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Advanced Uveal Melanoma: A Case Report Highlighting the Dilemma of Adjuvant Therapy

Nouhaila BOURRAS[1*], ZAKARIA Benoumrhar[1], S. Chabli, S. Laatitioui[1], M. Saadoune[1], S. Barkiche[1], N. Oumghar[1], M. Darfaoui[1], A. El Omrani[1], M. Khouchani[1]

[1]Radiotherapy Department, Oncology and Hematology Hospital; Mohammed VI University Hospital Center, Marrakech, Morocco

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***Corresponding author:** Nouhaila BOURRAS
Radiotherapy Department, Oncology and Hematology Hospital; Mohammed VI University Hospital Center, Marrakech, Morocco

Abstract **Case Report**

Uveal melanoma is the most common primary intraocular malignancy in adults, yet it remains a rare disease compared to cutaneous melanoma. It carries a high potential for local invasion and distant metastasis, with advanced presentations sometimes leading to orbital extension, optic nerve involvement, or even globe rupture. Histologically, it is characterized by malignant melanocytic proliferation with variable pigmentation and nuclear atypia. We report the case of a 60-year-old woman with an advanced uveal melanoma of the left eye, complicated by ocular rupture and orbital invasion, treated with orbital exenteration. Beyond its unusual and severe presentation, this case provides an opportunity to discuss the role of adjuvant therapy in such scenarios. Indeed, while surgery remains the cornerstone of management in extensive disease, the possible indications for postoperative radiotherapy or systemic chemotherapy remain an open question, particularly in the presence of high-risk features. This report underlines both the aggressive behavior of delayed-diagnosed uveal melanoma and the importance of multidisciplinary discussion to clarify the potential benefit of adjuvant treatment strategies aiming to improve long-term outcomes.

Keywords: Uveal melanoma, Orbital invasion, Exenteration, Adjuvant therapy, Radiotherapy, Chemotherapy.

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INTRODUCTION

Uveal melanoma is the most common primary intraocular malignancy in adults, accounting for the majority of ocular melanomas, yet it remains a rare tumor compared to its cutaneous counterpart. It arises from melanocytes of the uveal tract, most frequently the choroid, and is characterized by its potential for local invasion, orbital extension, and distant metastasis, particularly to the liver. While conservative eye-sparing treatments such as brachytherapy or proton beam therapy are preferred in selected cases, advanced presentations often require enucleation or orbital exenteration to achieve local control. Despite these measures, recurrence and metastatic spread remain major concerns, raising the question of whether adjuvant radiotherapy or systemic chemotherapy may offer additional benefit in high-risk patients. This case report presents an advanced uveal melanoma with orbital invasion, aiming to highlight both the pathological and therapeutic aspects of this disease, while discussing the potential role of adjuvant treatment strategies.

CASE PRESENTATION

We report the case of a 60-year-old woman, married and mother of five, with no significant medical or family history, who presented for further management of a left ocular melanoma. The disease had begun ten years earlier with progressive visual loss and ocular pain, eventually leading to blindness of the left eye, but the patient had not received documented follow-up. In January 2025, she was admitted with rupture of the globe.

Initial Orbital and cerebral imaging revealed a large intraocular mass measuring 30 × 20 × 23 mm, with scleral perforation, orbital fat invasion, and extension to the retrobulbar optic nerve and superior rectus muscle, findings highly suggestive of uveal melanoma.

