

# Yellow Nail Syndrome In an Elderly Sudanese Female: A Case Report

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## Abstract

Yellow nail syndrome is a rare lymphatic abnormality without a clear pathogenesis. Hereby, we report A 70-year Sudanese female who presented with recurrent cough, recurrent lower limb swelling and yellowish nail discoloration diagnosed as yellow nail syndrome but unfortunately passed away due to acute respiratory distress syndrome (ARDS).

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## Abstract

Yellow nail syndrome is a rare lymphatic abnormality without a clear pathogenesis. Hereby, we report A 70-year Sudanese female who presented with recurrent cough, recurrent lower limb swelling and yellowish nail discoloration diagnosed as yellow nail syndrome but unfortunately passed away due to acute respiratory distress syndrome (ARDS).

**Keywords:** Yellow nail syndrome; Acute respiratory distress syndrome; Lymphedema; Edema; ARDS

## Key Clinical message:

Whenever common causes are excluded; the co-existence of recurrent respiratory affection and non-pitting edema in patients of more than 40 years should raise suspicion of yellow nail syndrome even in absence of sinusitis, bronchiectasis or positive family history.

## Introduction:

Yellow nail syndrome is a very rare disorder that has been noticed since 1927 (1). It affects both sex equally, with age of more than 40 years is typical (2). The exact pathogenesis remains unclear but lymphatic system anatomical and functional abnormalities remain as the predominant theory, while other hypotheses suggest autoimmune, cancer and paraneoplastic roles (3). Also a very rare familial case has been reported (1).

Although it's only found in 27%.60% of patients The diagnosis depends on the presence of 2 out of; characteristic nail changes, respiratory tract infection and lymphedema. The latter occurs in up to 80% of cases and may be the first sign (1). The common Nail changes that have been described include nail discoloration (pale yellow to dark green), nail hyperkeratosis with loss of the lunula, onycholysis, proximal nail-fold erythema over curvature, cross-ridging, very hard and difficult-to-trim nail , increased nail thickness, and slowed longitudinal growth (1,3). Respiratory manifestations that are encountered include pleural effusion, bronchiectasis, chronic cough and frequent sinusitis (1).The condition may resolve spontaneously especially when it is paraneoplastic or cancerous (1).

Oral vitamin E, and fluconazole showed a good response, while intralesional steroids, oral zinc sulphate, and subcutaneous immunoglobulins showed promising data (1). Although The prognosis appears to be favourable; it requires extensive research.

## Case Presentation:

A 70-year Sudanese female, diabetic and hypertensive with a past history of ischemic stroke 7 years ago resulted in residual right-side weakness; presented complaining of fever and altered level of consciousness for 2 days with history of recurrent productive cough and recurrent right lower limb swelling for months. There is no family history of similar condition, or connective tissue disease. The patient is neither a smoker nor alcohol consumer. Her current medications included Glimepiride 4 mg and Losartan 50 mg.

Clinical examination revealed awake, confused patients (GCS 14/15) , otherwise clear neurological examination, BP 150/90 mmhg, pulse was 80 beats per minute, SPO<sub>2</sub> on 99% of room air. There was yellowish discoloration of her nails in both upper and lower extremities associated with separation from the nail beds (Figure 1 and 2). Chest examination revealed a right-side stony dullness, decreased air entry and diminished vocal resonance. Also, a pitting right lower limb oedema.

Laboratory investigations showed random blood glucose of 44 mg/dl, positive Blood Film for Malaria, normal Renal and Liver function tests. Chest radiograph revealed a moderate right sided pleural effusion (Figure

3). Therapeutic thoracentesis was done with 2 litres of a straw-coloured fluid removed, sent for microscopic examination which showed a hemorrhagic background pleural fluid, that's made of mixed mononuclear inflammatory cells with lymphocytic predominance and it was containing 3.0 g/dl proteins and 57.5 mg/dl glucose.

