Review Article

Nail Changes With Chemotherapeutic Agents and Targeted Therapies

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Abstract

Patients on Cancer chemotherapeutic agents often develop nail changes most of which are only cosmetic concern and disappear on drug withdrawal. But some nail changes can be painful and disabling thereby affecting quality of life substantially. Different components of the nail unit include the nail matrix, nail bed, nail plate, the hyponychium, lunula, the proximal and lateral nail folds. In this article we review the nail changes induced by chemotherapeutics and targeted anticancer drugs, preventive measures and treatment options available.

Keywords: *Anticancer drugs, chemotherapeutic agents, nail changes, nail toxicity, targeted therapies*

Nail covers the distal phalanx and the continuously dividing matrix cells generate the nail plate. Cancer chemotherapeutic agents may lead to nail changes as they affect these rapidly dividing nail matrix cells.[1] Nail changes have been reported to be the most common mucocutaneous adverse reactions of cancer chemotherapy and chemoradiation.[2] The nail changes are usually but not always transient and disappear on drug withdrawal. It may affect all the nails or some and shows a temporal relationship to drug intake. Different components of the nail unit include the nail matrix, nail bed, nail plate, the hyponychium, lunula, the proximal, and lateral nail folds. Presentation depends on the nail structure affected and severity of the insult.[3] Some of the nail changes are only a cosmetic concern while others may be symptomatic leading to severe pain. Usually several nails are involved and mostly fingernails are involved more commonly than toe nails except for some changes which are aggravated by pressure and trauma which are commonly observed on big toenail.

Pathophysiology

Finger nails grow at an average rate of 0·1 mm per day (3 mm per month) taking 4 to 6 months for complete regrowth and toenails at 0·03 mm per day (1 mm per month) taking 12 to 18 months for toenails. The nail changes are a past event relative to drug initiation and disappearance of inflicted changes does not coincide with drug interruption.

The clinical presentation of chemotherapeutic induced nail changes depends on the component of nail unit involved and the duration and severity of toxicity.

Pathogenesis of nail changes depending on part of nail unit affected is as follows:

Nail matrix: nail matrix is highly susceptible to damage from chemotherapeutic agents as it is formed of proliferating cells leading to defective nail plate production. Typical nail matrix changes include melanonychia, leukonychia, Beau's lines, and onychomadesis, and melanonychia due to arrest in epithelial proliferation or leukonychia due to abnormal keratinization.

Melanonychia: It refers to brownish or black pigmented bands in nail which can be transverse, longitudinal, or diffuse and mostly appear 1 to 2 months after chemotherapy initiation. Melanonychia occurs due to melanocyte activation in matrix epithelium.[3–5] Studies have reported diffuse hyperpigmentation of nails to be most common side effects.[6] Alternating bands of normal and hyperpigmented bands corresponding to the chemotherapy cycles may be seen[7] [Figure 1a] or alternating dark and white bands may

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also be seen corresponding to intermittent administration of drug [Figure 1b]. The pigmentary change is mostly reversible few months after stoppage of chemotherapeutic agent.

Leukonychia: It refers to white coloration of the nail plate which can be a true or apparent leukonychia. True leukonychia develops due to abnormal keratinization of the nail matrix [Figure 2] and apparent leukonychia develops due to abnormalities of the blood flow in the nail bed. Apparent leukonychia can present as half-and-half nail, Muehrcke's nails, or Terry's nails.

Beau's lines: Beau's lines are depressed linear bands on the dorsum of the nail plate that form due to arrest in mitotic activity of the nail matrix. The distance between Beau's line and proximal nail fold can guide about when the acute arrest in nail proliferation occurred and its depth can guide about the severity of insult. Onychomadesis is its most severe form in which a deep sulcus divides the nail plate into two parts [Figure 3].[7] Repeated chemotherapy cycles can lead to multiple beau's line on all/multiple nails.

Nail bed: Nail bed epithelium is responsible for adhesion of the nail plate to the underlying structures. Onycholysis refers to separation of nail plate from the nail bed. It results due to damage by toxins to the nail bed leading to nail plate detachment.[3,8]

Nail fold: Some drugs may interfere with proximal nail fold integrity exposing the nail matrix, leading to disordered nail growth. It may lead to granulation tissue formation with bleeding. It may manifest as paronychia or pyogenic granuloma like lesion [Figures 4a and 4b]. Its pathogenesis is largely unknown. It may be formed because of activation of angiogenic factors by the drugs.[4,8,9] The periungual lesions are initially sterile but bacterial infections (and rarely candida infection) may develop leading to purulent discharge. Pyogenic granuloma-like lesions are dose dependent, thereby regressing on dose reduction or treatment interruption, but in some patients may take upto several months to heal completely.