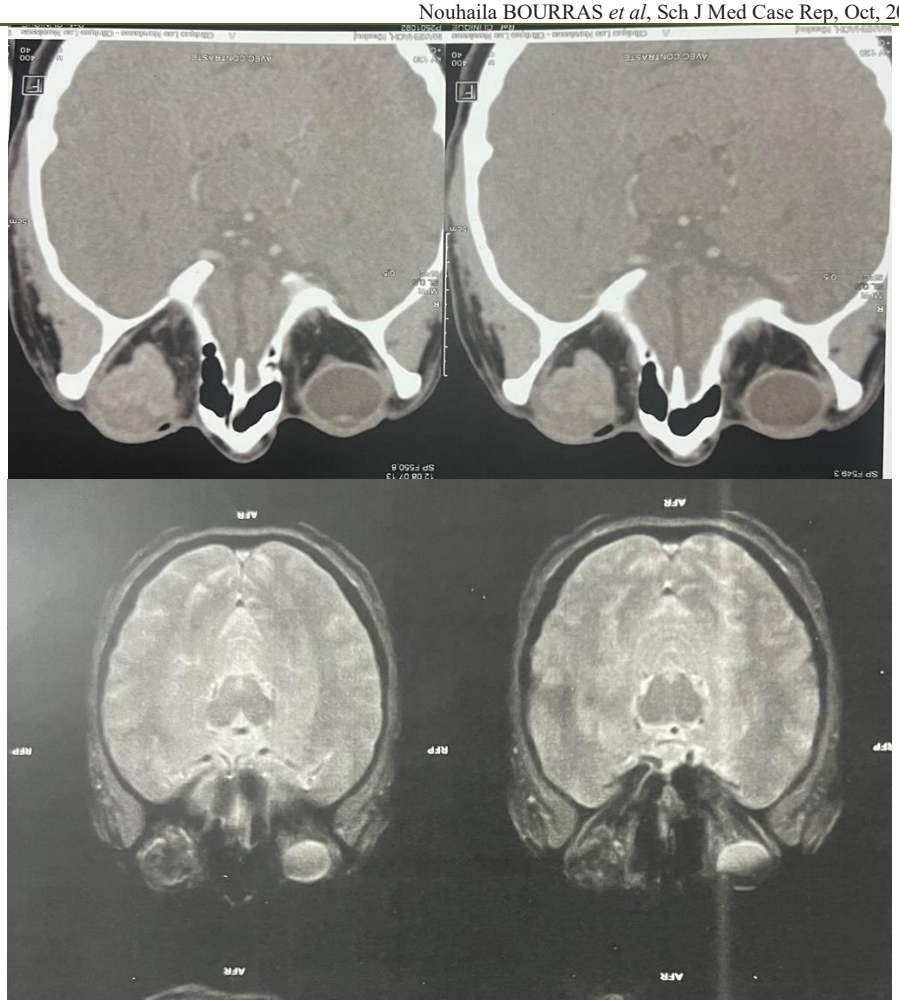

Figure 1 et 2: Left orbital mass causing globe rupture with infiltration of intra- and extraconal fat, retrobulbar optic nerve, and superior rectus muscle

The patient underwent emergency enucleation, which intraoperatively confirmed the extensive nature of the disease. Pathological examination of the specimen revealed a malignant melanocytic tumor, predominantly of mixed cell type, with infiltration of the choroid, orbital soft tissues, and regional lymph nodes, staging the disease as pT4bN1M0 according to the AJCC 8th edition criteria.

A postoperative FDG-PET scan was concerning for residual metabolic activity at the orbital apex. Consequently, the patient proceeded to a second, more definitive surgery: orbital exenteration. Histopathological analysis of the exenteration specimen showed only fibro-inflammatory tissue with no evidence of residual melanoma. However, surgical margins were noted to be close, ranging from 0.5 to 1.5 cm.

At follow-up, the patient was clinically stable, with a clean orbital cavity and a good general condition.

The question was whether to subject her to the potential side effects of adjuvant orbital radiotherapy for an uncertain benefit, or to place our trust in the surgery and commit to an exceptionally vigilant watch. After thorough discussion in a multidisciplinary tumor board and, a detailed conversation with the patient herself, we collectively chose a path of intensive surveillance: clinical exams, combined with orbital and cerebral MRI and a hepatic ultrasound every three months.

DISCUSSION

Uveal melanoma is the most common primary intraocular malignancy in adults, representing 80–90% of ocular melanomas, yet its overall incidence remains low at approximately 5-7 cases per million annually [1]. The choroid is the predominant site of origin, followed by the ciliary body and iris. Despite its rarity, this tumor is clinically significant due to its aggressive biological behavior and its strong predilection for hematogenous metastasis, most often to the liver [2].

