A curious case of Yellow Nail Syndrome

Radu Crișan-Dabija, Traian Mihăescu

University of Medicine and Pharmacy "Grigore T. Popa" Iași Clinic of Pulmonary Diseases

Correspondence: Radu Crisan-Dabija, University of Medicine and Pharmacy "Grigore T. Popa" Iași, Clinic of Pulmonary Diseases Iași, 30 dr. I. Cihac str., 700115 Iași, Romania e-mail: crisanradu@gmail.com twitter: @pneumo_iasi

Abstract

The Yellow Nail Syndrome is a rare clinical entity, first described in 1967 by P.D. Samman and W.F. White. The triad slow-growing dystrophic yellow nails, lymphedema and chronic respiratory disorders is the typical manifestation of the disease but some variations have been described as well as associations with chylothorax, chylous ascites, intestinal lymphangiectasia, thyroid abnormalities, malignancies and immunoglobulin A (IgA) deficiency. We present a case of a 55-years-old woman that had an insidious onset of respiratory disorders and chronic sinusitis, suspected to be infectious throughout the hospitalizations, associated with therapeutically neglected autoimmune thyroiditis.

Keywords: *yellow nails, pleural effusion, rare syndromes, lymphedema, bronchiectasis, chronical sinusitis*

Rezumat

Un caz curios de Sindrom al Unghiilor Galbene

Sindromul Unghiilor Galbene este o entitate clinică rară descrisă pentru prima oară în 1967 de către P.D. Samman and W.F. White. Triada: colorația galbenă a unghiilor asociată cu distrofie și creștere lentă a acestora, limfedem și tulburări respiratorii cronice reprezintă tabloul clinic obișnuit al patologiei însă literatura descrie și alte asocieri precum chilotoraxul, ascita chiloasă, limfangiectazia intestinală, tulburări tiroidiene, tumori maligne și deficit de IgA. În cadrul acestei lucrări prezentăm cazul unei femei de 55 de ani care a avut un debut insidios al patologiei respiratorii asociate cu sinuzită cronică, cu caracter bănuit infecțios de-a lungul spitalizărilor, asociată cu o tiroidită autoimună neglijată terapeutic.

Cuvinte-cheie: *unghii galbene, pleurezie, sindrom rar, limfedem, bronșiectazii, sinuzită cronică*

Introduction

The Yellow Nail Syndrome is a rare clinical entity, first described in 1967 by P.D. Samman and W.F. White[1]. The medical literature is scarce in case reports, as of 2009 there were around 150 clinical cases reports[2]. Believed to be a genetic disorder, its inherited nature has not been fully demonstrated. There were suppositions that the Yellow Nail Syndrome (YNS) is an inherited lymphedema with variate expression but the lack of published cases and retrospective studies does not sustain this theory. In a retrospective study, the actual genetic theory was rejected[3].

In most patients, the clinical onset is between the fourth and the sixth decade of life. The triad: slow-growing dystrophic yellow nails, lymphedema and chronic respiratory disorders is the typical manifestation of the disease but some variations have been described as well as associations with chylothorax, chylous ascites, intestinal lymphangiectasia, thyroid abnormalities, malignancies and immunoglobulin A (IgA) deficiency[4].

The literature also describes associations with bronchiectasis, recurrent pneumonias, bronchitis and sinusitis.

While the different clinical features of the syndrome may occur at wide intervals, the patients may not present the classical triad of symptoms.

Many therapeutical options have been tried, mostly for each symptom in part. A sustainable and typical therapy for the YNS has not been developed yet as the main cause of the disease remains unknown. Oral supplementation of vitamin E as well as topical treatment are known to reduce the nails' yellowness and diuretics or surgical pleuredesis are helpful in treating the pleural effusion, as the most common and long-term manifestation seems to be recurrent pleural effusion.

Case report

We present the case of a 55 years-old-woman, college-educated, working as a high school teacher, that presented to our clinic with 5 years of chronic coughing (1 year of dry cough and 4 years of cough with serous expectoration), slow growing toe and finger nails colored greenish – yellow and pleural effusion.

