Case Report

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A 9-Year-Old Patient with Yellow Nail Syndrome

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ABSTRACT

Yellow nail syndrome (YNS; OMIM 153300, ORPHA662) is a rare disorder that almost always occurs after 50 years of age, but juvenile or familial forms have been observed. It is characterized by the triad of typical yellow nail discolorations, lower limb lymphedema, and pulmonary manifestations like chronic cough, bronchiectasis, and pleural effusion. It may also be associated with autoimmune diseases, cancer, and other rare lymphatic disorders such as lymphedema-distichiasis syndrome or primary intestinal lymphangiectasia. We present the case of a nine-year-old boy with YNS and congenital onset of lymphedema of the lower left limb and foot. Since the age of 4, additional lymphedema on the right leg was diagnosed after several episodes of acute cellulitis. Yellow discoloration of the nail-plates of both thumbs and the feet appeared between age 4 to 5 years. So far, no pulmonary affections were observed. However, congenital adhesions of the tear canal were found. Despite the fact that most cases of YNS become apparent only after 50 years of age, this case demonstrates that early onset, even at birth, is possible. Presence of lymphedema at birth should trigger close follow-up to detect further alterations associated with YNS to ensure early and effective treatment of this syndrome.

Keywords: Lymphedema; Nail Discoloration; Yellow Nail Syndrome; Tear Duct Obstruction

Case Presentation

We report the case of a nine-year-old boy who was admitted to our clinic for the first time in October 2020 and again in May 2022 to our clinic. Detailed medical history revealed the presence of a most likely congenital lymphedema on the left lower limb and foot. Lymphedema of the right leg was diagnosed for the first time in April 2018, together with cellulitis of the right leg. It is noteworthy that cellulitis occurred several times before the initial lymphedema diagnosis. Repeated clinical, and abdominal and lung ultrasound exams did not reveal any additional pathological findings except for marginally increased lymph nodes in both groins. In July 2015, the patient underwent magnetic resonance tomography (MRT) of the legs demonstrating an increase of subcutaneous tissue associated with the known lymphedema but no other pathological findings. Discoloration of the nails on both thumbs and the feet were described for the first time in 2016. Together with the presence lymphedema of the lower limbs the diagnostic criteria for Yellow Nail Syndrome (YNS) were fulfilled [1]. Other causes of YNS including exposure to chemical agents such as titanium dioxide, or anti-rheumatic drugs, Candida-, Aspergillus- or dermatophyte-caused nail mycosis or planus lichen, psoriasis, alopecia areata, chronic paronychia, onychogryphosis and acquired pachyonychia were ruled out [2].

On his last admission to our institution, the patient presented in an age-appropriate general and nutritional state. He is known for constitutional dwarfism (127 cm, 27.4 kg [10th percentile]). No abnormalities in the head and neck region, and no pathologically enlarged peripheral lymph nodes were found. Cardiac, pulmonary, and abdominal findings were unremarkable. Furthermore, no orthopaedic or neurological abnormalities were found. The toenails were noted to have a yellowish discoloration (Figure 1). There was moderate soft

connective tissue volume increase of both thighs, predominantly on the left side with bulbous distension, which was found interspersed with connective tissue and only sparse pitting edema. Stemmer's skin fold sign on his left foot was positive. On the right lower leg, connective tissue volume was visible with only sparse pitting edema, moderate decontouring of the upper ankle joint and cushion-like collection of connective tissue in the dorsal region of the right foot. Stemmer's skin fold sign was positive with box toe deformity and widening of the dorsal toe skin fold (Figure 2).

