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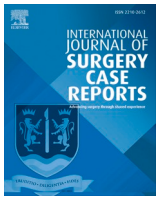

Case report

Progressive Acral Lentiginous Melanoma diagnosed via histopathology and surgically eradicated in a fingernail in a 69-year-old male - A Case Report

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ABSTRACT

Introduction and importance: Acral Lentiginous Melanoma (ALM) transpires in a profoundly scarce percentage of the population and is intercalated with a low survival rate. This is partly because such tumors are chiefly diagnosed at an advanced stage. Diagnosis is delayed largely due to the difficulties in recognizing the early histopathological signs and clinical presentations of Acral Melanoma.

Case presentation: We demonstrate the case of a previously healthy 69-year-old Middle Eastern male patient, who presented to our university hospital's Dermatology clinic with a papule under the right ring fingernail with spontaneous Onycholysis of the entire nail, suggesting a spontaneous malformation in his finger.

Clinical discussion: ALM is an abundantly rare subtype of melanoma that chiefly originates from the skin of the acral tissues. In this case it arose on the fingernail of a 69-year-old male, who has undergone 2 surgeries to eradicate the tumor with safe margins and as a ramification of successful follow-up for 6 months, has been deemed free of tumor recurrence or metastasis.

Conclusion: The aim of this article is to highlight the vitality of early detection, diagnosis, prognosis, and treatment of malignant Acral Lentiginous Melanoma in patients of all ages, especially with older patient populations.

1. Introduction

ALM is a comparatively infrequent form of skin melanoma but has been growing in incidence in recent years. Physicians classically diagnose it in the 6th and 7th decades of life. On the other hand, its incidence has been rapidly increasing also in young patients as well [1–4].

ALM constitutes approximately 2–3 % of all classes of melanomas, it typically arises on the soles, palms or inside and around the contour of the nails [1–4]. Its incidence is analogous in all races, but since the Asian and African populations do not have sun-related melanomas, therefore ALM is considered to have a high incidence rate in said groups, accounting for approximately 70 % of melanomas in African individuals. Acral Melanoma has been reported to be especially frequent amongst the Japanese population [5]. Reed was the pioneer scientist who first depicted it in 1976 [2,4].

Conventionally, it manifests as an asymmetric brown to black macular with irregular edges and is often diagnosed in advanced stages due to the difficulty of distinguishing it from normal or traumatic lesions, in addition to the difficulty of obtaining biopsy from these areas (extremities). The minority appeared to be sometimes non-typically pigment-free (amelanotic), in contrast to the lesion being pink, erythematous, or flesh-colored [6]. It presents a diagnostic challenge as it gets misdiagnosed with warts or Squamous Cell Carcinoma (SCC) and sometimes with Pyogenic Granulomas, chronic fungal Paronychia [7], Kaposi's Sarcoma, or Glomeruloma [8].

The work has been reported in line with the SCARE criteria and the revised 2020 SCARE guidelines [9].

Abbreviations: ALM, Acral Lentiginous Melanoma; SCC, Squamous Cell Carcinoma; H&E, Hematoxylin and Eosin; IHC, Immunohistochemistry; NM, Nodular Melanoma; SSM, Superficial Spreading Melanoma; LLM, Lentigo Malignant Melanoma.

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2. Presentation of case

2.1. Patient information

We illustrate the case of a 69-year-old Middle Eastern male patient who has a known medical history of Hypertension. Otherwise, he's previously healthy. The patient presented to the Dermatology clinic complaining of a protuberance under the right ring fingernail for a period of 4 months prior to his admission. It had rapidly increased in size during the three months prior to his clinical presentation, and this resulted in the spontaneous Onycholysis of the entire affected nail. The patient denied any associated pain or tenderness. Furthermore, there was not any accompanying nausea or episodes of vomitus. There was no history of bleeding disorders, alterations in his bowel habits, or reported symptoms of his genitourinary tract. He denies getting exposed to radiation or chemotherapy in the past. His family history is reported to be negative for similar incidences and for neoplastic occurrences mainly in the first and second-degree relatives. Moreover, he has negative drug and allergic histories except for medications to control his hypertensive situation. The patient has never been an alcoholic and isn't an active nor a previous smoker.

2.2. Clinical findings

Beginning via taking vital signs readings, they were all within normal values.

Through inspection, we depicted a bleeding, non-itchy, painless, and erythematous nodule situated along the entire nail bed of the right-hand ring finger accompanied by vivid rupture of the entire nail plate (Fig. 1). Examination of the axillary and cervical lymph nodes was negative as none were palpable. Clinical examination of the remaining fingers yielded negative results.