Her personal medical history includes:

- Childhood diseases (Paramyxovirus at 6 years old, Varicella at 8 years old)
- Infectious Hepatitis with Hepatitic Virus A (at 12 years old)
- Chronic sinusitis (22 years old)
- Cholecystectomy (43 years old)
- Autoimmune thyroiditis (at 50 years old)
- Feriprive anemia (since 2002)
- Known allergies: Iodine, pork protein
- Never smoked and consumes alcohol only occasionally.

In 2009 she presented to pulmonology ambulatory care for evaluation of the dry cough. The clinical exam revealed no abnormal respiratory sounds, the chest x-ray showed normal pulmonary fields. It was treated as a common cold.

One year later, the patient presented the same (chronic by now) dry cough and so in 2010 she had another X-ray examination that showed, in dynamics compared to the previous one, demineralization of all skeletal structures viewed within the chest X-ray field and a round thoracic kyphosis, bilateral apical pachypleuritis. Once again, an infectious disease was suspected but has been redirected to see an endocrinologist.

The visit to Endocrinology was delayed by patient's will and in 2011 she returned to her hometown Pulmonology Hospital, where a progression of respiratory pathology has been noticed as the imagery examination

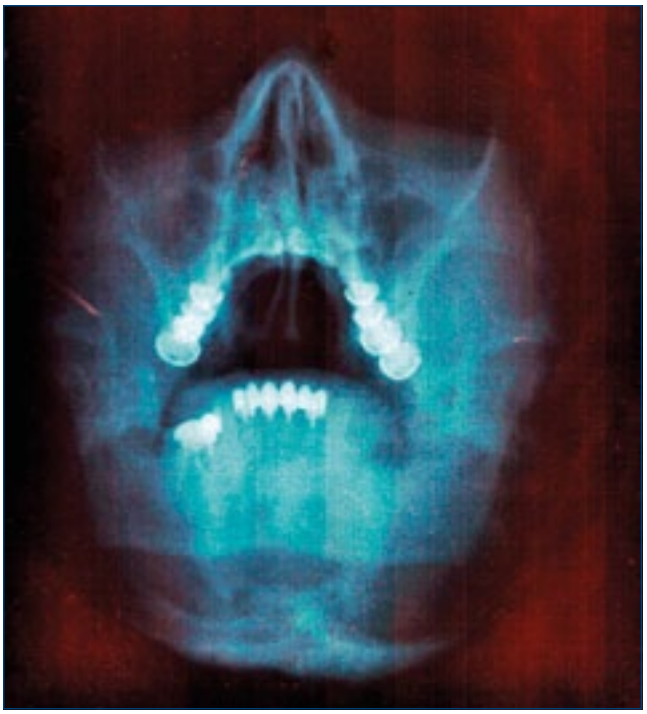

Figure 1. *Anterior Face Sinuses X-ray (2012)*

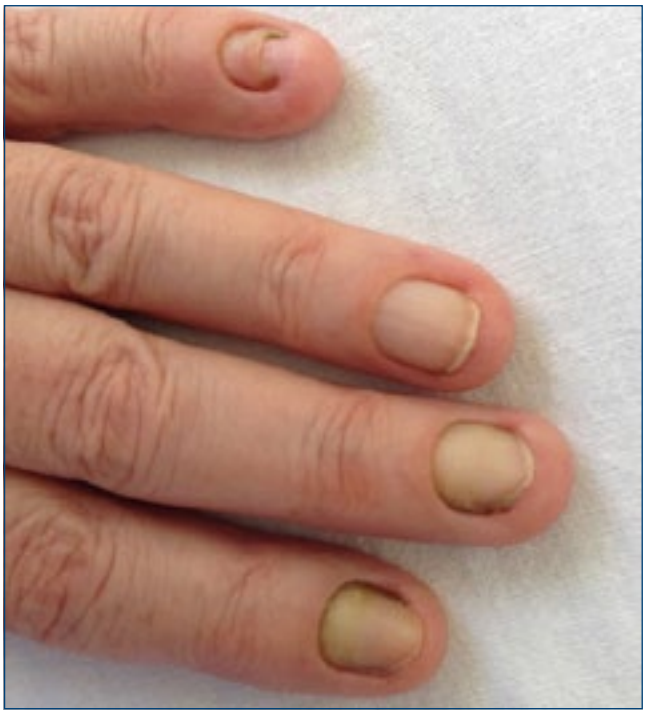

Figure 2. *Hand finger nails*

revealed discreet basal bilateral bronchiectasis, bilateral apical pachypleuritis, round thoracic kyphosis.