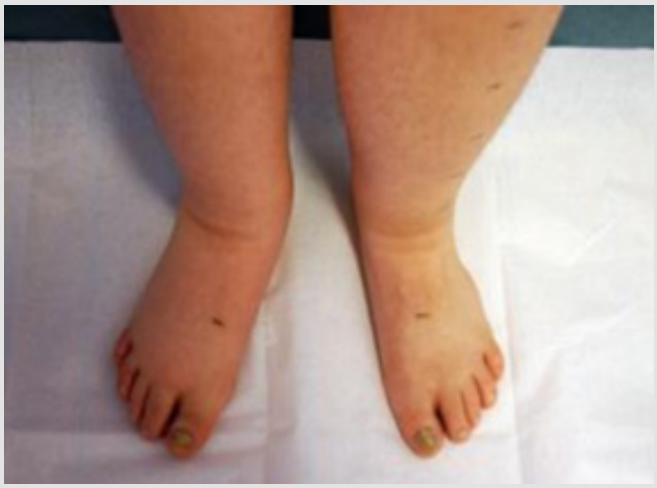

Figure 1: Typical nail discoloration in a 9-year-old boy with Yellow Nail Syndrome.

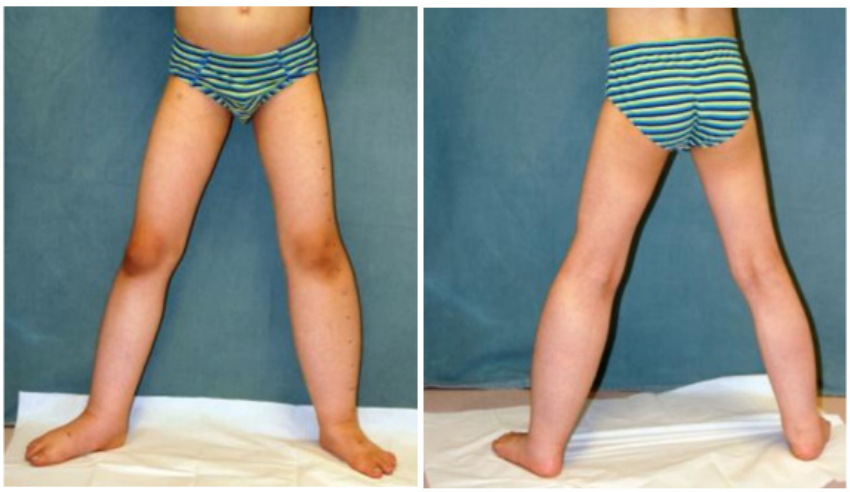

Figure 2: Lymphedema of lower limbs in a nine-year-old patient with Yellow Nail Syndrome.

Complete obliteration due to an adhesion of walls of the tear ducts on both sides was detected at the time birth. So far, neither distichiasis nor conjunctival changes or facial lymphedema have occurred. We initiated complex decongestive therapy with the aim of lymphedema volume reduction and improvement of fibrosis. This consisted of daily administration of low-stretch bandages, manual lymphatic drainage twice daily and specific skin care to both legs and feet. This was complemented by physical exercise. In addition, the patient and the accompanying parent were instructed with regards to self-treatment and self-bandaging that need to be performed on a regular basis at home together with continuing lymph therapy performed by an experienced lymph therapist. So far, the patient has not complained about pain or onycholysis associated with signs and symptoms of YNS and, at least for the moment, is not disturbed by the discoloration of the nails. Therefore, no medical treatment was initiated, in particular no oral vitamin E substitution [2].

Discussion

Yellow Nail Syndrome (YNS; OMIM 153300, ORPHA662) is a rare disease that comprises a clinical trial of yellow nails, lymphedema, and respiratory tract involvement. It was first reported by Heller in 1927 [3]. In 1964, Samman & White described a series of 13 patients, aged 25-65 years, who demonstrated abnormal nail-plate discolorations ranging from pale yellow to dark greenish associated with lymphedema [4]. Pleural effusion was added as a third diagnostic criterion by Emerson in 1966 [5].

Diagnosis

Among the three clinical YNS characteristics (yellow nail syndrome, respiratory tract involvement, lymphedema), only two are required to diagnose YNS [2]. However, these components are only present in 27-60% of the patients and may appear individually and sequentially [1,3-7].

Nail Discoloration

The most important clinical characteristic of the YNS is nail discoloration varying from pale yellow to dark green together with thickening of the nail plate making the nails very hard. There is a disappearance of the lunula because of nail hyperkeratosis and disappearance of the cuticle [8]. These alterations result in longitudinal nail growth that is half that of a normal nail and nail thickness that is double of that of a normal nail [9,10].