Vessels: Damage to the vascular network of nail bed may lead to splinter hemorrhages and subungual hematoma.[9] Splinter hemorrhages are more commonly observed in fingernails whereas hematomas are more common in toes and occur due to trauma. Thrombocytopenia secondary to cancer chemotherapy may also lead to the above changes.[3,5] Cancer chemotherapeutics may also lead to ischemic changes like Raynaud's phenomenon to digital gangrene.[4]

Nail bed and nail plate changes are observed to occur more commonly with cytotoxic chemotherapeutic agents than targeted anticancer therapies, whereas periungual lesions and paronychia are observed more with targeted anticancer therapies.

Grading of nail toxicity

The nail toxicities are classified using the NCI Common Terminology Criteria for Adverse Events version 4.03 (CTCAE v4.03) which includes five nail changes: paronychia, nail loss, nail ridging, nail discoloration, and nail infection.[10] Although this classification takes into account the impact on quality of life (QOL), it ignores some of the important chemotherapeutic agent induced nail changes, like painful nail bed hemorrhages. The Multinational Association of Supportive Care in Cancer Skin Toxicity Study Group [Table 1] has proposed grading scale for nail changes due to epidermal growth factor receptor (EGFR) inhibitors which takes into account the nail plate, nail folds, and digital tip changes.[11]

Each nail changes observed with different chemotherapeutic agents [Table 2] are summarized in table below.

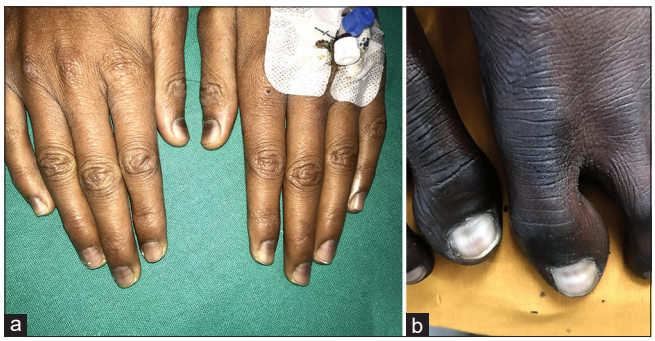

Figure 1: (a) Alternating dark and normal bands in patient on docetaxel; (b) Alternating dark and white bands on toenail in patient on daunorubicin

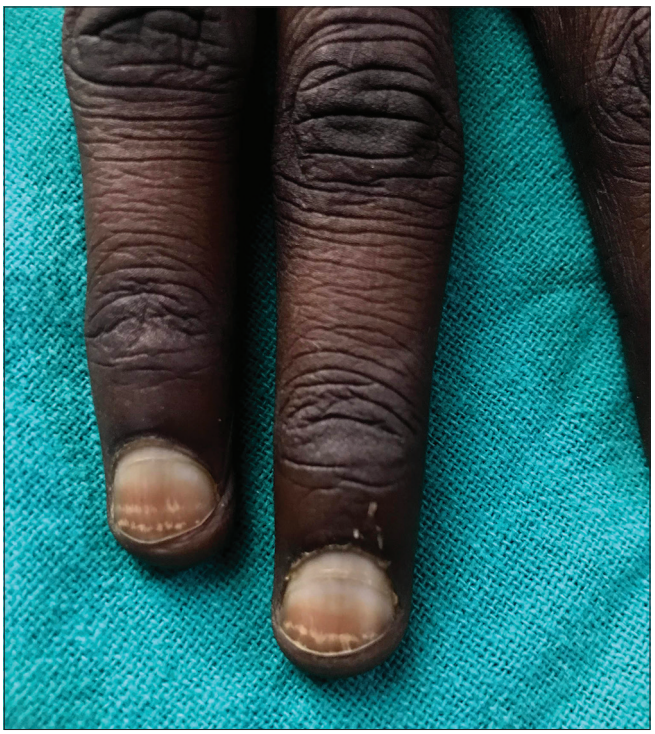

Figure 2: Transverse leuconychia bands corresponding to intermittent chemotherapy

