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Dear NSI members, Greetings from Nail Society of India!

As NSI enters in its 5th year of existence, we feel obliged, gratified and overwhelmed for your unconditional and constant support in our endeavor to fundate the mutual learning and sharing of expertise in the field of the Nail disorders. Publication of **ONYCHOSCOPE**, our biannual newsletter is to aggrandize this vision.

The diagnosis and management of **Non-dermatophytic OM (NDM)** remains enigmatic. In this issue, Dr Manjunath Shenoy, the invited faculty, will decipher the related complexities. Dr Sushruta Kathuria has comprehensively penned down 'What's new' in Nail. Be ready to exercise your grey cells to solve the 'Nail Maze' by Dr Khushboo Mahajan. The 'Photo-quiz' dealing with a common yet perplexing nail condition has been contributed by Dr Deepak Jakhar. This issue carries an interesting "Nail's Tale" contributed by Dr B Srinivas from Chennai.

The sincere intentions of NSI towards raising interest in Nail disorders has been recognized both at national and international levels. The fact is substantiated by the invite to be a **supporting organization for the 17th WCOCD** (World Congress of Cosmetic Dermatology) to be held in Bangalore, India for the first time in May 2017.

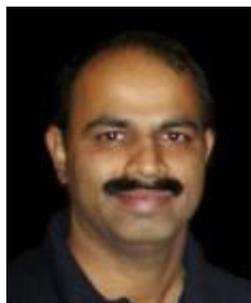
As you all know the **Annual National Conference of NSI 'ONYCHOCON'** has become a coveted event in the dermatologic academic calendar. And I feel privileged to invite you to **5th ONYCHOCON** that will be held in the most vibrant **PINK city of JAIPUR**, Rajasthan on **17th & 18th Dec, 2016**. The event will be hosted by very friendly, warm and hospitable **Prof Dinesh Mathur & Prof Manisha Nijhawan** and their team. Jaipur is the most enthralling historical *city and is an* epitome of magnificence and architectural heritage. It's definitely going to be an awesome amalgamation of learning and leisure. **Prof Iffat Hassan and her team** have contributed very graciously to the scientific program for **5th ONYCHOCON**. **Please block your dates!** So see you all during **5th ONYCHOCON**;
Adieu till then !

Archana Singal



Thanks giving get together post 3rd ISND & 4th ONYCHOCON

Onychomycosis by Non-Dermatophyte molds



Dr Manjunath Shenoy M,

Prof. & Head,
Dept. of Dermatology,
Yenepoya Medical College,
Yenepoya University,
Mangalore -575018. India.

Introduction:

Onychomycosis does not cause any life-threatening complications and is generally considered as a cosmetic problem. Apart from the disfigurement caused by the disease, it can also serve as a reservoir for cutaneous infections. Fungal agents other than dermatophytes often isolated from abnormal nails, were previously considered as colonizers or contaminants. However, currently it is proven that they are capable of causing nail disease. Non-dermatophytes are often accountable for a significant number of onychomycosis and in certain geographic locations they may outnumber that caused by dermatophytes. *Candida* is the most common non dermatophyte fungal genus isolated. Molds other than dermatophytes are frequently isolated from the infected nails. Some of these agents have been reported in association with invasive fungal diseases in neutropenic and immune-suppressed patients; hence focus has also been shifted towards the non dermatophyte molds (NDM).

Epidemiology and etiology:

There seems to be a great variation in the incidence of onychomycosis from one geographic area to another. Age, climate, occupation, travel, hygiene, chronic diseases and other factors play an important role. Among the chronic diseases, diabetes, peripheral arterial diseases and psoriasis may act as independent risk factors for onychomycosis. Agents causing onychomycosis also vary from one location to other. Undoubtedly, dermatophytes are the most common causative organisms. NDM are reported to be associated with nail infections in 2 to 17% in various studies. Incidence may be found to be higher in certain studies. Various NDMs that can cause onychomycosis are listed in **Table 1**.