Diagnosis of yellow nail syndrome with pleural effusion and complicating pneumonia was made.

The patient managed with Quinine infusion 600 mg T.D.S, 3rd generation cephalosporin, vitamin E and prophylactic dose of heparin, however the condition deteriorate progressively and the patient passed away on the fifth day of admission due to acute respiratory distress syndrome (ARDS).

## Discussion:

Yellow nail syndrome was first discovered in 1927, but the first case series of the disease was presented by Samman and White in 1964 (4). Thirteen cases were presented sharing the common features of thickened yellow nails with growth rates slower than normal ( $<0.25$  mm/week) in comparison to (0.5-1.2 mm/week) in normal individuals(4). Lymphedema presented in 10 out of the 13 cases, along with respiratory manifestations consistent with pleural effusion, bronchiectasis, and chronic sinusitis, which are late manifestations of the syndrome. Most cases of YNS are sporadic (5). With very little evidence supporting the hypothesis that YNS is an inheritable condition. Despite that, rare familial cases were reported with a doubted autosomal dominant transmission pattern. Very few juvenile cases of the disease were reported (6,7). In this section, we discuss the intersections of this patient's YNS presentation with cases reported in literature.

The presentation of this case is relatively late, as the patient presented at 70 years old. Patients of YNS usually present between their 4<sup>th</sup> and 6<sup>th</sup> decade of life(8). However, like known cases in literature(9,10), this case presents the classic triad of yellow nail syndrome consisting of: yellow and thickened nails (figure 1, figure 2), respiratory manifestations (figure 3), and lymphedema (figure 1 and 2). And like other cases of YNS, the case was diagnosed clinically, as Yellow nail syndrome's diagnosis is a clinical one (2). And as suggested by Hiller et al, can be made with two of the three known manifestations of the disease, as the observation of these signs may resolve overtime (11). Nonetheless, a diagnosis of the condition can't be made in the absence of nail abnormalities (2). And hence, based on the look of the patient's nails, chest radiograph, and lower limb swelling the diagnosis was confirmed.

The case was a sporadic case. No similar signs of the disease were reported in the patient's family. Patients also presented with ankle and foot oedema, as in the majority of the cases reported by Samman and White in their thirteen case series report (9) and 9 out of 17 cases presented by Bull et al (12). No rhinosinusitis was reported in this patient's condition.

The diseases known to be associated with YNS are malignancies, immunodeficiency states, connective tissue diseases, diabetes mellitus, thyroid dysfunction, hemochromatosis, obstructive sleep apnea, Guillain-Barre ´ syndrome, xanthogranulomatous pyelonephritis, tuberculosis, myocardial infarction, nephrotic syndrome, exudative enteropathy, hypoalbuminemia, and drugs (thiol compound therapy) (2). Comorbidities of patients presenting in this case intersects with this group in diabetes mellitus only. The patient also had hypertension and had a history of stroke. Hypertension is a comorbidity that was reported for other patients with YNS (13,14) although no association between the two conditions has been confirmed yet. In a case of an 65 year old man with hypertension and stroke, it was also suggested that the syndrome might be linked to the patient's cardiac pacemaker (14). However, all of these hypotheses are questionable..

The therapeutic thoracentesis of the patient showed a straw-colored fluid of two litres, which can expected in a pleural effusion patient and is consistent with the patient's presentation with fever, as lower respiratory tract infections, pneumonias, and bronchiectasis present in half of YNS patients(2,15). And hence as indicated by her symptoms, the patient had pneumonia.

Generally, analysis of pleural fluid of YNS patients is characterised by being transudative, with high protein content (2,16). Analysis of this patient's pleural fluid showed mixed mononuclear inflammatory cells with lymphocytic predominance. With 3.0 g/dl protein and 57.5 mg/dl glucose content. Previous findings in

literature entail that lymphocytic predominance is the rule when it comes to cellular analysis (8). The patients pleural fluid is also exudative by protein criteria and transudative by cholesterol and lactate dehydrogenase criteria as with previously known cases in Maldonado et al in which he performed high yield analysis of pleural fluid of 41 patients (8).