Cytotoxic agents

Alkylating agents

Classical alkylating agents (like Cyclophosphamide, ifosfamide and thiotepa): nail changes secondary to classical alkylating changes include nail pigmentation, Beau's lines, and onycholysis.[12,13] Nail pigmentation can occur in all age groups after oral or intravenous (IV) medication and can affect both finger and toe nails. It may vary from horizontal or longitudinal streaks to diffuse pigmentation.[14]

Platinum agents (like Cisplatin, carboplatin, and oxaliplatin)

Leukonychia, Beau's lines, and diffuse hyperpigmentation have been reported after cisplatin chemotherapy.[15] Pus discharge, onycholysis, and nail plate discoloration has been reported with weekly paclitaxel and carboplatin[16] and transverse leukonychia affecting fingernails described in a patient receiving paclitaxel and carboplatin on a 3-week basis.[17]

Antimetabolites

Pemetrexed: Report of longitudinal melanonychia after 2 months of treatment with pemetrexed which further evolved into complex pattern of nail pigmentation as well as onycholysis after further 3 months has been reported in a patient with non-small cell lung cancer.[18]

5-fluorouracil: Nail changes attributed to fluorouracil include Onycholysis, nail plate dystrophy, onychomadesis, transverse bands, paronychial pain and inflammation, and hyperpigmentation [Figure 5].[13,15]

Table 1: MASCC grading for nail toxicity due to EGFR inhibitors[10]

Grade	Nail plate changes	Nail fold changes	Digit tip changes
Grade 1	Onycholysis or ridging without pain	Disruption or absence of cuticle Orerythema	Xerosis and/or erythema without pain
Grade 2	Onycholysis with mild/moderate pain; Any lesion interfering with instrumental ADL	Erythematous/tender/painful nail fold changes Orpyogenic granuloma or crusted lesions	Xerosis and/or erythema with mild/moderate pain, stinging or fingertip fissures
Grade 3	Any changes interfering with self-care ADL		

ADL- activities of daily living

Table 2: Nail changes to different chemotherapeutic agent[4–7]

Nail changes	Drug implicated	Remarks
Nail matrix changes		
Melanonychia	Cyclophosphamide	Diffuse black pigmentation, longitudinal melanonychia, and dark grey pigmentation of the proximal part of the nail plate
	Doxorubicin	Alternating bands of dark brown and white lines and dark brown pigmentation in transverse bands
	Hydroxycarbamide (hydroxyurea)	Distal, diffuse dark brown pigmentation
	Taxanes	Orange discoloration due to hamorrhage in nail bed
	Busulfan, capecitabine, cisplatin, and bleomycin	
	Imatinib	Longitudinal, transverse, or diffuse melanonychia
True leukonychia	Doxorubicin, cyclophosphamide, and vincristine	
Beau's lines	Almost all cytotoxic agents	
Nail bed changes		
Onycholysis	Capecitabine, etoposide, mitoxantrone, or doxorubicin, targeted therapies (anti EGFR, MEK, and mTOR inhibitors)	
	Taxanes	Haemorrhagic onycholysis, may be associated with paronychia
	Anti-EGFR and MEK inhibitors	
Nail fold changes		
Paronychia	Anti-EGFR inhibitors, MEK inhibitors, mTOR inhibitors, capecitabine, methotrexate, and doxorubicin	
Vascular changes		
Raynaud's phenomenon/ digital gangrene	Bleomycin	May warrant drug cessation
Subungual splinter hemorhage	VEGR inhibitors	