NDMs rarely cause infections of both hands and feet; and are more likely to cause toe nail disease. *Aspergillus* species seem to be leading NDM isolated from the infected nails. In an Iranian study involving 463 ony-

chomycosis cases; *Aspergillus* was responsible for about one third of all cases of onychomycosis. *Aspergillus flavus* was the the most common species to be identified. Diabetics are especially at risk of toe nail onychomycosis and NDMs are the frequent isolates. In a recent study from Srilanka, *Aspergillus* species was isolated in 71% of the 255 mycologically confirmed toe nail onychomycosis in diabetics.

Table 1. Non-dermatophyte molds reported to cause onychomycosis

Aspergillus species
Scopulariopsis brevicaulis
Scytalidium
Alternaria species
Fusarium species
Cladosporium species
Curvularialunata
Acremonium species
Penicillium species
<i>Pyrenochaeta unguis-hominis</i>
Onychocolacandidensis

Among the various causative agents, some present a special affinity to keratin (pseudodermatophytes); eg. *Neoscytalidium dimidiatum* (*Scytalidium dimidiatum*) from tropical and subtropical are as and *Onychocolacandensis* from Northern America and Europe. Others are generally considered as saprophytes and most of the time considered as colonizers rather than real pathogens. Laboratories play an important role in identifying the species and confirming parasitism by the fungus in the infected nails.

Diagnosis:

Clinically dermatophytic and NDM infections are difficult to differentiate. Various clinical forms of onychomycosis as seen with dermatophytes infections namely distal lateral subungual onychomycosis (DLSO), superficial white onychomycosis, proximal subungual onychomycosis, and total dystrophic onychomycosis can also be seen with NDM infections. Tosti A reports that the patients with onychomycosis resulting from NDM presented most often with proximal subungual onychomycosis with paronychia, and hence one can clinically suspect the possibility of NDM infection. Immune suppression may not be a common association with NDM infections. Features that favor the diagnosis of NDM infections as com-

pared to dermatophytic infections are toe nail disease, absence of simultaneous finger and toe nail infection, absence of tinea pedis, presence of paronychia and nail plate discoloration.



Picture 1. Toe nail disease with paronychia suggestive of NDM infection.

Toe nails are particularly favored by NDM because they are prone to trauma and affected by peripheral arterial diseases. Presence of tinea pedis virtually rules out NDM infection, but there are exceptions. Tinea pedis may rarely be caused by *Scytalidium hyalinum* and certain other NDM. Paronychia is a common feature associated with infections by *Fusarium* and *Scytalidium dimidiatum*. Fungal melanonychia is an association with *Aspergillus niger* but has been reported in association with a number of dematiaceous and non-dematiaceous fungal agents. It is also seen with *Trichophyton rubrum* and *Candida* infections.

Diagnosis of NDM onychomycosis depends on the isolation and histopathologic demonstration of the fungal agents in the nail to confirm parasitism. Culture allows the identification of the species involved in nail infection. Before attributing any pathogenic role to non-dermatophytic molds, it is essential to precisely evaluate their pathogenicity through appropriate samples and mycological diagnosis. In other words diagnosis of NDM infections should only be considered after it is corroborated by direct microscopic examination, culture, and histo-mycology. This can be done by the histopathologic examination using periodic acid-Schiff staining (PAS) of the nail clips. NDM infections should be confirmed if the same agent is isolated repeatedly or more than five colonies in two consecutive samples. NDMs generally grow faster as compared to dermatophytes and species identification can be done within a week. This is an advantage over the dermatophytic infections which generally require not less than 2 weeks for the culture yields.

Treatment:

There is no consensus regarding the treatment of NDM onychomycosis. This is because of the variety of agents that cause the infection. It is ideal that the antifungal sensitivity of the agents be detected before treating which is not always feasible. We have to follow the evidence from published literature and extrapolate the information for our patient care.