Pulmonary Manifestations

Respiratory tract involvement occurs in 56-71% of cases [4-6]. The most common lung conditions with YNS are chronic cough in 56% and pleural effusion in 14-46% of the patients [4,5]. Valdés et al. reported that 68,3% of pleural effusion were bilateral, serous in 75% and milky (chylothorax) in 22% and generally rich in proteins (exudates) [11]. Bronchiectasis is seen in 44% [12]. Further pulmonary manifestations associated with YNS include chronic sinusitis (41%), bronchitis, and recurrent pneumonias (22%) [4,6,11-13].

Lymphedema

Lymphedema occurs in 29-80% of the patients with YNS [4-6]. In one third of the patients, it is the first manifestation [4-6]. Lymphedema is typically located bilaterally in the lower limbs, below the knee, and clinically does not differ from primary lymphedema [5,6,13]. Lymphedema can also involve the arms or the face [12]. The excess lymph accumulation leads to a fibroblast stimulation with a consecutive fibrosis [14,15]. As a pathognomic sign of lymphedema, Stemmer's skin fold sign is positive and pitting edema can be found in the lower limb [16]. Cellulitis is the most important complication in lymphedema and associated with worsening of the edema [16].

Pathogenesis

The pathogenesis of YNS is incompletely understood. Less than 400 cases have been published and the prevalence is estimated 1:1.000.000 [2]. Mainly individuals over 50 years of age are affected and there is no sex predominance [3-5]. YNS in children is only rarely described [17-25]. In these cases, clinical manifestation can be congenital or develop during childhood. Very few reported familial cases are reported with a suspected genetic cause but could not be proven until now [3]. With the majority of evidence stemming from case reports and only very few clinical studies available, the etiology of YNS continues to remain unclear. It was hypothesized that either innate or acquired lymphatic impairment may be the cause of lymphedema and pleural effusion. This notion is based on the observation of a high rate of lymphatic morphological abnormalities and reduced regional nodal tracer uptake in patients with YNS [26,27]. Defective lymphatic drainage may be responsible for the sclerosis of the nail matrix tissue in the presence of ectatic lymphatic vessels explaining the thickening and slow growth of the nails observed in YNS [17,28]. However, other authors have attributed the clinical findings of YNS to protein leakage due to microvasculopathy rather than functional lymphatic impairment [29]. Recent publications point to a role of titanium, in particular titanium dioxide, stemming from titanium implants such as inlays, crowns or joint implants, food (e.g. chewing gum), or cosmetics such as sunscreen, shampoo or toothpaste. On the other hand, despite autopsy findings of titanium in liver, spleen, lymph nodes, and the lung, there was no detectable association with YNS [2].

Molecular Genetics of YNS

Finegold and colleagues identified a mutation in the FOXC2 gene in affected members of a family with lymphedema-distichiasis syndrome [30]. However, none of the patients were reported as having yellow nails. On the other hand, the same mutation was found in 7 affected members of another family with lymphedema-distichiasis syndrome, with 3 patients having yellow nails. Although these findings indicate a phenotypic overlap between lymphedema-distichiasis syndrome and lymphedema-YNS, the phenotypic classification of autosomal dominant lymphedema does not appear to reflect the underlying genetic causation of these disorders, as they may be allelic [30]. Rezaie and colleagues suggested that lymphedema with yellow nails is not a distinct disorder but rather in the spectrum of lymphedema-distichiasis syndrome [31]. Despite the fact that 6 of the 7 patients in the family reported to having yellow-nail syndrome and also had distichiasis characteristic of the lymphedema-distichiasis syndrome, no FOXC2 mutations was were found in 4 additional families with lymphedema and yellow nails, leading to the view that yellow discoloration of the nails is not uncommon with lymphedema but does not necessarily indicate a diagnosis of so-called 'yellow nail syndrome,' in which the nail changes are very specific [30].