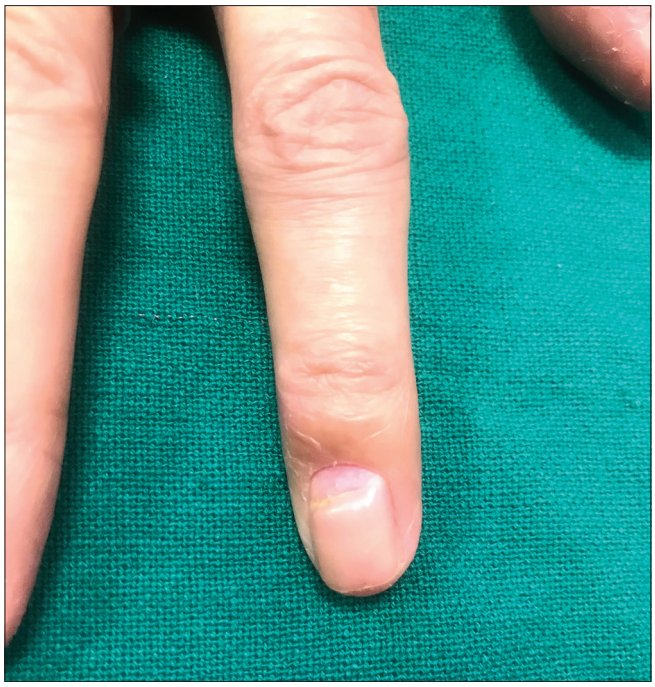

Figure 3: Onychomadesis

Capecitabine: Onycholysis and onychomadesis are the nail toxicities described after capecitabine therapy.[19] Nail toxicities are observed in about 7% of cases with capecitabine. Sunset appearance of the nail with erythema and edema along with onycholysis has also been described.[20] Periungual inflammation, paronychia, and pyogenic granuloma can develop after capecitabine.[21]

Tegafur: There are reports of blackish discoloration of lunula of fingernails after 4 weeks of oral tegafur administration in a patient with colon cancer.[22]

Topoisomerase inhibitors

Anthracyclines

Daunorubicin: Transverse dark pigmented bands[23] [Figures 6a and b] and transverse leuconychia (Mee's lines)[24] of the fingernails and toenails have been reported following daunorubicin administration. Alternating dark and white bands may be seen corresponding to intermittent administration of Daunorubicin [Figure 1b].

Doxorubicin: Beau's lines, longitudinal pigmented bands, onycholysis, nail loss, periungual inflammation, and periungual pyogenic granulomas have been described after doxorubicin.[25,26]

Etoposide: Nail bed pigmentation, Beau's lines, and onycholysis are some reported side effects of etoposide.[4,15]

Topotecan: Topotecan and irinotecan are effective chemotherapeutic drugs for treatment of solid tumors. Topotecan is given as IV infusion lasting five days every three weeks. In a case report, nail pigmentation was observed after topotecan.[27,28]

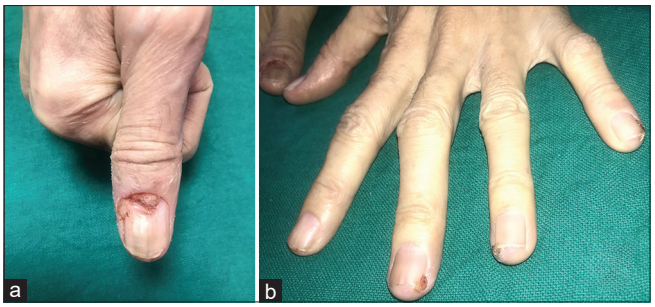

Figure 4: (a) Proximal nail fold paronychia with pyogenic granuloma like lesions secondary to Gefitinib; (b) Granulation tissue at lateral nail fold with EGFR inhibitors

Antimitotic agents

Taxanes

Taxanes are one of the most common cancer chemotherapeutic agents causing nail toxicity. Most of the cases have been attributed to docetaxel after variable schedule like weekly, 3-weekly, and undefined schedules of administration or combination therapy. Minisini *et al*.[29] have reported an overall incidence of 44% for taxane-induced nail changes with some series reporting it as 89% with 3 treatment cycles. The nail toxicity may be severe enough to affect QOL, leading to treatment discontinuation.

Docetaxel: Various nail changes have been reported with docetaxel as shown in Table 3. Two hypotheses have been suggested to explain taxane-induced nail toxicity: neurogenic inflammation due to neuropeptides release or the effect of prostaglandins via sympathetic fibers. It was observed in a woman with breast cancer involving right braxial plexus treated with docetaxel that severe nail toxicity affected all nails except the nails of the right hand.[29] It was observed in a study that the nail toxicity improved with treatment of a cyclooxygenase-2 inhibitor, which favors the hypothesis of the role of prostaglandins.[30] The presence of nail toxicity was found to be strongly associated with the number of cycles given, weekly regimen, and its cumulative dose.[31] The cumulative hazard of developing nail toxicity increased above 10% after 2.8 months to upto 40% at 6 months.[32] Winther *et al*.[33] on studying the patients with metastatic breast cancer treated with docetaxel reported that 58.1% of patients with some nail toxicity increased to 88.5% in those receiving an additional three cycles of docetaxel. Although most of the patients had major cosmetic concerns with the nail changes, about 32% patients had functional difficulty interfering with daily activity. Because studies comparing weekly and three-weekly regimens did not show any difference in the incidence of nail toxicity, nail changes in the weekly treatment arm affected the QOL to the extent that it was the major reason for withdrawal from these studies.[33]