Antifungal drugs, terbinafine and itraconazole, have been used in the treatment of NDM infections. Both are found effective to the treatment of *Scopulariopsis brevicaulis* and *Aspergillus* species infections. *Fusarium* species may also show a good response to itraconazole and terbinafine. According to a Srilankan study by Ranawaka RR et al, both itraconazole and terbinafine were partially effective on NDM onychomycosis with a clinical cure of 54-65%. They used itraconazole 400 mg daily or terbinafine 500 mg daily for 7 days in a month; two pulses for fingernails and three pulses for toenails.

Topical treatment with ciclopirox nail lacquer may also be effective and may work better if combined with chemical or surgical avulsion of the nail. Tavaborole, a novel boron containing topical antifungal solution has also been found beneficial in the treatment of toe-nail onychomycosis.

Photo Quiz

Q. A 35 year male presented with a skin colored, asymptomatic, subungual growth over the right great toe for the past three months (Fig 1). There was a slow increase in its size with partial lifting up of the nail plate. The X-ray images did not show any bony connection. The onychoscopic picture is shown (Fig 2) (50X; Dinolite 413ZT).

1. What is your diagnosis?
2. What are the onychoscopic findings seen?
3. What could be the best treatment strategy for such a lesion?



Answer on Page - 8

Efinaconazole is a new triazole topical antifungal which seems to be having advantage over other topical agents in onychomycosis. In vitro studies by Jo Siu WJ et al found that the drug was active against *Trichophyton*, *Microsporium*, *Epidermophyton*, *Acremonium*, *Fusarium*, *Paecilomyces*, *Pseudallescheria*, *Scopulariopsis*, *Aspergillus*, *Cryptococcus*, *Trichosporon*, and *Candida*. Its low keratin affinity may be responsible for its nail penetration and fungicidal activity. It is currently not available in India but it could be the most effective topical agent with lesser chances of antifungal resistance.

Conclusion:

NDM nail infections are common and can be diagnosed by following certain criteria. There is no definite consensus regarding the treatment. Therapeutic response to available topical and systemic antifungals has been proven. More information regarding the diagnosis and treatment is likely to be available in near future.

Excerpts from Nail Literature

NAIL: WHAT'S NEW?

The Efficacy and Prognostic Factors for Long Pulse Neodymium: Yttrium-Aluminum-Garnet Laser Treatment on Onychomycosis: A Pilot Study.

Lu S, Zhang J, Liang Y, Li X, Cai W, Xi L. *Ann Dermatol*. 2016; 28: 406–408.

A study to compare the effect of a Fotona™ long-pulse Nd:YAG 1064-nm laser (Dualis SP; Fotona, Ljubljana, Slovenia) with topical 5% amorolfine nail lacquer in onychomycosis in order to evaluate the efficacy of these noninvasive therapies on onychomycosis was conducted. Patients included in the study had dystrophic nails clinically consistent with onychomycosis, confirmation of onychomycosis by a positive culture, a direct smear, or both and should not have received topical antifungal medications within 3 months nor any systemic antifungal medications within 6 months. A total of 31 patients with 96 affected nails (28 fingernails and 68 toenails) completed the trial. Subjects in group one were treated with long pulse Nd:YAG 1064-nm laser (Fotona) by using these following parameters: 35~80 J/cm² (applied fluence), 35 ms (pulse duration), 4 mm spot size, and 1 Hz frequency. The entire nail

plate in all 10 fingernails or 10 toenails were treated with 3 passes for each session and four sessions were executed once a week. Patients in this group underwent two courses (each course was separated by interval of 4 weeks) of treatment. Subjects in group II were treated with topical application of 5% amorolfine nail lacquer twice a week for 12 weeks. There was no significant difference in the recovery result between both groups after 6 months with $\geq 90\%$ newly grown nail with negative fungal examination in 7 nails (11.1%) in laser group and 6 nails (18.1%) in amorolfine group.