Therapeutic Approaches

Improvement of the frequently unaesthetic nail appearance together with the associated pain, which at least in part is due to onycholysis, may be the primary goal in patients with YNS. Treatment is based on systemic or topical administration of vitamin E [32,33]. Although YNS is not caused by fungi, antifungals have been used to treat this condition [34]. The treatment of pulmonary manifestations depends on the underlying pathological changes and includes physiotherapy and antibiotic therapies where needed. Vaccinations against flu, Covid-19, and pneumococci are strongly recommended. The treatment of lymphedema is based on the complex decongestive therapy as described by Földi, et al. [16].

Summary and Conclusion

The Yellow Nail Syndrome is a very rare entity of nail discoloration, lung manifestation or sinusitis and lymphedema. It is mostly isolated but can also be associated with other diseases such as autoimmune diseases, immunodeficiencies or cancers or can be induced by drugs [2]. In the case of our nine-year-old patient we only found congenital lymphedema on both legs and the typical nail alterations but no manifestations in the respiratory system. Treatment of his lymphedema is currently sufficient for symptom relief and prevention of skin infections. At this stage the patient does not wish for treatment of the nail discolorations with vitamin E. Our patient demonstrates an unusual finding i.e. bilateral tear duct occlusion due to adhesion of the walls of the duct. Only one further case in a patient with YNS and involvement of the tear ducts could be identified in an extensive literature search [35]. In this patient, obstructed palpebral puncta and invisible orifices were found. In this case report we describe a further tear duct obstruction resulting from adhesion of the tear duct walls. Given the sparsity of evidence on YNS, further research is required to better understand, diagnose and treat this rare syndrome.

Conflicts of Interest Related to this Publication

- Ulrike Walz-Eschenlohr: None.
- Susan Witt: None.
- Thomas Dieterle: None.

References

1. Pavlidakey GP, Hashimoto K, Blum D (1984) Yellow nail syndrome. J Am Acad Dermatol 11: 509-512.
2. Vignes S, Baran R (2017) Yellow nail syndrome: a review. Orphanet J Rare Dis 12: 42.
3. Hoque SR, Mansour S, Mortimer PS (2007) Yellow nail syndrome: not a genetic disorder? Eleven new cases and a review of the literature. Br J Dermatol 156: 1230-1234.
4. Maldonado F, Tazelaar HD, Wang CW, Ryu JH (2008) Yellow nail syndrome: analysis of 41 consecutive patients. Chest 134: 375-381.
5. Piraccini BM, Urciuoli B, Starace M, Tosti A, Balestri R (2014) Yellow nail syndrome: clinical experience in a series of 21 patients. J Dtsch Dermatol Ges 12: 131-137.
6. Nordkild P, Kromann-Andersen H, Struve-Christensen E (1986) Yellow nail syndrome-the triad of yellow nails, lymphoedema, and pleural effusions. A review of the literature and a case report. Acta Med Scand 219: 221-227.
7. Varney VA, Cumberworth V, Sudderick R, Durham SR, Mackay IS (1994) Rhinitis, sinusitis and the yellow nail syndrome: a review of symptoms and response to treatment in 17 patients. Clin Otolaryngol Allied Sci 19: 237-240.
8. Baran R (1978) Pigmentations of the nails (chromonychia). J Dermatol Surg Oncol 4: 250-254.
9. Samman PD, White WF (1964) The yellow nail syndrome. Br J Dermatol 76: 153-157.
10. Moffitt DL, de Berker DA (2000) Yellow nail syndrome: the nail that grows half as fast grows twice as thick. Clin Exp Dermatol 25: 21-23.
11. Valdés L, Huggins JT, Gude F, Ferreiro L, Alvarez-Dobaño JM, et al. (2014) Characteristics of patients with yellow nail syndrome and pleural effusion. Respirology 19: 985-992.
12. Douri T (2008) Yellow nail syndrome in two siblings. Dermatol Online J 14: 7.
13. Paradisis M, Van Asperen P (1997) Yellow nail syndrome in infancy. J Paediatr Child Health 33: 454-457.
14. Szuba A, Rockson SG (1998) Lymphedema: classification, diagnosis and therapy. Vasc Med 3: 145-156.
15. Zampell JC, Aschen S, Weitman ES, Yan A, Elhadad S, et al. (2012) Regulation of adipogenesis by lymphatic fluid stasis: part I. Adipogenesis, fibrosis, and inflammation. Plast Reconstr Surg 129: 825-834.
16. (2010) In: Földi M, Földi E, Kubik S (Eds.)., Lehrbuch Lymphologie: Für Ärzte, Physiotherapeuten und Masseure/med. Bademeister (7th Edn.)., Urban & Fischer in Elsevier.
17. Magid M, Esterly NB, Prendiville J, Fujisaki C (1987) The yellow nail syndrome in an 8- year-old girl. Pediatr Dermatol 4: 90-93.
18. Göçmen A, Küçükosmanoglu O, Kiper N, Karaduman A, Ozçelik U (1997) Yellow nail syndrome in 10-year-old girl. Turk J Pediatr 39: 105-109.
19. Yalçin E, Dogru D, Gönç EN, Cetinkaya A, Kiper N (2004) Yellow nail syndrome in an infant presenting with lymphedema of the eyelids and pleural effusion. Clin Pediatr (Phila) 43: 569-572.
20. Cebeci F, Celebi M, Onsun N (2009) Non classical yellow nail syndrome in 6-year- old girl: a case report. Cases 2: 165.
21. Nanda A, Al-Essa FH, El-Shafei WM, Alsaleh QA (2010) Congenital yellow nail syndrome: a case report and its relationship to nonimmune fetal hydrops. Pediatr Dermatol 27: 533-534.
22. Siddiq I, Hughes DM (2012) Yellow nails, lymphedema and chronic cough: yellow nail syndrome in an eight-year-old girl. Can Respir J 19: 35-36.
23. Cecchini M, Doumit J, Kanigsberg N (2013) Atypical presentation of congenital yellow nail syndrome in a 2-year-old female. J Cutan Med Surg 17: 66-68.
24. Dessart P, Deries X, Guérin-Moreau M, Troussier F, Martin L (2014) Syndrome des ongles jaunes: deux cas pédiatriques. Ann Dermatol Venereol 141: 611-619.