2.3. Diagnostic assessment

Biopsy of the lesion was taken, and histopathological analysis via Hematoxylin and Eosin (H&E) revealed an Acral Lentiginous Melanoma measuring 1.5 cm in its greatest dimension with a thickness of 0.7 cm. It was invading the surrounding bone and muscle tissues with a mitotic rate of 12 mm^2 (Fig. 2A-B-C-D-E). Immunohistochemistry (IHC) via stains like (HMB-45: positive - Actin: Negative, Desmin: Negative, CD99: Negative, LCA: Negative). The tumor was identified with a radial and vertical growth phase, with perineural and lympho-vascular invasion, in addition to regression of approximately 10 % of the neoplastic mass (Fig. 3A-B).

Fig. 1. Preoperative image depicting a soft, bleeding, non-itchy, painless, and erythematous nodule situated along the entire nail bed of the right-hand ring finger accompanied by vivid rupture of the entire nail plate (*Black Arrow*).

2.4. Therapeutic intervention

Based on the patient's previous clinical picture, a surgical intervention was decided. The surgeries were performed at our tertiary university teaching hospital by a Reconstructive Surgery consultant specialized with such cases with 20 years of experience. The operations were carried-out under local anesthesia with no perioperative complications. The patient underwent two surgeries, two months apart. The first surgery was performed within 3 weeks of diagnosis, where the distal phalanx was excised, and biopsies were taken. The result according to histopathology was stated as an ALM infiltrating the surrounding nerves, lymphatic vessels, muscles, and bones. As for the second surgery, the entire finger was amputated down to the fourth metacarpal head, with scraping of the excised edges. Samples were sent for microscopic analysis. Histopathology result of the latter yielded negative results for neoplasia at the resection border and confirmed the findings stated in the preoperative biopsy report.

The patient's wound has been carefully taken care of and professionally dressed by a professional to insure adequately rapid wound healing and avoidance of wound infection. Furthermore, the patient has been followed-up in the outpatient clinic for six months. Regular CT scans and clinical examinations were done and insured no current recurrence has taken place.

3. Discussion

Acral Lentiginous Melanoma (ALM) is a profoundly rare subtype of melanoma that chiefly develops from the skin of the acral tissues. This neoplasm spreads to involve the soles, palms, and nail beds. Its incidence reflects only the scarcity of data gathered from such cases as it occurs merely in 4 to 6 % of all confirmed diagnoses of melanoma in populations of Caucasian descent [10]. We are currently still discovering the genetic etiology behind the variations existing in ALM [11]. Nonetheless, there are numerous factors that may influence the pathogenesis of this type of melanoma and they're still poorly comprehended. Nevertheless, scientific research has established chronic inflammatory processes, iatrogenic causes, and trauma, to be risk factors for developing ALM [12]. To roughly compare ALM to the aggressive Superficial Spreading Melanoma (SSM), ALM tends to occur in older age group patients, has less pathological nevi, and is less correlated to the blunt exposure to the sun and in turn developing sun burns than patients with SSM. Additionally, patients who develop ALM are found to have a higher family and previous histories of non-cutaneous malignancies [13].

The major classification of malignant melanoma stems primarily from the histological and clinical findings in visiting patients into four classical subtypes: Lentigo Malignant Melanoma (LMM), Nodular Melanoma (NM), ALM, and SSM.

ALM is favored to occur in white Caucasian population groups, but it has a higher affinity to arise in Asian populations. Based on previously published research articles, ALM constitutes 1 to 7 % of all malignant melanomas in White Caucasian population groups, whereas it makes-up 50 % of which in Asian populations [14–16].

ALM is the rarest of the previously mentioned subtypes of melanoma and the pioneer behind depicting this specific type of pathology was Reed in 1976 [17]. ALM repeatedly arises from cutaneous skin of the soles and palms. The most frequently involved site by ALM is the plantar surfaces and followed by the subungual region. Furthermore, the Hallux is the most affected digit followed by the Thumb [18].

NM is evidently the worst and most aggressive subtype of melanoma based on its biological pathophysiology. It possesses a rapid growth rate and a malignant potential for metastasis. It is conventionally discovered at an advanced stage in terms of local manifestation. Unfortunately, it is correlated with high mortality and poor prognosis. This results in a major challenge for physicians to early recognize and treat it in an early