DLSO responded better than other clinical forms ($p < 0.05$) while great toenail, and patients with concomitant tinea pedis showed worse response to the laser treatment ($p < 0.05$). The authors suggest that long pulse Nd:YAG laser is equivalent to topical nail lacquer alone for onychomycosis and produces satisfactory results.

Efficacy and safety of tavaborole topical solution, 5%, a novel boron-based antifungal agent, for the treatment of toenail onychomycosis: Results from 2 randomized phase-III studies.

Elewski BE, Aly R, Baldwin SL, González Soto RF, ich P, Weisfeld M, Wiltz H, Zane LT, Pollak R. *J Am Acad Dermatol*. 2015; 73:62-9.

Tavaborole topical solution, 5% is a novel, boron-based pharmaceutical approved by the Food and Drug Administration (FDA) in July 2014 for the treatment of toenail onychomycosis caused by *Trichophyton rubrum* and *T. mentagrophytes*. Tavaborole targets fungal cytoplasmic leucyl-transfer ribonucleic acid (tRNA) synthetase, essential for protein synthesis. It has broad-spectrum antifungal activity and more than 1000-fold greater selectivity for the fungal leucyl-tRNA synthase than the mammalian leucyl-tRNA synthetase. Two phase-III, multicenter, randomized, double-blind, vehicle-controlled, parallel-group trials of identical design were conducted: 1 at 27 sites in the United States and Mexico from December 2010 to November 2012 (study 1; NCT01270971) and the other at 32 sites in the United States and Canada from February 2011 to January 2013 (study 2; NCT01302119). Patients 18 years of age or older with distal subungual toe nail onychomycosis involving 20% to 60% of at least 1 target great toenail (TGT)

were eligible if they had a positive potassium hydroxide (KOH) wet mount and positive culture for dermatophytes, greater than or equal to 3-mm clear nail measured from the proximal nail fold to the most proximal visible mycotic border, and distal TGT thickness 3 mm or less. Eligible patients were randomized 2:1 to receive tavaborole or vehicle, and applied study treatment to the TGT and all other affected toenails once daily for 48 weeks. The primary efficacy end point was complete cure of the TGT defined as completely clear nail and negative mycology at week 52. Secondary end points included completely or almost clear nail of the TGT, negative mycology of the TGT, and completely or almost clear nail plus negative mycology, each determined at week 52. Tavaborole was significantly more effective than vehicle for all primary and secondary efficacy end points, and produced higher rates of negative culture and negative KOH at week 52 versus vehicle. A significantly greater proportion of patients achieved complete cure of the TGT at week 52 with tavaborole versus vehicle in study 1 (6.5% vs 0.5%; $P = .001$) and study 2 (9.1% vs 1.5%; $P < .001$). In conclusion, these studies demonstrate that tavaborole, a novel, first-in-class; boron-based pharmaceutical approved by the FDA for the treatment of toenail onychomycosis, has a favorable benefit-risk profile and is an attractive option for the treatment of onychomycosis of the toenail as a result of dermatophytes.

Efficacy and Safety of Calcipotriol/Betamethasone Dipropionate Ointment for the Treatment of Trachyonychia: An Open-Label Study.

Park JM, Cho HH, Kim WJ, Mun JH, Song M, Kim HS, Ko HC, Kim BS, Kim MB. *Ann Dermatol.* 2015; 27: 371-5.

A prospective open-label study was conducted to evaluate the efficacy and safety of an ointment consisting of calcipotriol plus betamethasone dipropionate for the treatment of trachyonychia. Forty seven patients with trachyonychia were enrolled after ruling out other nail disorders and onychomycosis. Patients applied the calcipotriol plus betamethasone dipropionate ointment (Daivobet; LEO Pharma A/S, Ballerup, Denmark) once daily onto the proximal nail fold without occlusion for 6 months. Among the 47 total patients, 39 (83.0%) patients with total of 432 nails completed the

