatment modality. Its association with pregnancy is more challenging. Proton therapy or brachytherapy are more suitable for these situations. However, IMRT could be a good alternative. Early detection by the ophthalmologist remains crucial for a conservative approach. Access to care, health insurance and material and human resources are indicators and

mandatory conditions for early diagnosis and therefore conservative treatments.

References

- [1] Zografos L, Uffer S. Tumeurs intraoculaires. Société Française d'Ophtalmologie et Masson, Paris, 2002: 281-313.
- [2] Gaudy marquestre C; Monestier S; Grobl J. Mélanome. EMC (Elsevier Masson SAS, Paris), Dermatologie, 98-595-A-10, 2007.
- [3] Shukla S, Acharya S, Dulani M. Pregnancy and melanoma. Journal of Clinical and Diagnostic Research. 2015 May, Vol-9 (5): ED09-ED10
- [4] Charif chefchaouni M. Mélanome de l'iris et grossesse. Journal français d'Ophtalmologie Vol 26, N3- mars 2003 pp. 277-280
- [5] Driscoll MS, Grant-Kels JM. Hormones, nevi and melanoma: an approach to the patient. J Am Acad Dermatol. 2007; 57: 919-931.
- [6] Tang JY, Spaunhurst KM, Chlebowski RT, et al. Menopausal hormone therapy and risks of melanoma and nonmelanoma skin cancers: Women's Health Initiative randomized trials. J Natl Cancer Inst. 2011; 103: 1469-1475.
- [7] Gupta A, Driscoll MS. Do hormones influence melanoma? Facts and controversies. Clin Dermatol. 2010; 28: 287-292.
- [8] Laver NV; McLaughlin ME; Duker JS. Ocular Melanoma. Arch Pathol Lab Med. 2010; 134: 1778-1784
- [9] Tarlan B; Kiratli H;. Uveal Melanoma: Current Trends in Diagnosis and Management. Turk J Ophtalmol. 2016 Jun; 46 (3): 123-137
- [10] Mudhar HS; Dherty R; Salawu A; Sisley K; Rennie IG. Immunohistochemical and molecular pathology of ocular uveal melanocytoma: evidence for somatic GNAQ mutations. Br J Ophthalmol 2013 Jul; 97 (7): 924-8
- [11] Stodell M; Thompson JF; Emmett L; Uren RF; Kapoor R; Saw RPM. European Journal of Surgical Oncology (EJSO); Volume 43, Issue 8 August 2017, Pages 1517-1527
- [12] Shields et al. "Choroidal nevus transformation into melanoma: analysis of 2514 consecutive cases." Arch Ophthalmol. 2009 Aug; 127 (8): 981-7
- [13] Margo CE. "The Collaborative Ocular Melanoma Study: an overview. Cancer Control.". Cancer Control 2004 Sep-Oct; 11 (5): 304-9.
- [14] Stannard C; Sauerwein W; Maree G; Lecuona K. Radiotherapy for ocular tumours. Eye (Lond). 2013 Feb; 27 (2): 119-127.
- [15] Kaliki S; Shields CL; Shields JA Uveal melanoma: Estimating prognosis. Indian J Ophthalmol. 2015 Feb; 63 (2): 93-102.