Congenital yellow nail syndrome presenting with eyelid lymphedema and fetal hydrops

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INTRODUCTION

Yellow nail syndrome (YNS) is a rare disorder characterized by a triad of yellow dystrophic nails, lymphedema, and chronic respiratory manifestations.[1]

YNS often occurs in adults older than 40 years, with no sex predominance. However, few pediatric cases have been reported.[1] We describe a child having congenital YNS with several features, including congenital nail dystrophy, pleural effusion, and eyelid and lower-limb lymphedema.

Abbreviations used:

CAM: clarithromycin
YNS: yellow nail syndrome

CASE REPORT

A 14-year-old boy born to nonconsanguineous, healthy parents presented with a past history of fetal hydrops and neonatal respiratory distress. Physical examination at birth showed noticeable edema of the eyelids with bilaterally decreased breathing sounds of both lungs. Radiography showed bilateral pleural effusions, which resolved with the use of diuretics after a few weeks. During the patient's first year of life, the family described slow growth of the nails, with a progressive yellow discoloration and a lymphedema of the lower limbs. He also presented with nasopharyngitis, serous otitis, and cough associated with respiratory distress that required multiple hospital admissions. He was partially improved by physiotherapy, antibiotics, and traditional asthma treatment.

He has been presenting with 2 to 3 episodes of bronchitis per winter, which is controlled with antibiotics (amoxicillin-clavulanic acid). Respiratory function tests showed mixed obstructive and restrictive syndrome.

Lymphedema of the lower limbs was noted and classified as minimal stage I, according to the classification of the International Society of Lymphology, and evolved, with eyelid lymphedema by relapse without obvious triggering factors (Fig 1, *A* and *B*). Affected nails showed onycholysis and a yellow-green discoloration (Fig 2, *A* and *B*). Therefore, the diagnosis of YNS was established.

Additional workup was done to eliminate other causes, such as Njølstad syndrome. Additional investigation findings included normal karyotype; no microdeletions at chromosome locus 10q26.3; upper gastrointestinal endoscopy with biopsy samples, which were normal; normal metabolic workup, echocardiogram, and abdominal ultrasonography results; negative results on Epstein-Barr virus and cytomegalovirus polymerase chain reaction; and negative results for parvovirus B19 toxoplasmosis and syphilis serologic analyses.

Laboratory investigations showed a T-cell lymphopenia of 830/mm^3 (normal range 1500-4000/

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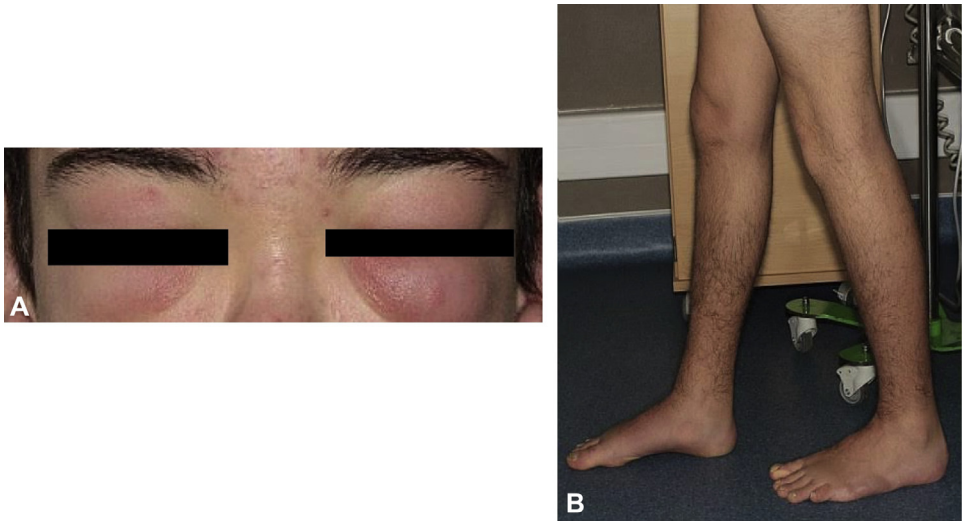

Fig 1. The patient at 14 years of age with lymphedema of (**A**) the eyelids and (**B**) the lower limb, stage I according to the classification of the International Society of Lymphology.