Histologically, uveal melanoma is composed of malignant melanocytic cells that may appear spindle-shaped, epithelioid, or mixed. The epithelioid subtype is generally associated with a poorer prognosis. The AJCC staging system classifies any ciliary body involvement and tumor size >15mm with EOE as T4b disease, placing our patient in the highest local risk category [3].

Management of uveal melanoma depends on tumor size, location, and extent. Conservative treatments such as brachytherapy, proton beam radiotherapy, or local resection are often employed in small to medium-sized tumors, aiming to preserve the eye and vision [4].

In contrast, large tumors or those with orbital extension usually require enucleation or orbital exenteration, as in our patient [5]. However, the discovery of close margins post-operatively presents a classic therapeutic dilemma. Adjuvant orbital radiotherapy could be considered to mitigate the risk of local recurrence. While some studies, such as a retrospective analysis by Finger *et al.,* suggest that adjuvant plaque brachytherapy or external beam radiation can improve local control in the setting of positive or close margins, no randomized data exists to demonstrate a conclusive overall survival benefit [6]

The decision to utilize adjuvant therapy following complete surgical excision remains a complex and debated aspect of managing advanced uveal melanoma. It is well established that conventional adjuvant chemotherapy offers little benefit, a fact attributable to the distinct biology of this cancer. Uveal melanoma is primarily driven by mutations in the GNAQ or GNA11 genes, which activate downstream signaling pathways like PKC and MAPK. This molecular profile renders it inherently resistant to traditional chemotherapeutic agents [7]. Consequently, the current standard of care appropriately excludes adjuvant chemotherapy.

This recognized therapeutic gap has accelerated the development of more precise, molecularly tailored strategies. In recent years, significant attention has turned to targeted therapies, such as MEK and protein kinase C inhibitors, and to immunotherapies, including checkpoint inhibitors targeting PD-1/PD-L1 and CTLA-4. These modalities have yielded promising results in the treatment of metastatic disease [8, 9]. These advances provide a strong rationale for the ongoing clinical trials that are now investigating the potential adjuvant role of these agents, signaling a shift towards a more personalized and biology-driven treatment paradigm

In our patient, exenteration achieved local control, with histology showing no residual tumor but narrow margins. Given the absence of clear evidence supporting adjuvant radiotherapy or chemotherapy, a strategy of close observation was chosen, with regular clinical exams, combined with orbital and cerebral MRI and a hepatic ultrasound every three months.

The focus, therefore, shifts to early detection of metastatic disease, primarily in the liver. Emerging data suggests that early intervention with liver-directed therapies (immunoembolization, selective internal radiation therapy) or enrollment in clinical trials for metastatic disease upon first detection can improve outcomes [10].

Furthermore, the frontier of UM treatment now includes investigational adjuvant therapies targeting the specific biology of the disease. Clinical trials are ongoing evaluating adjuvant immune checkpoint inhibitors and targeted agents like the MEK inhibitor selumetinib [11]. The results of such trials are eagerly awaited, as they may finally provide an evidence-based adjuvant strategy for high-risk patients like the one described.

Our approach reflects the balance between avoiding overtreatment and ensuring vigilant follow-up in a patient whose condition is currently stable and whose performance status remains good.

CONCLUSION

This case of advanced uveal melanoma with orbital extension highlights the limitations of our current therapeutic arsenal once the disease progresses beyond the globe. It reinforces the importance of early detection and lifelong follow-up for all uveal melanoma patients. While radical surgery remains the primary option for local control, the decision regarding adjuvant treatment must be personalized through multidisciplinary discussion and shared decision-making with the patient. The future of managing high risk uveal melanoma lies not in broader local therapy, but in better molecular stratification and the development of effective systemic therapies that target the unique biology of this disease. For now, in the absence of proven adjuvant options, a proactive and meticulous surveillance plan, undertaken in partnership with a motivated patient, represents our most prudent course of action.

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