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Case Report

Internal Medicine Section

Yellow Nail Syndrome: An Unusual Cause of Pleural Effusion

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ABSTRACT

Yellow Nail Syndrome (YNS) is a rare clinical syndrome characterised by the classical triad of thickened and dystrophic yellow nails, pleural effusion, and primary lymphoedema. It usually occurs in older adults of over 50 years but there is no sex predilection. This was a case report of a 21-year-old male, who presented with dyspnoea on exertion, dry cough and abdominal distension for past 15 days and bilateral lower limb swelling for past two years. On general examination, patient had pallor with bilateral non pitting oedema of lower limbs and had yellow thick and dystrophic nails. There was clinical evidence of pleural effusion and ascites. Pleural fluid analysis showed lymphocytic and exudative picture with low Lactate Dehydrogenase (LDH) and Adenosine Deaminase (ADA) levels and was negative for malignancy. Duodenum second part (D2) biopsy showed Primary Intestinal Lymphangiectasia (PIL). Hence, a final diagnosis of YNS was confirmed. Symptomatic management was done, following which the patient had relief of symptoms and in subsequent follow-ups the patient was doing better. A detailed clinical history with investigations helps in attaining the diagnosis. Although there is no definitive treatment, diagnosis helps in avoiding unnecessary treatment and symptom based management helps in improving the quality of life of the patient.

Keywords: Dystrophic nails, Lymphangiectasia, Lymphoedema, Non pitting oedema

CASE REPORT

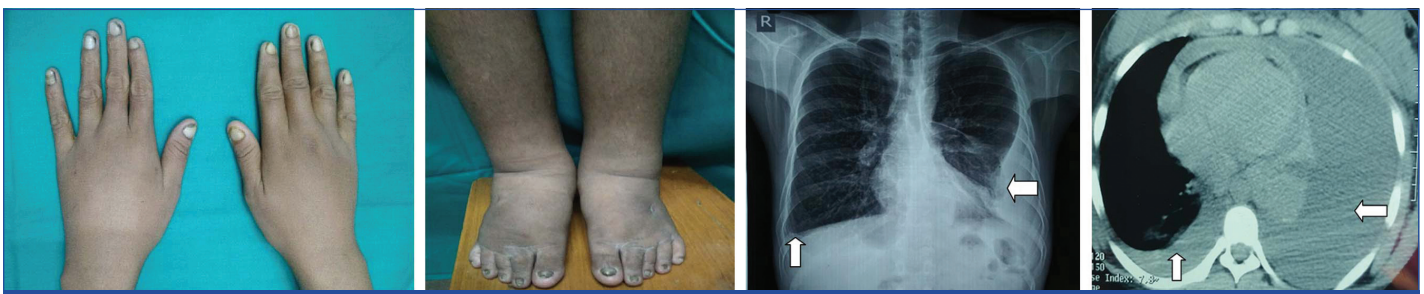
A 21-year-old male presented to the Department of Pulmonary Medicine with complaint of dyspnoea on exertion, dry cough and abdominal distension for past 15 days and bilateral lower limb swelling for past two years. He had no co-morbidities and his past medical and family history were unremarkable. He had been previously treated with antifilarials for his swelling, suspecting it to be filariasis due to high endemicity.

On physical examination he had a blood pressure of 126/76 mmHg, pulse rate of 78/min, respiratory rate of 34/min, temperature 37.8°C and oxygen saturation 98% at room air. On general examination, the patient had yellow thick and dystrophic nails [Table/Fig-1] and pallor with bilateral non pitting oedema of lower limbs [Table/Fig-2]. There were no palpable cervical, axillary or inguinal lymph nodes. On respiratory system examination, there was decreased tactile fremitus in the left mammary, infra-axillary and infrascapular area. Stony dull percussion was noted and diminished vesicular breath sounds were also noted. On Gastrointestinal (GI) system examination, there was ascites with no hepatosplenomegaly. All other system examinations were normal.

Complete haemogram showed haemoglobin 8.7 g/dL (reference range: 12-15 g/dL), raised Erythrocyte Sedimentation Rate (ESR) of 29 mm in 1st hour (reference range: 0-20 mm in 1st hour) and C-Reactive Protein (CRP) of 85 mg/L (reference range: <5 mg/L) [1,2]. Renal Function Tests (RFT) and urine analysis were normal. Liver Function Tests (LFT) showed hypoalbuminaemia with albumin of 2.1 g/dL (reference range: 3.5-5 g/dL [1]. Thyroid Function Tests (TFT) were normal. Sputum for Acid Fast Bacilli (AFB) and Cartridge Based Nucleic Acid Amplification Test (CBNAAT) detected no mycobacteria. Mantoux test was negative. His serology panel were non reactive. On chest roentgenography, the patient had a homogeneous opacity in the left middle and lower zone obliterating the left costophrenic angle and slight blunting of right costophrenic angle [Table/Fig-3].