6-month study. At baseline, 30 (6.9%), 147 (34.0%), and 255 (59.0%) patients were in stage II (moderate roughness), III (marked roughness), and IV (severe roughness), respectively. At the end of treatment, 18 (4.2%) nails achieved complete remission and 94.4% (408/432) of the nails achieved partial remission. Of the nails with partial remission, 195 (45.1%), 131 (30.3%), and 88 (20.3%) were in stage I, II, and III, respectively. The mean±standard deviation physician global assessment score decreased significantly from baseline to the end of treatment ($3.5±0.8$ to $1.7±0.9$, respectively, $p<0.05$). The limitations of this study were that fungal cultures were performed only for patients who had clinical signs suggestive of dermatophytes or candidal onychomycosis and there is no data about recurrence or conditions after treatment cessation. The authors concluded **that topical calcipotriol/betamethasone ointment is an effective and safe treatment for trachyonychia that can be used as monotherapy.** Further double-blinded and placebo-controlled studies are required to confirm the effectiveness of calcipotriol/betamethasone ointment for the treatment of trachyonychia.

Dermoscopy of nail fold and elbow in the differential diagnosis of early psoriatic arthritis (sine) psoriasis and early rheumatoid arthritis.

Errichetti E, Zabotti A, Stinco G, Quartuccio L, Sacco S, De Marchi G, Piccirillo A, De Vita S.J *Dermatol.* 2016 May 30.

This study was aimed to investigate possible dermoscopic differences in vascular appearance of nail fold and elbow (a classic site of repeated trauma) in psoriatic arthritis (PsA) and rheumatoid arthritis (RA). Fifteen patients with PsA without psoriasis, 12 patients with RA and 12 controls were included in the study. The nail fold vascular appearance was studied. The presence of diffuse reddish background with or without sparse dotted vessels was significant in the PsA, whereas the evidence of parallel dotted/short linear vessels ("fish school-like" pattern) or irregular/ramified, blurry, purple vessels were significant in RA. None of these patterns were detected in the control group. Regarding the elbow, the pattern significantly associated with PsA consisted of diffusely distributed, red, dotted vessels. On the other hand, RA patients and

controls displayed similar dermoscopic findings, with three possible vascular patterns being observed: (i) irregular, blurry, purple vessels; (ii) avascular appearance; and (iii) sparse, dotted, purple vessels. In conclusion, **dermoscopy may be a useful supportive tool for differentiating early PsA without psoriasis from RA.**

Dermoscopy and Onychomycosis: guided nail abrasion for mycological samples.

Bet DL, Reis AL, DiChiacchio N, Belda Junior W. An Bras Dermatol. 2015; 90:904-6.

It is known that sample for mycological examination of onychomycosis should be performed at the most proximal portion of the nail lesion, where there is a higher probability to find the fungus responsible for the nail invasion. However it may be uncomfortable and even painful for the patient, because it requires progression of instruments under the nail plate. Localized abrasion is a technique that allows obtaining suitable material of the proximal part of the lesion through a vertical piercing on the nail plate, with little or no discomfort for the patient. This case demonstrates the utility of dermoscopy to guide local abrasion to obtain better quality samples. Dermoscopy in a 58 year-old female patient with two previous negative mycological tests showed an irregular longitudinal white streaked pattern with a yellowish central spike, suggestive of onychomycosis. A vertical perforation was done with an electric drill at this central spike until the local resistance decreased and the nail became brittle. Sample collected from this site showed hyaline septate hyphae on direct examination with KOH. On culture, *Trichophyton rubrum* was seen confirming the diagnosis of onychomycosis. **Thus, dermoscopy can be a useful tool to locate the best proximal site for mycological sampling thru abrasion.**

Nail disorders in older people, and aspects of their pharmaceutical treatment.