25. Al Hawsawi K, Pope E (2010) Yellow nail syndrome. Pediatr Dermatol 27: 675- 676.

26. Marks R, Ellis JP (1970) Yellow nails: a report of six cases. Arch Dermatol 102: 619-623.

27. Bull RH, Fenton DA, Mortimer PS (1996) Lymphatic function in the yellow nail syndrome. Br J Dermatol 134: 307-312.

28. DeCoste SD, Imber MJ, Baden HP (1990) Yellow nail syndrome. J Am Acad Dermatol 22: 608-611.

29. Maldonado F, Ryu JH (2009) Yellow nail syndrome. Curr Opin Pulm Med 15: 371-375.

30. Finegold DN, Kimak MA, Lawrence EC, Levinson KL, Cherniske EM, et al. (2001) Truncating mutations in FOXC2 cause multiple lymphedema syndromes. Hum Mol Genet 10 :1185-1189.

31. Rezaie T, Ghoroghchian R, Bell R, Brice G, Hasan A, et al. (2008) Primary non-syndromic lymphoedema (Meige disease) is not caused by mutations in FOXC2. Eur J Hum Genet 16: 300-304.

32. Ayres Jr S, Mihan R (1973) Yellow nail syndrome: response to vitamin E. Arch Dermatol 108: 267-268.

33. Williams HC, Buffham R, du Vivier A (1991) Successful use of topical vitamin E solution in the treatment of nail changes in yellow nail syndrome. Arch Dermatol 127: 1023-1028.

34. Baran R, Thomas L (2009) Combination of fluconazole and alpha-tocopherol in the treatment of yellow nail syndrome. J Drugs Dermatol 8: 276-278.

35. Ayata A, Ünal M, Ersanli D, Bilge AH (2008) Ocular findings in yellow nail syndrome. Can J Ophthalm 43: 493-494.

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