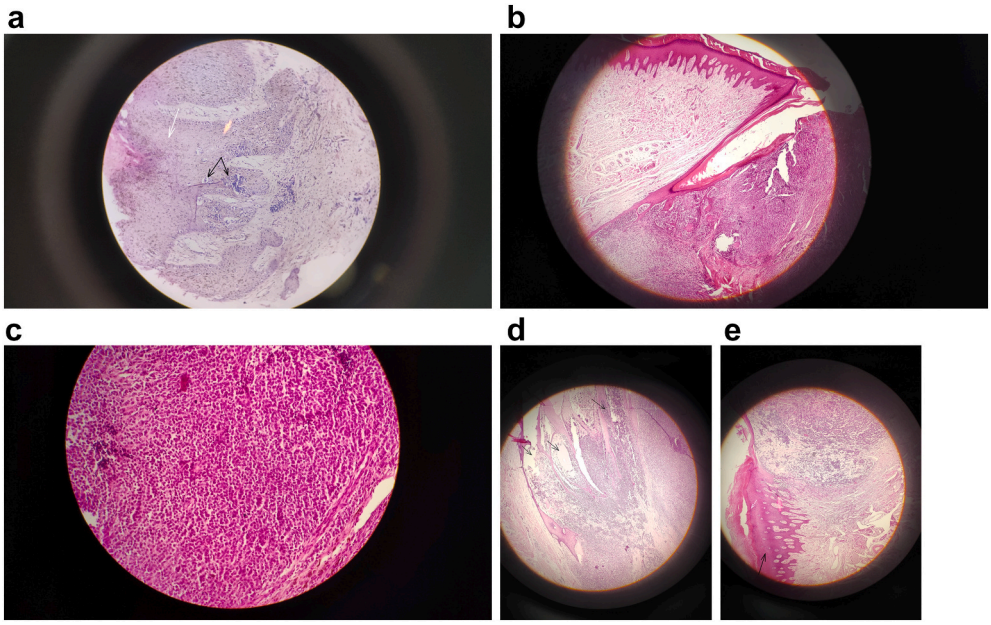

Fig. 2. A: H&E staining revealing epidermal hyperplasia (*White Arrow*), atypical Melanocytes are arranged solitarily and in irregular nests in all levels of the epidermis "Pagetoid Scatter" (*Black Arrows*). Infiltration of the papillary dermis by solitary single cell nests.
B: H&E staining revealing cellular extension along the follicles.
C: H&E staining revealing epithelioid cells are large and round with abundant eosinophilic cytoplasm. Prominent vesicular nuclei and large nucleoli are seen.
D: H&E staining revealing marked elongation of Rete Ridges (*Black Arrows*).
E: H&E staining revealing epidermal hyperplasia (*Black Arrow*) and melanoma in-situ. Single lesioned cells near the dermal epidermal junction. Marked replacement of the basal layer by atypical Melanocytes especially around the periphery (*White Arrow*).

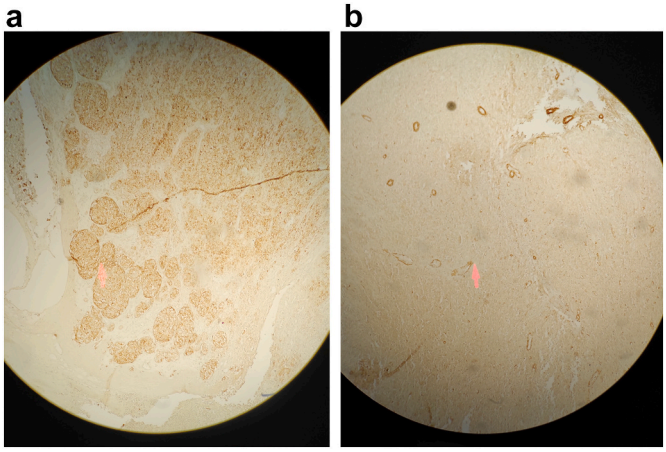

Fig. 3. A: IHC staining positive for HMB-45.
B: IHC staining negative for Actin.

stage [19]. NM constitutes approximately 15–30 % of all types of melanomas and it is the second most prevalent type after SSM. With regards to melanomas with a thickness of over 2 mm, NM makes-up 40–50 % of them which renders NM the primordial cause of melanoma-related fatalities [20]. The occurrence rate of NM increases exponentially with increasing age. It is classically discovered in males who are older than 50 years of age, especially if they suffer from skin damage due to sun exposure. NM primarily arises in the lower limbs or the head and neck regions of the body [21].

The gross description of NM involves the typical patient presentation which is an asymmetric/symmetric, elevated, homogenously pigmented, organized regular border, hypo-/amelanotic nodule or papule, which evolves at a high rate and consequently causes ulceration or hemorrhaging [22]. With regards to its morphology, NM lesions can present in variety of colors such as grey, black, brown, blue, pink, distinctive shades of the same color or multiple colors, or as an amalgamation of different colors together. As for the surface texture of the lesion, it could be rough, smooth, or scaly. Physiologically, melanocytes are the main regulatory force behind keratinocytes' proliferation and differentiation, thus, a high keratinocytes' turnover consequently results in the scaly texture of said lesions [23].