Haemorrhagic onycholysis is the characteristic nail toxicity induced by taxanes observed more commonly with docetaxel than with paclitaxel.[36] Taxane-related onycholysis

Table 3: Chemotherapeutic agents and their nail changes[9,10,24,29,34,35]

Class of chemotherapeutic agent	Subclass/Drug	Nail changes
Alkylating agents	Cyclophosphamide, ifosfamide, and thiotepa	Nail pigmentation, Beau's lines, and onycholysis
	Platinum agents: Cisplatin, carboplatin, and oxaliplatin	Leukonychia, Beau's lines, and diffuse hyperpigmentation, pus discharge, onycholysis, and nail plate discoloration
	Dacarbazine	Melanonychia
Antimetabolites	Antifolate: Pemetrexed	Longitudinal melanonychia onycholysis
	Antifolate: Methotrexate	Acute paronychia pigmented horizontal bands extensive onycholysis
	Fluropyrimidine: 5-fluorouracil	Onycholysis, nail plate dystrophy, onychomadesis, transverse bands, paronychial pain and inflammation, and hyperpigmentation
	Fluoropyrimidine: Capecitabine	Onycholysis and onychomadesis Periungual inflammation, paronychia, and pyogenic granuloma
	Fluoropyrimindine: Tegafur	Blackish discoloration of lunula
	Busulphan	Brownish tinge to the lunula and nail plate or inducing longitudinal nail bands
	Hydroxyurea	Pigmentation of the nails
Topoisomerase inhibitors	Anthracyclines: Daunorubicin Doxorubicin	Transverse leuconychia (Mee's lines), Beau's lines, longitudinal pigmented bands, onycholysis, nail loss, periungual inflammation, and periungual pyogenic granulomas
	Dactinomycin	Beau's lines
	Topotecan	Nail pigmentation
	Etoposide	Nail bed pigmentation, Beau's lines, and onycholysis, nail bed pigmentation, Beau's lines, and onycholysis
Antimitotic agents	Taxanes Docetaxel Paclitaxel	Onycholysis, transverse leukonychia, purulent discharge, acute paronychia, nail ridging, beau's lines, subungual hemorrhages, and hyperpigmentation of hyponychium
	Vincristine	Cause leukonychia, Beau's lines, Mees' lines, and onychodermal bands
	Etoposide	Nail bed pigmentation, Beau's lines, and onycholysis.
BCR-ABL inhibitors	Imatinib	Hyperpigmentation, affecting all of the fingernails
Epidermal growth factor receptor inhibitors	Cetuximab, erlotinib, panitumumab, Gefitinib, and lapatinib	Paronychia, pyogenic granuloma like lesions, onycholysis, melanonychia, brittle nails, nail cracking, onychoschizia, and onychorrhexis
MEK inhibitors	Binimetinib Cobimetinib Trametinib	Paronychia, pyogenic granuloma like lesions, onychoschizia, onychorrhexis, brittle nails, nail cracking, and onycholysis
mTOR inhibitors	Everolimus Temsirolimus	Paronychia, pyogenic granuloma like lesions, nail plate thinning, onychodystrophy, brittle nails, distal onycholysis, and diffuse yellow nail discoloration
VEGFR inhibitors	Sorafenib Sunitinib Pazopanib Bevacizumab	Splinter subungual hemorrhages
Miscellaneous agents	Bleomycin	Hyperpigmentation, onycholysis, Beau's lines, and raynaud's phenomenon

may at times be associated with inflammatory erythema of dorsum of hands, perimalleolar, and Achilles areas, known as periarticular thenar erythema with onycholysis (PATEO syndrome).[37] Docetaxel-induced finger and toenail changes can be reduced by using an Elasto-Gel frozen glove and sock during docetaxel infusion, but once toxicity develops, only conservative measures can be taken.[38,39]