Patient's chest radiograph shows moderate right sided pleural effusion (figure 3). This radiographic finding is particularly similar to a case reported by Maldonado et al where the patient's pleural effusion was bilateral but particularly larger in the right chest (2).

Although not all known cases of yellow nail syndrome present with lymphedema, some cases do indeed present without it (9,12). The likelihood of the lymphadenopathic theory of the disease still prevails. The presentation of this case can be regarded as supportive of this theory, although confirmatory integrity of this theory still remains a question under investigation.

Cases of YNS's respiratory manifestations are treated with postural drainage, other pulmonary hygiene measures, and antimicrobials (2). Treatment of pleural effusion depends on the severity of the effusion. Therapeutic thoracentesis might suffice in management. With pleurodesis coming as an option for recurrent effusion patients (2). The use of topical steroids or vitamin E has been described though the evidence supporting their use remains scarce (8,17).

No definitive treatment for YNS was confirmed until now. However, several treatment regimens for the disease were proposed in literature, but they remain as treatment efforts for individual cases. Fluconazole, vitamin E, and topical steroids have been the most popularly used treatments for YNS. But their ascribed treatment properties are still under question due to scarcity of supportive evidence (8,17,18). Another effort by Algain et al (18) suggested terbinafine and topical minoxidil as curative treatments for the disease that promote the formation and enhance barriers and thus reduce peripheral swelling in a first of its form remarks. Like many other cases with the disease (2), this case was managed with supportive treatments to ameliorate the severity of the symptoms. Specifically, regarding the patient's treatment for YNS, along with the therapeutic thoracentesis, she was treated with vitamin E. The patient took Glimepiride 4 mg and Losartan 50 mg. For her diabetes and hypertension, quinine for her Malaria, 3rd generation cephalosporin for her pneumonia, and a dose of heparin as prophylaxis for her hypertension. Despite efforts, the patient's condition deteriorated quickly and she passed away due to an episode of acute respiratory distress syndrome (ARDS). Up to our knowledge, there is no published literature linking yellow nail syndrome to a specific fatal complication.

The course of the disease is generally known to be benign; the prognosis of yellow nail syndrome cases shows decreased life longevity in comparison to control population (2). And although when presented to the clinic the patient underwent the proper investigations to diagnose the syndrome and was managed with the up to date known management of the disease, this late presentation and hence identification of the patient's condition might have affected her prognosis, along with the patient's co- morbidities and age which might have further complicated the condition and our understanding of the progression of the case.

## Conclusion:

Yellow nail syndrome is a syndrome that presents with yellow thickened nails, respiratory manifestations, and lymphedema. In this case, the patient has presented in the 8<sup>th</sup> decade of her life as a sporadic case with the classic triad of the disease with no complications. Patients' pleural profile and chest radiograph matched that of patients in existing literature. Also, the case had a history of hypertension, diabetes, and stroke. Although diabetes has been noted to be associated with yellow nail syndrome. There is no conclusive evidence regarding its relation to hypertension despite a number of noted cases up until now. Patient passed away after an episode of acute respiratory distress syndrome (ARDS). No similar reports of this specific case of death were found in literature.

## Declarations:

## Consent to participate:

Both verbal and written consents to participate and to publish this information were obtained from the patient.

#### **Consent to publish:**

Consent for publication was obtained from all authors.

#### **Availability of data and materials:**

The datasets used and \ or analysed during the current study are available from the corresponding author on reasonable request.

#### **Competing interests:**

The authors have no conflict of interest to declare.

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#### **Authors contribution:**

AA, MYY and IA: Took history, did investigations and participated in writing first draft.

MMF, KAH and MTA: Wrote first and final drafts.

SAG, EBS and DHO: wrote and revised final draft.

All authors contributed significantly in the study.

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