Murdan S. Int J Pharm. 2016; pii: S0378-5173(16)30402-1. doi: 10.1016/j.ijpharm.2016.05.022

Changes in the nail due to aging can be inherently due to old age or due to other concomitant diseases common in old age. Some of the changes are alterations in the nail plate's colour, contour, thickness, fragility, sur-

face features, cell size, chemical composition and growth rate with toenails and fingernails showing different effects. The incidence of onychomycosis and brittle nails is considerably higher in older people. The literature about aging and the incidence of nail psoriasis is inconclusive, although, it is clear that as one gets older, the negative impact of nail psoriasis on one's quality of life decreases. Pharmaceutical treatment of the diseases comprises local and systemic therapies, sometimes in combination. Systemic therapies have the inherent disadvantages of adverse systemic effects, drug interactions and the need for monitoring, disadvantages which are especially problematic for older people who are more likely to suffer from co-morbidities and be on other medications. Topical therapy avoids such disadvantages. However, the success rates of commercially available preparations are low, and older people may need help with their application. It is also proposed that **regular inspection and grooming of nails should become part of routine care of older people, as these would provide opportunities to identify and treat any problems at an earlier stage.**

Compiled by

Dr. Sushruta Kathuria

Specialist, Deptt of Skin & STD,

VMMC & Safdarjung Hospital, New Delhi.



NAIL'S TALE



Dr B Srinivas, Chennai

*'My name is nail
I grow like the snail
I am your finger guard
And am pretty hard
I get you a grip
And let you rip
When it comes to scratch
I am yet to meet my match
Take a look at me
There is not much to see
Yet I'm a screen to project*

*Many a bodily defect
When I resemble a club
There is trouble with lub & dub
I may look like a spoon
And of half the moon
When I am white
Anaemia is in sight
As I turn yellow
Lung disease will follow
I turn red green or blue
To give the doctor a clue
About many a dermatoses
Poisons and mycoses
With lots of pit
It's Psoriasis you bet!
A glance and Doc will tell
If one is ill or well
I like manicure, pedicure & filing
Especially when I am not ailing
Painting me is in fashion
And many a woman's passion
Docs, take a good look
You can read me like a book!
A sure way to fail
Is to ignore the nail!*

5th ONYCHOCON

Annual National Conference of Nail Society of India (NSI)

17-18th December, 2016

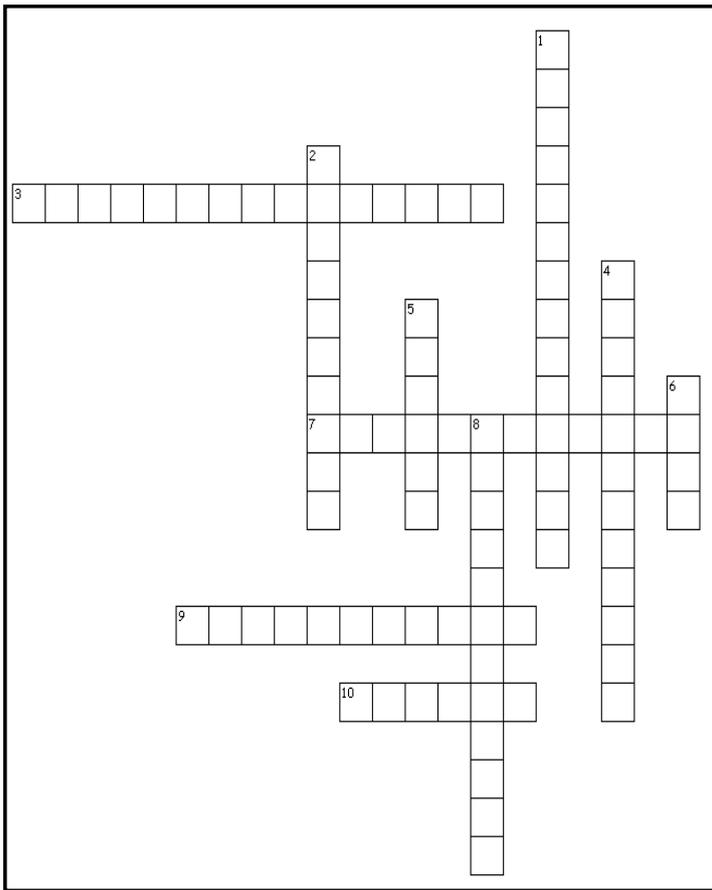
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NAIL MAZE



Across

3. Excessive thickening with increased curvature of nail plate is called as.
7. Accelerated nail growth and longitudinal beading seen with this antifungal.
9. Most abundant lipid in nails.
10. Micronychia seen in this syndrome which is specific in short statured females.