Ultrasonography (USG) of thorax and whole abdomen confirmed bilateral pleural effusion and ascites, respectively. Contrast Enhanced Computed Tomography (CECT) of thorax showed bilateral pleural effusion (left>right) without any obvious parenchymal involvement [Table/Fig-4].

The CECT of the whole abdomen showed oedematous jejunal mucosa with mesenteric adenitis and ascites. Electrocardiogram (ECG) and echocardiography were within normal limits. Pulmonary function testing showed restrictive pattern. Pleural fluid was straw coloured and pleural fluid analysis showed lymphocyte predominance (95%) and exudative picture by pleural fluid protein criteria with value of 5.7 g/dL. Pleural fluid glucose was normal with low Lactate Dehydrogenase (LDH), which was 145 U/L and Adenosine Deaminase (ADA) was 19.20 IU/L. Pleural fluid AFB smear and CBNAAT detected

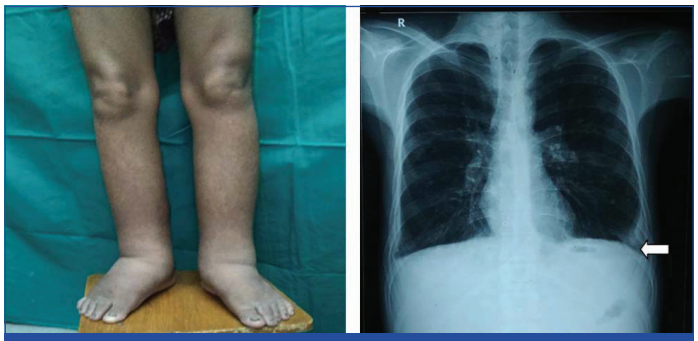


[Table/Fig-1]: Yellow dystrophic nails in the finger of both hands; **[Table/Fig-2]:** Primary chronic bilateral lymphoedema in the patient; **[Table/Fig-3]:** Chest roentgenography of the patient showing bilateral pleural effusion (left>right) [white arrows]; **[Table/Fig-4]:** Contrast Enhanced Computed Tomography (CECT) of thorax showing bilateral pleural effusion (left>right) [white arrows]. (Images from left to right)

no mycobacteria. Pleural fluid cell block study was negative for malignancy. Pleural biopsy showed lymphocytic cellular infiltrates with no evidence of granuloma or malignancy. Ascitic fluid analysis was predominantly lymphocytic with Serum Ascites Albumin Gradient (SAAG) of 0.8 g/dL (reference range: cut-off 1.1 g/dL) [3]. Ascitic fluid ADA levels were low and cytology was negative for malignancy. Ascitic fluid AFB and CBNAAT detected no mycobacteria. The Doppler USG of lower limbs showed subcutaneous tissue swelling but no vascular abnormality. From patient's clinical history, examination and investigations, the final diagnosis was confirmed to be a case of Yellow Nail Syndrome (YNS). The treatment planned was mainly supportive, based on patient's symptoms. Due to patient's persistent hypoalbuminaemia, an upper GI endoscopy was planned to exclude intestinal causes of malabsorption. Upper GI endoscopy was done by the Surgery Department and biopsy taken from D2 showed Primary Intestinal Lymphangiectasia (PIL).

Symptomatic management was given to the patient in the form of packed red cell transfusion (2 units), therapeutic thoracentesis (total 2.4 litres aspirated in 2 days), therapeutic paracentesis (1.4 litres once). Diuretics (inj. frusemide 20 mg twice daily for 7 days) and oral antibiotics (tab. azithromycin 500 mg once daily for 5 days) were also added. Patient also received 100 mL of 20% human albumin for 5 days. After consulting with the gastroenterologist, patient was also started on subcutaneous octreotide (250 mcg daily for 5 days). Patient's clinical symptoms gradually improved with the treatment and he was discharged after 7 days of hospital stay. Patient was advised to take low-fat diet like green leafy vegetables, fruits, legumes etc. with supplementary medium-chain triglycerides, mainly dairy products.

