

# Metastatic acral melanoma with retroperitoneal and liver metastases: Diagnostic challenges and therapeutic dilemmas in a resource-limited clinical setting of district Swat, Pakistan

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## Abstract

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Acral melanoma is a rare subtype of cutaneous melanoma that often presents late in resource-limited settings. We report a 67-year-old woman from District Swat, Pakistan, with a 5-year history of a neglected pigmented plantar lesion who presented with jaundice and weight loss. CT imaging showed a large para-aortic retroperitoneal mass causing hydronephrosis and periampullary compression with biliary dilatation, along with liver metastases. Trucut biopsy revealed metastatic melanoma (S100+, HMB-45+, SOX10+). Molecular testing for BRAF V600 mutation was recommended but not performed due to unaffordability. Nivolumab monotherapy (anti-programmed cell death protein 1 [anti-PD-1]) was started, as dual immune checkpoint blockade was unaffordable, and a ureteric stent was placed. The patient was subsequently lost to follow-up. This case highlights diagnostic complexity and therapeutic inequities in metastatic acral melanoma in a resource-limited setting.

**Keywords** Acral melanoma; Retroperitoneal metastasis; Obstructive jaundice; Nivolumab; Financial toxicity.

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## Introduction

Cutaneous melanoma is an aggressive malignancy with a rising global incidence, as highlighted in recent large-scale epidemiologic analyses.<sup>1</sup> Acral melanoma, which arises on the palms, soles, or nail apparatus, accounts for a small proportion of melanomas overall but constitutes a substantially higher proportion of melanoma cases among individuals with darker skin types, including Black

and Asian populations.<sup>2-4</sup> Unlike sun-exposed cutaneous melanoma, acral melanoma is not associated with ultraviolet radiation exposure.

Delayed recognition, limited access to dermatologic care, and diagnostic challenges contribute to late presentation in many low- and middle-income countries. According to contemporary ESMO (European Society for Medical Oncology) guidelines, systemic therapy selection for metastatic or clinically non-resectable melanoma is individualized based on tumor burden, functional performance status, and molecular profiling, particularly the presence of actionable mutations

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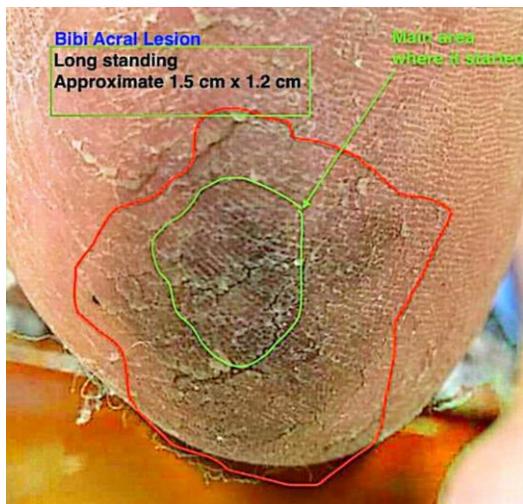
such as BRAF V600.<sup>5</sup> We report a patient from District Swat, Pakistan, with a long-standing plantar lesion presenting with retroperitoneal and hepatic metastases, highlighting diagnostic challenges and therapeutic constraints in a resource-limited setting.

### Case Report

A 67-year-old woman from District Swat, Pakistan, presented with progressive jaundice and unintentional weight loss over several months. She reported a painless, asymmetric, brown to blackish pigmented lesion on the plantar surface of the foot for many years, which had been neglected due to limited access to specialized healthcare.

On examination, she was jaundiced. Local examination showed a 1.5X1.2 cm irregular pigmented lesion on the sole.

Contrast-enhanced CT abdomen revealed a large para-aortic retroperitoneal mass encasing the right ureter, causing hydronephrosis and compressing the peri-ampullary region with biliary and pancreatic duct dilatation, along with liver lesions consistent with metastases and bulky adrenal glands. Lymphoma was initially suspected.



**Figure 1** Annotated clinical photograph of an acral pigmented lesion on the heel at first presentation. The long-standing lesion measures approximately 1.5 × 1.2 cm. The central darker area indicates the probable site of origin with surrounding hyperkeratosis and fissuring.



**Figure 2** Close-up view of the heel lesion demonstrating irregular pigmentation with hyperkeratosis and fissuring at first presentation.



**Figure 3** Lateral/ oblique view of the heel lesion at first presentation showing pigmentation over the weight-bearing area.

Trucut biopsy of the retroperitoneal mass confirmed metastatic malignant melanoma (S100+, HMB-45+, SOX10+). Testing for BRAF V600 mutation was advised to guide targeted therapy but could not be pursued due to unaffordability. A ureteric stent was placed for obstruction, and nivolumab, an anti-programmed cell death protein 1 (anti-PD-1) agent, was initiated as single-agent immunotherapy every two weeks, because dual immune checkpoint blockade was financially unfeasible. The patient was counseled regarding immune-related toxicities and scheduled for response assessment after 8-12 weeks but was subsequently lost to follow-up.

## Discussion

Melanoma is less common in South Asian populations compared with fair-skinned populations; however, acral melanoma represents a disproportionately higher proportion of melanoma cases among individuals with darker skin types.<sup>2,3,10</sup> SEER-based analyses have demonstrated distinct epidemiologic and anatomic patterns of melanoma in Asian populations.<sup>9</sup>

Although visceral metastases are recognized in advanced melanoma, presentation with bulky retroperitoneal metastatic disease causing obstructive jaundice is uncommon and may mimic other malignancies such as lymphoma, creating diagnostic uncertainty. Adequate tissue sampling with focused immunohistochemistry (S100, SOX10, HMB-45/Melan-A) remains essential in ambiguous cases.

Visceral (non-CNS) metastases correspond to AJCC stage IV (M1c) disease. For unresectable stage III/IV melanoma, ESMO-endorsed first-line options include immune checkpoint inhibitors (anti-PD-1 monotherapy or dual immune checkpoint blockade such as nivolumab plus ipilimumab) and, in BRAF V600-mutant tumors, BRAF/MEK inhibitor combinations.<sup>5,6</sup> Evidence specific to acral melanoma suggests variable responses to immune checkpoint inhibitors compared with non-acral melanoma subtypes.<sup>7</sup>

In Pakistan, where most patients pay largely out of pocket for cancer care, financial toxicity significantly affects treatment initiation and continuity. Limited access to molecular testing and combination immunotherapy may alter adherence to international guideline-recommended therapy and adversely impact outcomes.<sup>8</sup>

## Conclusion

This case is noteworthy due to the uncommon combination of delayed recognition of a

longstanding plantar lesion, presentation with bulky retroperitoneal metastatic disease causing obstructive jaundice with hepatic involvement, and substantial diagnostic and therapeutic limitations imposed by financial constraints in a resource-limited setting.

While acral melanoma itself is biologically distinct and less common overall, the convergence of advanced visceral metastasis at first presentation and constrained access to molecular testing and dual immunotherapy underscores critical inequities in melanoma care. Strengthening early detection, improving access to molecular diagnostics, and expanding subsidized systemic therapy programs are essential to reduce preventable morbidity and mortality in low-resource settings.

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## Author's contribution

**SJS,PK:** Substantial contribution to management of the case and manuscript writing.

**CJA,I:** Substantial contribution to identification and management, literature review of the case. Critical review of the manuscript.

**ARK, JM:** Identification and management of the case. Critical review of the manuscript.

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