Since the symptoms intensified and associated serous expectorations, headaches and periods of shortness of breath, an X-ray of anterior sinuses was performed. It showed an intense opacification of frontal sinuses, obstruction of nasal fossae, opacification of maxillary sinuses. She was prescribed antibiotics and once again, the indication of seeing an endocrinologist was made.

In 2012 she went to "Marius Nasta" Institute of Pulmonology in Bucharest with the same worsened recurring symptoms that chronically re-appeared within one year's period. At the chest X-ray examination a pulmonary nodule diffuse delimited superior, latero-cardiac in the anterior segment of her left lower lobe, and minimum bilateral pleural effusion was described.

Prior to this hospital presentation, the patient was consulted by an endocrinologist. She was diagnosed with autoimmune thyroiditis and levothyroxine was prescribed. Pleural effusion was considered secondary to autoimmune thyroiditis (therapeutically neglected – the patient interrupted the treatment by herself). The clinical diagnose was pneumonia of the left lower lobe in the context of sinusitis. She was thus treated with antibiotics and NSAID (Non-Steroid Antiinflamatory Drug). After this hospital admission, one month later she attended her treatment follow-up. Chest X-ray showed the persistence of minimum bilateral pleural effusion and minimum pericarditis. Thoracentesis evidentiated a transudate-like pleural liquid. The blood tests showed normal blood biochemistry and normal blood cell count.

Thoracic CT described bilateral pleural effusion, pericarditis, no mediastina lymphadenopathy, normal liver and normal suprarenal gland.

In 2014 she presented herself at our clinic with a cough, serous expectoration and mild shortness of breath. Based on prior documentation and anamnesis, she had two new symptoms: persistent swelling of lower limbs and eyes and slow growing yellow-colored nails.

Thoracic imagery showed the same aspect of pleural effusion. The pleural liquid extracted by thoracentesis showed no tumor cells, inflammatory cells present with the proportions of 84% lymphocytes and 16% eosinophils.

To exclude an autoimmune systemic pathology the blood antinuclear antibodies (ANA-test) were dosed and the result showed a value of 1/100 titer – upper limit values.

The ORL examination described unhomogenous opacification with hypertrophy of the mucosa from the maxillary sinus and demineralization of the sinus walls.

The patient was prescribed oral doses of Vitamin E – 1000 IU per day with little clinical effect.

Discussions

The Yellow Nail Syndrome (YNS) is a rare condition with erratic occurrence and manifestations, hence its difficult diagnosis and the many traps of clinical assessment. Very little data, most of it coming from the case reports, show no predilection for a particular gender, group of population or age. It is believed to occur after the age of 40 (most clinical cases published describe patients over 40 years old) and the evolution is highly unpredictable.

A journal article from 2006 raised the possibility that YNS can be associated with tuberculosis – given a case report from Spain[5] but there were no further associations between YNS and infection with *Mycobacterium tuberculosis* in other cases reported. The life expectancy is believed to be greatly reduced for the patients with YNS[6] compared to