Down

1. Shell nail syndrome is associated with this ILD.
2. Extension of proximal nail fold on nail plate.
4. Most effective systemic drug in psoriatic nail disease.
5. This triad of nails seen in psoralen induced photo onycholysis.
6. These lines in nails are seen in Arsenic poisoning.
8. Most prominent band in acrocyanosis.

Compiled by

Dr. Khushbu Mahajan, Assistant professor,
NDMC medical college & Hindu Rao Hospital, Delhi.

Acknowledgement: **Dr. Sukriti Sharma**
DNB student, Hindu Rao hospital, Delhi

Please mail your answers to nailsocietyofindia@gmail.com. Prize winners will be announced in the next issue of Onychoscope.

Solution to the nail maze from Onychoscope Vol. 5, Issue 1, January 2016

NAIL MAZE

Across

2. excavation in distal nail in a triangular pattern
5. thick nails
6. idiopathic hypertrophic osteoarthropathy
9. leuko-onycholysis paradermatitica
10. pretibial myxoedema, exophthalmos, finger clubbing

Down

1. increased local expression of this AMP in nail
3. drug that causes red or purple discolouration of nails
4. drug that causes faster nail growth
7. median nail dystrophy
8. long nails
9. hardness of nails is due to this mineral

And the winner are!

- **Tanvi Gupta**
- **Himanshu Gupta**

Corrigendum for Answer to Nail Maze (Vol. 4, Issue 2, July 2015)

Dr. SM Qazi, Gurbinder Banga, Amit Kumar Dhawan, Prashansa Jaiwal, Kenit Ardesna had also submitted the correct entry

Answer to Photo Quiz

Diagnosis: Subungual wart

Subungual warts are asymptomatic benign fibroepithelial tumors caused by Human papilloma virus, commonly by HPV-1, 2 and 4. They present with a rough keratotic surface and are contagious. More frequently they are seen at the lateral aspect of proximal nail fold, but it's not uncommon to find them on hyponychium. From there, they grow slowly to involve the nail bed, finally elevating the nail plate. Bony erosions resulting from warts have been reported.

Differential diagnoses includes acquired digital fibrokeratoma, subungual keratoacanthoma, squamous cell carcinoma and subungual corn.

Onychoscopy shows a rough keratotic surface with thrombosed blood vessels seen as reddish-brown or black dots and/or dilated vessels. Onychoscopy can also provide a clue regarding the extent of wart below the nail plate.

Treatment strategies: Treatment of unguinal warts can be disappointing because of recurrence. Options include topical trichloroacetic acid, imiquimod, cantharidin, 5-fluorouracil and silver nitrate. Intralesional bleomycin 1mg/ml is an effective technique and we preferred it in our patient. We used multiple puncture technique to minimize the side effects. Other treatment modalities which have been tried include paring, cryosurgery, electrodesiccation, CO₂ laser, pulse dye laser, photodynamic therapy. Oral immune modulators like zinc sulphate (10mg/kg/day) and cimetidine can be added as an adjuvant. Consistent follow-up is however necessary even after successful therapy to ensure complete disappearance.



Dr. Deepak Jakhar
Post Graduate Student
UCMS & GTBH

Important Announcement

5th ONYCHOCON 17-18th december 2016
Jaipur, Rajasthan

Editorial Board Members



Dr Archana Singhal



Dr Chander Grover



Dr Shikha Bansal