Yellow Nail Syndrome

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Described in adults by Samman and White in 1964 [1], the yellow nail syndrome (YNS) presents as a triad: yellow nails, lymphedema, and pleural effusions [2].

Yellow Nails

1. Systemic drugs such as bucillamine, gold, methotrexate, penicillamine, and tiopronin are possibly associated with YNS [3]. A thorough drug history should be available for potential drug association followed by discontinuation of the offending agent.
2. Exposure to titanium dioxide (found in foods, personal care items, medications, dental and surgical devices [4]) is associated with YNS and has been detected in the nails [5].
3. Association with a paraneoplastic disease is still controversial, and some consider it a coincidental event. The YNS-to-cancer-diagnosis interval ranges from days to years, with gradual development of the complete YNS triad.

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Various types of cancers have been associated with YNS such as the following:

Breast	Melanoma
Bronchial carcinoma	Multiple myeloma after hematopoietic stem cell transplantation
Endometrium	Non-Hodgkin lymphoma
Gallbladder	Renal cell carcinoma
Larynx	

Yellow nails are the main clinical manifestation (88% of the cases) leading to YNS diagnosis. However, the time between the first clinical sign and nail discoloration hinders affirmation of the YNS diagnosis. Early in the YNS course, YNS is more frequently associated with pleural effusion and lymphedema than in patients with drug-related YNS.

Xanthonychia is unsightly and varies from pale yellow (Fig. 1.1) to a more or less dark (Fig. 1.2) and greenish color.

The nail plate becomes thickened with enhanced transverse overcurvature, sometimes with a notable hump and cross-ridging with a hard (″Scleronychie″ syndrome of German authors) and difficult-to-trim nail plate. Onycholysis may be followed by nail shedding.

The cuticle may disappear leading to erythema of the proximal nail fold causing a chronic paronychia. The lunula is no longer visible due to nail hyperkeratosis. Interestingly, the nail grows half as fast and twice as thick.

The color of the nail is due to lipofuscin, a pigment arisen from colorless lipid precursors and

R. L. Baran (ed.), *Advances in Nail Disease and Management*, Updates in Clinical Dermatology,
https://doi.org/10.1007/978-3-030-59997-3_1

Fig. 1.1 Pale yellow nails in YNS

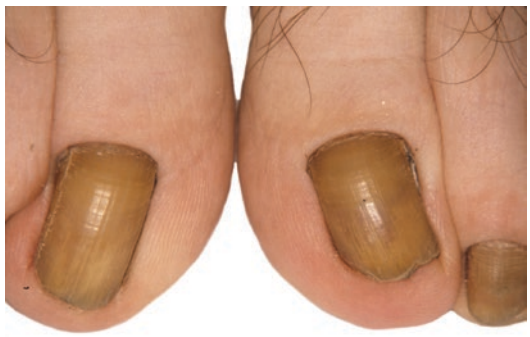

Fig. 1.2 Dark yellow nails in YNS

transformed by oxidation in tissue to produce varying degrees of yellow.

Contrasting with xanthonychia of the YNS that often improves without specific therapies [6] *in about one-half of patients but may relapse, the other varieties of yellow nails are transient* [7].

Specific investigations should be performed:

Rule out nail fungal or *Pseudomonas* infection
Complete blood count
Urinalysis and evaluation of proteinuria
Immunoelectrophoresis
Thyroid-stimulating hormone
Waaler-Rose test for serum rheumatoid factors
Chemistry profile with blood creatinine
Sinus and chest radiography and CBCT
Ear, nose and throat and pulmonary investigations
Liver enzymes and alkaline phosphatases

If the YNS is restricted to nail involvement, the following treatment algorithm should be considered:

- Fluconazole 300–400 mg weekly, associated with alpha-tocopherol (1000u daily) for best results.
- Intra-matrix triamcinolone once per month especially if there is a chronic paronychia.
- Zinc (300 mg/day) may be effective.
- Clarithromycin 300–400 mg daily.

These treatments can be in addition to those used for lymphedema and respiratory disorders.

Lymphedema

Lymphedema is observed in approximately 40% of cases and involves mainly the lower limbs. The face is rarely affected and the eyelids are only exceptionally. The most distal body parts are always more severely affected than proximal parts. Characteristic of lymphedema is the disproportion between lymphatic fluid and the capacity of lymphatic vessels. Stemmer's sign that shows the inability to pinch the skin on the dorsal side or the base of the second toe is pathognomonic.

Manuel lymphatic drainage on each leg for 45 minutes daily followed by placement of a multilayer compression bandage on each leg induced a slight improvement after 1–3 weeks of treatment followed by a compressive garment to stabilize lymphedema volume. In some cases, addition of a low-pressure compression pump may be useful [8, 9].

In cases refractory to conservative management, surgery has been proposed for moderate cases using excision of edematous subcutaneous tissue down to the muscle fascia with skin flaps used as closure. For severe and rare cases, resection of all edematous tissue to muscle fascia with skin grafting taken from the excised tissue has given good results [3].