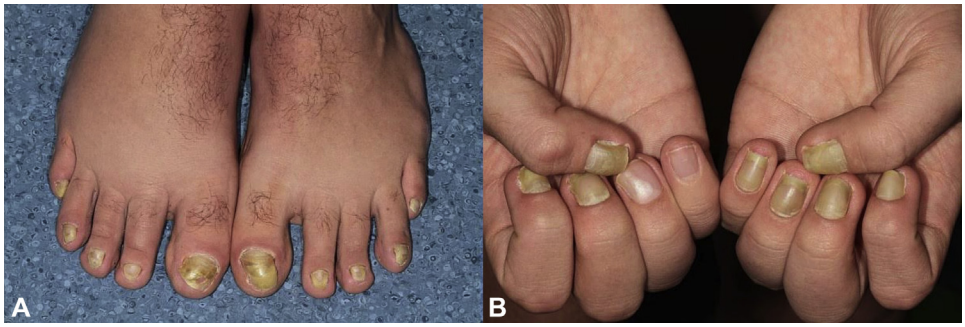

Fig 2. Yellow-green nail discoloration on (**A**) feet and (**B**) hands.

mm^3) predominant on $CD4^+$ at 193/μL (normal range 480-1320/μL) and a decrease in the proportion of memory B lymphocytes at 9.3% (normal range 23.0%-49.0%). Measurement of immunoglobulin concentrations showed a normal value for IgG but decreased values for immunoglobulin M at 0.34 g/L (normal range 0.54-1.53 g/L) and IgA at 0.66 g/L (normal range 0.76-2.42 g/L).

All the other values of the full blood count, 24-hour urine protein, renal, and hepatic function tests were normal, except for a serum albumin level of 33.7 g/L (normal range 39-49 g/L).

Abdominal ultrasonography showed normal kidneys with a good corticomedullary differentiation. Echocardiography findings were normal, with no sign of portal hypertension.

Lymph magnetic resonance imaging showed a dysplasia/hyperplasia of the lymphatic ducts in the lower limbs and a bilateral hydrocele. The chest CT showed bronchopulmonary dysplasia, emphysema, and septal thickening with a collapsed right basal pyramid.

Because of his low IgM and immunoglobulin A concentrations, the patient received a monthly intravenous immunoglobulin infusion for 6 months with no response. Clarithromycin (CAM) 400 mg/d was initiated a month ago. Currently, the disease is stable and no improvement has been seen since clarithromycin was started.

DISCUSSION

YNS is a rare clinical entity of unknown etiology consisting of the triad of dystrophic yellow nails, lymphedema, and pleural effusion. Only one third of patients are seen with this classic triad.[1] YNS is rare in children and, to our knowledge, the congenital form has rarely been reported. Association of fetal hydrops with YNS has been described in 4 previous reports.[2,3] To our knowledge, our patient is the youngest to present the classic triad associated with fetal hydrops. However, lymphedema of the eyelids has been described in 6 adult patients with this syndrome and in 1 child.[4] To this day, our patient is the only one with YNS presenting with lymphedema

of the eyelids since birth. The youngest case described in the literature was a 7-month-old girl.[4]

Njølstad cases may have a similar clinical presentation and are autosomal recessive conditions with possible prenatal onset (fetal hydrops and chylothorax) and severe respiratory manifestations during infancy that evolves into mild asthma. Lower-limb lymphedema appears during the first year of life and facial abnormalities are variable,[5] but the association of pulmonary manifestations, lymphedema, and yellow nail staining is quite characteristic of YNS.

YNS treatment options are based on anecdotal evidence and case reports. Some observations report the efficacy of immunoglobulin administration in patients with immunoglobulin deficiency, with an improvement of lymphedema and a decrease in the frequency and severity of infections.[6,7] There was no significant response for our patient after 6 months of treatment.

In a recent publication, Matsubayashi et al[8] reported the effectiveness of CAM in patients with YNS. CAM has both anti-inflammatory and antibacterial effects. The researchers conducted an observational study involving 5 patients with YNS and treated them with CAM. Nail discoloration and the respiratory manifestations improved in most patients. Therefore, CAM was initiated for our patient, without significant change in 1 month. However, the nail improvement in previous studies was between 1 month and 3 years and also corresponded to better control of respiratory manifestations.

Other treatment options include oral or topical vitamin E and oral zinc, which have been reported to be effective for treating yellow nails. They can be combined with fluconazole. Pleural effusion can be treated surgically (pleurectomy, pleurodesis). Lymphedema treatment is based on elastic compression and manual lymph drainage.[1,9]

Because of the paucity of pediatric patients, yellow nail syndrome is often misdiagnosed in infancy. This syndrome should be considered in children with unexplained exudative pleural effusions and localized lymphedema, even in the absence of nail changes.[4] Furthermore, it can arise in association with multiple diseases, such as neoplastic, endocrine, or immune deficiencies.[1] Therefore, thorough interdisciplinary evaluation and clinical follow-up are indicated. We also believe this syndrome should be considered in the differential diagnosis of nail dystrophies in pediatric patients. The congenital onset and events such as fetal hydrops should steer investigations toward a genetic etiology in YNS.

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