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CANCER OF THE NAILS: NOVEL TECHNIQUES AND PROTOCOLS FOR NAILS CANCER TREATMENT: PRESENT VIEWPOINTS

Harsh Sharda*, Sarfraz Ahmed, Raja Babu, Anjali Negi, Vinita Pandey and Divyanshu

G.I.P.E.R, Uttarakhand.

***Corresponding Author: Harsh Sharda**

G.I.P.E.R, Uttarakhand.

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ABSTRACTS

Compared to lesions in other areas of the skin, benign or malignant neoplastic lesions are uncommon in the nail area. Even with advancements in diagnostic methods, misdiagnosis or inappropriate treatment might cause their diagnosis to be delayed or ignored for days, weeks, or even years. Malignant tumors are unquestionably the most significant lesions since a delayed diagnosis or course of therapy can significantly alter the patient's prognosis. Benign or malignant neoplastic lesions are rare in the nail region as compared to other skin locations. Even with improvements in diagnostic techniques, a patient's diagnosis may be postponed or disregarded for days, weeks, or even years due to a mistake or inadequate treatment. Undoubtedly, malignant tumors are the most important lesions since a postponed diagnosis or treatment plan might drastically change the patient's prognosis. Using careful examination and modern diagnostic methods, including onychoscopy, biopsy, and histopathology, will help identify SCC and prevent the invasive progression. X-ray is important to investigate the bone invasion to determine the best surgical approach that will have satisfying cosmetic and functional outcomes. Nevertheless, local excision with sufficient surgical margins, best if using Mohs surgery, is usually sufficient and superior to amputation of the distal phalanx.

KEYWORDS: benign, malignant, misdiagnosis, neoplastic, diagnostic, lesions, onychoscopy, biopsy, histopathology.

INTRODUCTION

The nail plate is created by continuously dividing matrix cells, and the nail covers the distal phalanx. Chemotherapy for cancer agents that interact with these fast-dividing nail matrix cells may cause alterations to the nail. The most frequent mucocutaneous adverse effect after cancer chemotherapy and chemo radiation has been documented to be nail alterations.[1] Withdrawing from drugs causes the nail alterations to disappear, however they are typically not permanent. The condition might impact all or some nails and exhibits a correlation with drug consumption over time. The nail matrix, nail bed, nails plate, hyponychium, lunula, and the proximal and lateral nail folds are some of the several parts of the nail unit. The degree of the insult and the damaged nail structure determine how the nail is shown.[2] A portion of the nail modifications are purely aesthetic. An essential component of the digital space, both functionally and aesthetically, is the nail piece of equipment. All the cells that comprise its tissues have the potential to develop into neoplastic lesions, despite its rarity.[3] Benign and malignant tumors that cause deformities and stunt nail growth are both considered nail neoplasms. They exhibit varying signs and symptoms. The most significant nail apparatus lesions in terms of the prognosis are malignant tumors.[4] Melanoma and squamous cell carcinoma are two of the malignant neoplasms of the nail apparatus; melanoma accounts for 0.18% to 7% of cutaneous melanomas, while squamous cell carcinoma has 0.0012% prevalence.[5]

Research Methodology

This systematic literature review was conducted with the aim of identifying and classifying the most onyochoscopy, biopsy, histopathology based methods for nail cancer detection.[6] Systematic literature reviews gather extant research and evaluate it using predetermined standards. These reviews aid in ascertaining the current state of knowledge within the relevant field of study.[7] Every piece of information gathered from original sources is arranged and examined. When systematic literature is finished, it offers a more reasonable, logical, and solid response to the research's central question.[8]

Pathophysiology

Risk factors for SCC development include trauma, chronic sun exposure, radiation, burning, genodermatoses, tobacco, immunosuppression, and HPV

infection.[9] Immune suppression is crucial, as immunocompromised patients present with the tumor at a younger age and have a shorter history.[10] HPV is increasingly implicated in the pathogenesis of SCC of the nail unit, with type 16 being the only detected subtype.[11]

Clinical sign and symptoms

SCC, a slow-growing tumor, typically originates from the subungual region, proximal or lateral nail folds, and hyponychium, with mild symptoms and varying clinical features depending on its location.[10]

1. Erosion of the nail bed without pain that manifests as a distal onycholysis area that oozes from under the nail and is yellow in color.[11]
2. In long-standing lesions, the clinical aspect becomes that of large nail bed erosion associated or not with a nodule.[12]
3. Rarely (3% of the cases), SCC can appear as a band of longitudinal erythromycin. All reported cases of this clinical presentation were in situ SCC, clinically indistinguishable from the more common erythronychia due to onychopapilloma.[13]
4. SCC involving multiple digits is an exceptional presentation, also known as synchronous SCC.[14]

Over 20% of cases have bone involvement, with peaks in immunocompromised patients like AIDS patients.[15] Pain may occur when bone invasion is present. Lymph node involvement is less common in 2% of patients.[16]

Distinctive Diagnosis

SCC, an uncommon tumor, often mimics benign nail conditions. Diagnosis is delayed due to lack of knowledge, painless history, and higher frequency of benign illnesses.[17] Differential diagnoses include granuloma, onychomycosis, and onychopapilloma.[18] Viral warts are crucial to rule out suspected SCC, with hyperkeratotic and exophytic papules or nodules.[19]