Respiratory Disorders

The most common respiratory manifestations of YNS are, in descending order, chronic cough, bronchiectasis, pleural effusion, recurrent pneumonia, and restrictive lung disease (mainly due to the presence of a pleural effusion).

Acute or Chronic Rhinosinusitis

Acute and chronic rhinosinusitis are very common and present with daily mucopurulent rhinorrhea, nasal obstruction, and frequent postnasal drip. Acute sinusitis is treated with antibiotics such as *amoxicillin*, *clavulanate* (1.5–3 g/day), *doxycycline* (200 mg/day), or *fluoroquinolone* (levofloxacin 500 mg/day, moxifloxacin 400 mg/day); a surgical procedure such as *meatal antrostomy* may be necessary.

Pulmonary Manifestations

Chronic cough is certainly the most common pulmonary manifestation. *Physiotherapy* training helps patients self-manage their chronic expectoration [6].

Pleural effusions are bilateral in 68.3%. The appearance of the fluid is serous in 75%, milky (chylothorax) in 22%, and purulent (empyema) in 3.5%. Pleural effusions were described as an exudate in 95% and transudate in 5%. For nonmalignant effusion, *tetracycline* is the most practical option.

OK-342 [10], a hemolytic streptococcal preparation treated with penicillin, has been used successfully in Asia. Octreotide 30 mg, once a month, and lanreotide have generated positive response.

Pleural effusions and lymphedema, refractory to conservative management, can be treated with more invasive procedures: chemical pleurodesis, "PleurX® catheter," and pleurovenous shunt all appear to be most effective [11].

Bronchiectasis

Chest CT scan is the best tool for examination. Management includes antibiotics and bronchodilators. Antibiotics used are azithromycine 250 mg × 3 times weekly or clarithromycin 400–600 mg/day for some years.

Recurrent Pneumonia

Vaccinations against flu and pneumococci are highly recommended. Bilateral apical fibrosis and patchy alveolar disease are rarely encountered.

Pulmonary function studies are usually normal or may show a moderate-to-severe restrictive syndrome owing to pleural effusions.

YNS in Children

Pediatric forms of YNS are rarely reported [12]. YNS may be congenital (present at birth) or develop before the age of 10 years. Familial forms of YNS have very rarely been described, affecting two siblings or a family with eight cases in four sibships over two generations. There are very few reported familial cases which mimic a dominant inheritance pattern, but they have not been supported by any genetic evidence. In very rare cases, YNS may be associated with intellectual disability or fetal hydrops, suggesting a more complex syndrome [13].

References

1. Samman PD, White WF. The "Yellow nail" syndrome. Br J Dermatol. 1964;76:153–7.
2. Vignes S, Baran R. Yellow nail syndrome: a review. Orphanet J Rare Dis. 2017;12:42.
3. Mishra AK, George L. Yellow nail syndrome in rheumatoid arthritis: an aetiology beyond thiol drugs. Oxford Med Case Rep. 2016;3:37–40.
4. Berglund F, Cazlmark B. Titanium, sinusitis and the YNS. Biol Trace Elem Res. 2011;143:1–7.
5. Decker A, Doly D, Scher RK. Role of titanium in the development of YNS. Skin Appendage Disord. 2015;1:28–30.

6. Maldonado F, Tazelaar H, Wang C-W, et al. Yellow nail syndrome. Analysis of 41 consecutive patients. Chest. 2008;134:375–81.
7. Chiriac A, Naznean A, Podoleanu C, Stolnicu S. Transient yellow discoloration of the nails for differential diagnosis with yellow nail syndrome. Orphanet J Rare Dis. 2017;12(1):article 159.
8. Szolnoky G, Lakatos B, Husz S, et al. Improvement in lymphatic function and partial resolution of nails after complex decongestive physiotherapy in yellow nail syndrome. Int J Dermatol. 2005;44:501–3.
9. Polat AK, Dang HT, Soran A. YNS treatment of lymphedema using low pressure compression. Lymphat Res Biol. 2012;10(1):30–2.
10. Yamagishi T, Hatanaka N, Kamemura H, et al. Idiopathic yellow nail syndrome successfully treated with OK-432. Intern Med. 2007;46:1127–30.
11. Kurin M, Wiesen J, Mehta AC. Yellow nail syndrome: a case report and review of treatment options. Clin Respir J. 2017;11:405–10.
12. El Alami J, Galicier L, Huynh S, Frumholtz L, Bagot M, de Masson A, Vignes S, Bouaziz JD. Congenital yellow nail syndrome presenting with eyelid lymphedema and fetal hydrops. JAAD Case Rep. 2019;5:1010–2.
13. Nanda A, Al-Essa FA, El-Shafel WM, Alsaleh QA. Congenital yellow nail syndrome: a case report and its relationship to nonimmune fetal hydrops. Pediatr Dermatol. 2010;27(5):533–4.