Paclitaxel

Nail changes secondary to paclitaxel are similar to docetaxel including onycholysis of finger and toenails which may be extensive, transverse leukonychia, purulent discharge, acute paronychia, nail ridging, Beau's lines, subungual hemorrhages, nail pain, and hyperpigmentation of hyponychium.[17,40] There is an increase in the incidence of paclitaxel-induced nail abnormalities probably due to increased use of weekly schedules and the side effects were not associated with fewer cycles or 3-weekly schedules.[4]

Vincristine: Vincristine has been reported to cause leukonychia, Beau's lines, Mees' lines, and onychodermal bands.[15]

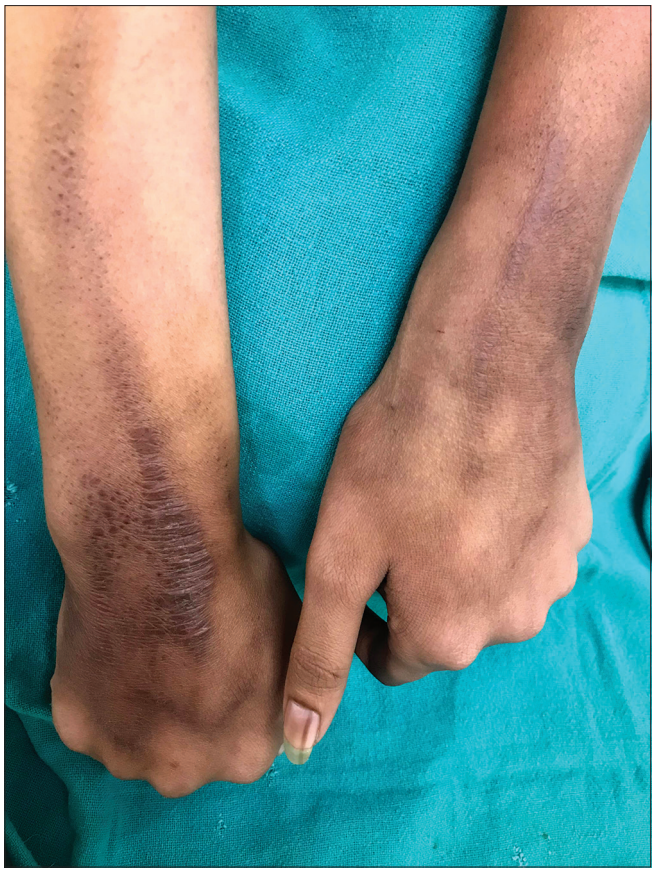

Figure 5: Longitudinal melanonychia in patient on 5 fluorouracil. Also note serpentine pigmentation on forearm

Miscellaneous agents

Bleomycin: Hyperpigmentation, onycholysis, Beau's lines, raynaud's phenomenon have been reported with bleomycin.[15,41] Intralesional bleomycin used for treatment of periungual warts may lead to nail dystrophy.[42]

Targeted Therapies

Epidermal growth factor receptor inhibitors

EGFR inhibitors are members of type 1 tyrosine kinase receptor family and are used for treatment of solid organ malignancies. These include cetuximab, erlotinib, panitumumab, and lapatinib. They are associated with various cutaneous adverse effects including nail toxicities. The overall incidence of nail toxicities (all grades) with EGFR inhibitors is 17.2% and of high grade nail toxicity is 1.4% with relative risk of 76.94 and 13.11, respectively.[34] Nail changes typically develop after 2 or more months of drug exposure. Almost all patients on EGFR inhibitors are at risk for same irrespective of the tumor type and has been reported with latest EGFR inhibitors (lapatinib, pertuzumab, and afatinib) as well. It may involve multiple or all 20 nails.[35]

The nail changes observed are independent of the type of EGFR inhibitor used. It may affect all. Various nail changes

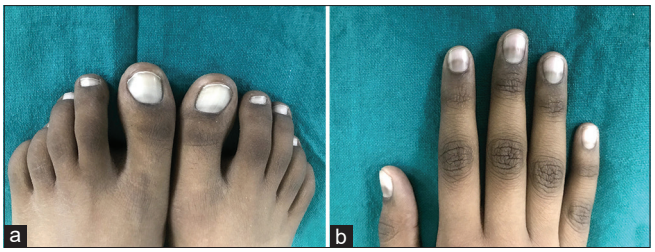

Figure 6: (a and b) Transverse melanonychia in patient of AML on cytarabin and daunorubicin

can be observed in the entir]e nail unit which includes-

- Nail fold–paronychia and periungual granulation tissue
- Nail bed–onycholysis
- Nail matrix–melanonychia and brittle nails.