During follow-up visit over 10 months with last visit 15 days back, there was resolution of pleural effusion [Table/Fig-5] and ascites. Patient was advised oral vitamin E 800 mg per day for 1 month and pressure stockings of the lower limbs which showed significant improvement in lymphoedema [Table/Fig-6]. For his nail symptoms, patient was started on tropical therapy with clobetasol 0.05% for 5 days a week and is undergoing treatment till next follow-up visit.



[Table/Fig-5]: Mild reduction of lymphoedema with treatment on follow-up visit.
[Table/Fig-6]: Chest roentgenography showing near complete resolution of pleural effusion with treatment on follow-up visit (white arrow). (Images from left to right)

DISCUSSION

The diagnosis of YNS is by exclusion and is purely based on clinical features which consists of yellow dystrophic nails, pleural effusion and primary lymphoedema [4-6]. It was first described by Samman and White in 1964, who included only nail discolouration, while Emerson in 1966, added pleural effusion to the diagnostic criteria [5-7]. Around 100 cases of this syndrome have been reported in last 35 years with an estimated prevalence <1/1,00,000 cases [3,8,9]. The primary aetiology of YNS remains obscure and available data suggests anatomic or functional abnormality in lymphatic system as the predominant underlying mechanism [10]. Data from a recent study have suggested microvasculopathy with protein leakage as a more likely explanation for the symptoms in YNS [10].

Very few familial cases reported in the literature supports autosomal dominant pattern of inheritance, although there is no supportive genetic evidence [5]. In a few cases, mutation in *Forkhead Box Protein C2 (FOXC2)* gene has also been identified [11]. It usually occurs in older adults of over 50 years but there is no sex predilection [5]. The presence of nail changes with at least one of the other features from the triad is necessary to make the diagnosis [6]. It usually affects middle-aged individuals [5]. It has been associated with multiple clinical conditions such as malignancy, connective tissue diseases, endocrinopathies, tuberculosis, haemochromatosis and Guillain-Barré Syndrome (GBS) [8]. The supporting hypothesis for possible mechanism is by microvasculopathy of protein leakage [7,8,12]. In the present case, the patient was a young male of 21 years and presented with all the clinical features simultaneously.

Nail changes usually includes dystrophic slow growing nails and it might be the only symptom in about 10% cases [4,10]. In the present case, both upper and lower limb nails were involved. Nail changes seem to result from impaired lymphatic drainage of the fingers and toes [4]. It is important to perform mycological tests in these patients as there are cases where they have been treated with long duration of antifungals without any improvement and later had been diagnosed with YNS [4].

Lymphoedema is usually primary and occurs in about 80% of cases and most frequent site of involvement is the lower limbs and the involvement is usually bilateral [10]. It is usually a late presentation but has been reported as the first symptom to appear in around 33% of cases [4,10]. In the present case, lymphoedema was the first symptom which was noticed and had been misdiagnosed as filariasis.

Pleural effusion occurs in 36% of cases and is the initial presentation in about 30% of cases [10]. Pleural fluid characteristics usually show lymphocytic predominant pattern with low LDH levels [13,14]. Chowdhury N et al., in their study, reported pleural fluid to be neutrophilic even with multiple pleural fluid aspirations [10]. In the present case there was associated bilateral pleural effusion with similar pleural fluid characteristics.

Treatment of YNS is controversial and includes the treatment of the underlying disease as well as its symptoms and reports published showed spontaneous remission of symptoms in 7-30% of cases [15]. In the present case, treatment was both of the disease and its related symptoms. Lotfollahi L et al., reported a case of YNS who had resolution of symptoms on treatment with octreotide [15]. In our case also, treatment with octreotide showed significant improvement in the patient's clinical symptoms. Although a wide variety of trial-based treatments are being currently going on for YNS, but a definitive treatment is yet to come.

CONCLUSION(S)

Yellow nail syndrome, although rare, should always be suspected in patients with chronic lymphoedema and pleural effusion, as they are the most common and early features to be encountered by the physician. A detailed clinical history with investigations helps in attaining the diagnosis. Although there is no definitive treatment, diagnosis helps in avoiding unnecessary treatment and symptom based management helps in improving the quality of life of the patient. This case signifies the utility of nail examination in the field of pulmonary medicine as chronic bilateral pleural effusion with nail changes is the dictum of YNS as was seen in this case.

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