Diagnostic technique

Nail dermoscopy (onychoscopy) is a noninvasive method used to observe the nail unit and evaluate nail diseases. It reduces unnecessary excisions of benign lesions and can detect alterations in SCC, such as onycholysis, irregular vascularity, and hemorrhages.[20] However, onychoscopy does not diagnose periungual warts or SCC, as they share similar signs. However, it reduces difficulties for differential diagnosis compared to onychopapilloma, onychomatricoma, and subungual exostosis.[21] Vascular polymorphism is a key feature in SCC, characterized by clustering of dot-like to glomerular vessels. Clinical and dermoscopic presentations include irregular borders, hyperkeratosis, splinter hemorrhages, white longitudinal lines, nail thickening, and a polycyclic/fuzzy lesion edge.[22] These presentations are not exclusive to SCC but can also be observed in other diseases like onychomatricoma or onychopapilloma. The onychoscopy criterion is significantly associated with SCC series.[23] Ex vivo fluorescence confocal microscopy (FCM) is a recent method used to investigate nail tumors.[24] It has been found to correlate well with malignant epithelial tumors, such as invasive SCC, and less favorably with minimally invasive SCC.[25] This technique is suggested for intraoperative diagnosis and surgical margin assessment, offering an alternative to classic Mohs surgery.[26] Radiological examination is crucial for evaluating underlying bone involvement, which is an indicator for amputation in less than 20% of patients.[27] X-rays may show compression rather than true bone invasion. Soft tissue masses with osteolytic defects are often seen in SCC, while MRI is superior for identifying exact location and extension, adding value in local staging for SCC.[28] A heterogeneous hypoechoic mass with irregular contours and posterior acoustic enhancement best represents SCC.[29] Accurate diagnosis of SCC requires a painful biopsy and histopathologic evaluation.[30] However, many dermatologists are reluctant to perform biopsies, leading to patients being misdiagnosed and delayed treatment by an average of 4 years.[31] Nail biopsy is particularly important for recurrent and persistent warty lesions, allowing early diagnosis and preserving maximal digit function, avoiding extensive surgery.[32]

Histopathology

SCC of the nail presents with irregular and incomplete keratinization, superficial ulceration, atypia, single cell necrosis, and pathological mitoses.[33] The epidermis shows vacuolated superficial keratinocytes with pyknotic raisin-like nuclei. In the late stage, deep invasion of the bone can be observed, and this type is negative for HPV DNA.[34] Subungual keratoacanthoma (KA) is a differential diagnosis of SCC, with irregular stratification and normal maturation of epithelial cells. KA also has lip formation and elastic fibers, indicating rapid growth.[35]

Treatment

Squamous cell carcinoma (SCC) is a rare and challenging disease that can be treated with various options, including surgical excision, microscopically controlled surgery (Mohs surgery), therapeutic radiation, and nonsurgical alternatives.[36] Surgical excision is the mainstay treatment for invasive SCC, while Mohs micrographic surgery is indicated for noninvasive SCC due to its minimal residual scarring, reduced number of unnecessary amputations, and patient quality of life preservation.[37] Wide surgical excision with no less than 4 mm of normal tissue from the tumor margin can be used for lesions without bone involvement.[38]

Postoperative complications of Mohs surgery include graft infection, delayed wound healing with severe pain, hypersensitivity to mechanical shock, mildly increased sensitivity to cold, loss of fine touch sensation, and epidermal inclusion cysts.[39] Due to the rarity of SCC, treatment guidelines have not been established. Nonsurgical treatment options include photodynamic therapy, 5% fluorouracil cream, or 5% imiquimod cream after curettage, but they are characterized by high

incidence of relapses and absence of control of histological margins. Radiation therapy may be helpful in cases of polydactylous disease or where surgery is difficult, especially in immunocompromised patients.[40] Photon irradiation using a water bath is recommended for extensive disease but has been limited due to concerns regarding toxicity. Chemotherapy is indicated only in metastatic disease.[41]

Amputation of the distal phalanx has the highest cure rate and is indicated in cases of long-standing carcinoma or bony involvement.[42] Recurrence is reported in only 3.5% of patients after Mohs surgery and 4% after wide surgical excision, higher than skin SCC. Factors contributing to this discrepancy include high-risk HPV, surgical procedure difficulty, and challenging pathology interpretation.[43]

RESULTS

Physicians need to maintain heightened awareness, and chronic, non-healing lesions of the digits should be viewed with suspicion. Rapidly growing ulcerative lesions should be considered as potential malignancy. The prognosis of SCC is very good if it is recognized at an early stage, highlighting the need for clipping away the nail plate and taking a biopsy in patients with chronic or recurrent oozing from under the nail that fails to respond to any previous conservative treatment. Nail dermoscopy is useful in looking for longitudinal melanonychia or erythronychia, irregular vascularity, and hemorrhages. Moreover, it is helpful to better visualize the onycholytic nail plate and subungual hyperkeratosis with high magnification that permits observation of the aspect of the color and shape. It is not a specific method for diagnosis, but it is helpful in differential diagnosis in some conditions such as onychomatricoma and onychomycosis. Another important role of dermoscopy can be the selection of the biopsy site.

CONCLUSION

Pathological confirmation is crucial for early diagnosis and treatment of Spinal Cord Tumor (SCC), with pain indicating bone invasion. X-rays are necessary for bone involvement. There is no consensus on the optimal treatment due to the rarity of SCC. Treatment is based on tumor extension and underlying structures involvement.[44] Microscopic surgery and local removal are recommended for superficial lesions, while large excisions are recommended for bone infiltration patients. Recurrence is higher in the nail unit due to residual HPV or incomplete tumor excision, requiring strict and long follow-up.[45]

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