Of these, most common nail changes seen on EGFR inhibitors include paronychia and periungual granulation tissue which may lead to onycholysis and onychodystrophy.[34]

Mechanism for nail changes with EGFR inhibitors is postulated to be through its inhibitory effect on EGFR dependent pathways in keratinocyte leading to altered differentiation and migration of epidermal cells, thereby inhibiting keratinocyte proliferation and inducing apoptosis of keratinocytes in and around nail unit.[43] This leads to thinning of the periungual tissue. The nail plate pierces through the thinned out epithelium, thereby inciting inflammation.

Periungual lesions are observed gradually after about 4 to 8 weeks of starting EGFR inhibitors treatment which is late in comparison with other cutaneous side effects like folliculitis developing within first week of treatment initiation.[44–46] First, acute paronychia appears with periungual swelling, tenderness, and oozing which may progress into granulation tissue on the lateral nail folds. The periungual changes are observed most commonly on big toes though any digit may be involved due to repeated microtrauma. Some of the changes are just a cosmetic concern but a few especially the periungual changes can be debilitating severely affecting QOL and essential daily self care activities warranting dose reduction. Drug interruption is not recommended given the long half life of drug and slow growth of the nail plate.[46]

MEK (mitogen-activated protein kinase) inhibitors

Nail changes with MEK inhibitors can be due to inhibition of EGFR in the nail matrix.[43] MEK inhibitors can affect all nails and the nail changes include brittle nails, nail cracking, onychoschizia, onychorrhexis, onycholysis, and perinungual inflammation.[43,44,47,48] There are no prospective studies on incidence of these lesions but authors have reported its frequency and severity to be lower than EGFR inhibitors. MEK inhibitors exhibit side effects similar to EGFR inhibitors like folliculitis, painful fissuring of

fingertips, or hair changes probably due to inhibition of the MAP-kinase pathway.[47]

mTOR(mammalian target of rapamycin) inhibitors

In view of the role of mTOR signalling downstream of EGFR, MAPK, and PI3K pathway, its side effect profile closely resembles that of EGFR inhibitors and MEK inhibitors which includes nail plate thinning, onychodystrophy, brittle nails, distal onycholysis, diffuse yellow nail discoloration (xanthochromia), and periungual lesions.[49,50] A study has shown incidence of 22% for periungual lesions with mTOR inhibitors.[51]

BCL-ABL (breakpoint cluster region protein- Aberlson murine leukemia viral gene) inhibitors

BCL-ABL inhibitors like Imatinib can lead to finger as well as toenail melanonychia which can be longitudinal, transverse, or diffuse [Figure 7].[52] The probable mechanism of action is c-KIT blockade by imatinib which has role in melanogenesis.[53] This may also explain pigmentatory alteration observed with imatinib.[44]

VEGFR (Vascular endothelial growth factor) Inhibitors

Splinter hemorrhages have been frequently reported (incidence 25%-75%) with VEGFR inhibitors[54] and have been seen more commonly with sorafenib than sunitinib or pazopanib.[45,55] Fingers nails are affected more commonly than toenails. Splinter hemorrhages develop within first few weeks of therapy and disappear as the nail progressively grows despite continued treatment.[44] The mechanism of development of subungual hemorrhages has been hypothesized as impaird repair of nail bed capillaries from the trauma sustained by repeated micro injuries due to VEGFR inhibition.[54] Splinter subungual hemorrhages do not need any definite treatment.