NM can initially develop as a continuously expanding nodular lesion with dark pigmentation. It is conventionally a resultant of sun exposure in typically sun exposed areas of skin. Nonetheless, it occurs in covered areas of the body, but in a much less frequency [24].

When it comes to establishing a diagnosis for ALM and NM, incisional or punch biopsies are commonly the initial diagnostic modalities.

The microscopic pattern of said biopsies especially in the skins of soles and palms has a distinctive morphological appearance comprising of ridges and furrows [25].

Further diving into establishing a definitive diagnosis for ALM, immunohistochemistry is a well-established and reliable diagnostic method. Stains for melanocytes include HMB-45, Melan-A and S-100. If we are fortunate enough to catch the lesion in its early stages, we would be able to have positive staining for HMB-45 due to the solitary presence of Melanocytes in the Crista Profunda Intermedia layer of the skin [26].

The gold standard treatment for malignant melanomas is surgical excision of the lesion along with safety margins [27].

Upon definitive establishment of said diagnosis, any physical remnants of lesion along with the biopsy scar -if any- ought to be excised in order to eliminate any local seedings of the neoplasm. Furthermore, we must excise adequate free margins but the extent of said margins relies heavily upon tumor thickness. For example, in situ neoplastic lesions, a safe margin for excision ranges from 0.5 to 1 cm of normal cutaneous skin. Additionally, razor thin melanomas of thickness less than 1 mm will necessitate a 1 cm free margin of surgical excision to limit recurrence. Moreover, neoplastic lesions with thickness between 1 and 2 mm will warrant a 1–2 cm free margin local excision. In contrast, melanotic neoplasms of the digits of the palms and soles will demand digital amputation [28,29].

We must emphasize a core principle which is vital for tumor staging, and that is lymph node mapping which involves sentinel lymph node scanning for any tumor involvement [30].

When we discuss prognosis, it is crucial to note that histopathological analytical characteristics of ALM such as the growth phase, the presence of microscopic satellites, and mitotic activity are indicators of poor prognosis for patients [31].

Metastasis of malignant melanoma typically includes the lymph nodes draining the affected area. Lymph nodes which are first involved are the surrounding area nodes. Unfortunately, distant nodal metastasis is common. In descending order, the skin and subcutaneous nodes are

the most involved with a rate of 59 % followed by the lungs (36 %), the brain (20 %), hepatic involvement comprises 20 %, and bone with a 17 % metastasis rate [32,33].

The cornerstone in determining patient survival who suffers from malignant melanomas is culminated in tumor staging and lesion thickness at the time of patient diagnosis. Early detection of said neoplasia whilst lesion thickness is minimal leads to an overall higher survival rate [10,34,35].

Amongst the various types of malignant melanoma discussed earlier, ALM seems to have the worst prognosis. However, according to published literature, there doesn't seem to be any notable differences gender favorability in prognosis between males and females [10].

4. Conclusion

NM is the most aggressive subtype of malignant melanoma, and it can easily be mistaken for benign lesions or non-melanotic skin neoplasia especially if the lesion was hypomelanotic.

ALM is a rare and distinguished form of cutaneous malignant melanoma that is diagnosed in older patients and at a more advanced stage than other melanomas, thus, culminating in a worse prognosis.

The scarcity of data on ALM and NM warrants further studying, thorough consideration, informed clinical assessment and performing patient educating programs to early detect and diagnose this malignancy before it metastasizes.

Documentation of such cases is paramount so that researchers can further dive into the pathogenesis, preoperative diagnostic options, and postoperative patient care. Said neoplasms should be kept in mind as core differential diagnoses when presented with any suspicious skin lesions to limit morbidity and mortality associated with this pathology.

Abbreviations

ALM	Acral Lentiginous Melanoma
SCC	Squamous Cell Carcinoma
H&E	Hematoxylin and Eosin
IHC	immunohistochemistry
NM	Nodular Melanoma
SSM	Superficial Spreading Melanoma
LLM	Lentigo Malignant Melanoma

Availability of data and materials

The datasets generated during and/or analyzed during the current study are not publicly available because the Data were obtained from the hospital computer-based in-house system. Data are available from the corresponding author upon reasonable request.

Provenance and peer review

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Ethical approval

This study is exempt from ethical approval in our institution.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

CRediT authorship contribution statement

OA, RA, MA, AI: Conceptualization, who wrote, original drafted, edited, visualized, validated, and literature reviewed the manuscript.

AB: Dermatology consultant, supervision, project administration, and review of the manuscript.

OA: The corresponding author who submitted the paper for publication.

All authors read and approved the final manuscript.

Registration of research studies

Not applicable in our case.

Guarantor

Omar Al Laham.

Declaration of competing interest

None.

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