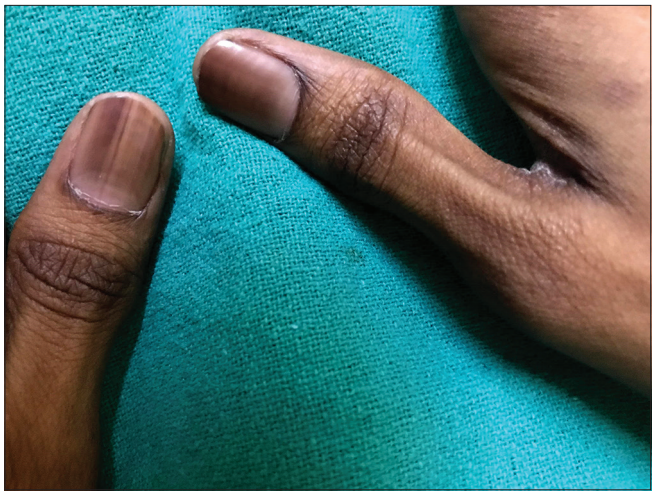

Figure 7: Longitudinal melanonychia secondary to imatinib

Management

It is important to counsel the patient before starting chemotherapeutic agent about the potential nail side effects and brief them about preventive strategies. Preventive measures to avoid/decrease chemotherapeutic induced nail toxicity focus on minimizing the pressure, trauma, and friction on the nail unit. These include avoiding irritants like frequent water immersion, wet work, corrosive chemicals, avoiding aggressive manicure, acetone, artificial nails, nail biting, cutting nails too short, and encouraging frequent application of emollients like petroleum jelly to the nail plate, filing the edges to smoothen the corners of nail plate, and promoting wide and comfortable footwear. It is important to maintain appropriate hygiene to avoid secondary infection. Use of frozen glove and socks can be effective preventive measure for taxane-induced toxicity.[38] Dark-colored nail may prevent photo-induced onycholysis, but it is yet to be established. Treatment with biotin may be helpful, but it is yet to be established.[56]

Most of the nail toxicities once developed can be managed conservatively. Since nail growth is a slow process, there is no effective means to reverse nail abnormalities arising secondary to transient arrest of nail matrix mitotic activity. It is important to counsel the patient that the nail changes will disappear with the nail growth but this may take months. Usually, it is not recommended to withdraw the drug as it takes several months for the nail changes to improve but if toxicity is severe, reduction or cessation of the offending drug may be necessary. Management of different nail toxicities has been briefly described in Table 4.

Conclusion

Nail changes are frequently observed in patients treated with anticancer agents. The cytotoxic chemotherapeutic agents mostly affect the nail plate and bed, whereas the targeted therapies mostly involve the periungual tissue. Patients can be informed about the expected side effects based on the chemotherapeutic agents and explained preventive strategy to minimize the side effects. Nail changes can at times be debilitating affecting the QOL and so treating physician should be aware of changes expected and timely intervention needed.

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Conflicts of interest

There are no conflicts of interest.

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Table 4: Management of different drug induced nail toxicities[4,8,38,39,57,58,59,60]

Drug induced nail toxicity	Management
Drug-induced onycholysis	keep nails short
	debridement for moderate onycholysis
	local application of antimicrobial solutions
	avoid contact with irritants
	if haematoma limited to <25% of the visible nail-drain with sharp scalpel or by hot paper-clip cautery touched at center of dark spot.
Drug-induced paronychia and periungual inflammation	Topical application of corticosteroids and calcineurin inhibitors
	antibiotics if culture positive/infected
	vinegar soaks/dilute bleach soaks to prevent secondary infection
	oral tetracyclines prescribed for folliculitis due to EGFR inhibitors may be helpful.[42]
	topical adapalene gel has been found promising in few case reports, but further studies needed.
Pyogenic granuloma like lesions	pain
	monitor effect on activities of daily living
	Topical liquid nitrogen, topical steroids, or weekly 10% aqueous silver nitrate
	electrodesiccation
	88% phenol or 35% trichloroacetic acid topical, or liquid nitrogen applications
	intralesional triamcinolone acetonide followed by chlorhexidine lotion twice daily
	topical or oral antibiotic if superinfected
	surgical treatment - removal of part of the nail together with the matrix may be needed with physical destruction of excessive granulation tissue.
	dose adjustments needed if lesions are painful, several, or persistent
Nail pigmentation	pigmentation may persist unchanged for years even after drug withdrawal
	only a cosmetic concern
	Application of colored nail varnish helps to conceal the pigmentation and hardens the nails to prevent fragmentation.
Nail plate changes	reduce contact with water
	wear cotton gloves under plastic or rubber gloves before any wet work
	Topical applications of nail lacquer containing hydroxypropyl chitosan may increase linear nail growth and improve nail keratin quality (as shown in psoriatic nail dystrophy).

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