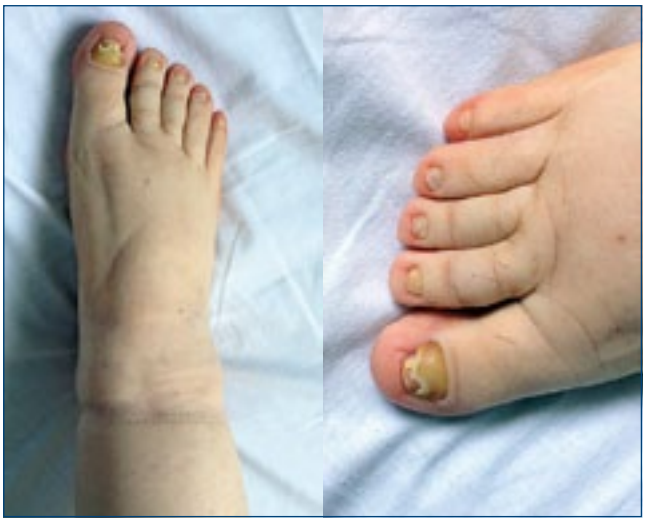

Figure 3. *Toe nails and edema*

the general population. The complex possible factors that precede the onset of the syndrome along with the complex general manifestations make the diagnosis and management of the disease difficult and challenging. Multiple-case report from 2012[7] the authors underline the fact that all 5 patients diagnosed with YNS presented chronical sinusitis. Since this case report shows that chronical sinusitis was present during the patient's youth, it may lead to a clinical possibility that this particular comorbidity can be added as a frequent occurrence along with the classical triad: yellow nails, lymphedema and chronic respiratory symptoms.

Still, the most important clinical manifestation that accelerates the presentation to the hospital remains the unexplained cause of the edema or the respiratory symptoms. In an article from 1972, Hiller and Rosenow[8] suggested that the diagnosis of the YNS can be strongly suggested in the presence of two out of the three manifestations if the clinical onset lacks another plausible explanation, but the presence of slow-growing yellow nails is a crucial condition for the correct diagnosis.

The pathogenesis of YNS is poorly understood. Structural or functional lymphatic abnormalities and increased vascular permeability to albumin are a proposed pathologic mechanism.

Since Yellow Nail Syndrome has been described in previous case reports as secondary to another condition (e.g., connective tissue disease, a thyroid disorder or malignancy), the fact that a mistreated thyroid disease has been in this patient's history for about 3 years might be considered as the onset of YNS.

Also, YNS has been reported as an adverse effect of medicines such as penicillamine, bucillamine or gold sodium thiomalate[9]. In the light of this theory, the suspicion of side effects due to long-term antibiotics use has been raised but the medication was administered intermittently and with long periods between the cures.

The particularity of this case consists primarily in the atypical onset of the disease: first the chronic cough associated with autoimmune thyroiditis – two apparently separate clinical entities. Then, the bronchiectasis and the acute sinusitis appeared. The pleural effusion was fist associated with a lower lobe pneumonia and later, after its persistence, the connection with the thyroid pathology was made. After almost 5 years of symptomatology, the yellow coloration of the nails and the lymphedema appeared, finally completing the diagnosis of Yellow Nail Syndrome.

Vitamin E treatment had little effect but other therapeutical options described in the literature (itraconazol, for example) also showed modest results[10]. Nail changes seem to result from impairment of lymphatic drainage of the fingers and toes. The yellowish color is probably due to lipofuscin pigment, resulting from lipid oxidation of free radicals[11].

Conclusions

YNS is a controversial syndrome that is usually associated with an autoimmune condition: in our case autoimmune thyroiditis. Pulmonary manifestations were classic but sinusal manifestation exacerbated year by year. Probably, if the patient would have taken the autoimmune pathology seriously from the onset, the debut of the syndrome might have been delayed. Even so, there is no certainty that the nails coloration or the persistence of the pleural effusion would have an earlier or a later onset.

Further reports and focus on the immunology of the syndrome is needed in order to understand how to delay if not prevent the onset in suspected patients.

Disclosure: The authors take full responsibility in the information presented in this article and acknowledge that they have the written consent of the patient to publish the medical data in this paperwork. ■

References

1. Samman P. D, White W. F. The 'yellow nail' syndrome. *Br J Dermatol* 1964, Vol. 76, pp. 153-157.
2. Maldonado F, Ryu J.H. Yellow nail syndrome. *Curr Opin Pulm Med* 2009, Vol. 15, pp. 371-375.
3. Hoque S.R, Mansour S, Mortimer P.S. Yellow nail syndrome: not a genetic disorder? Eleven new cases and a review of the literature. *Br J Dermatol*. Vol. 156, Issue 6, June 2007, pp. 1230 - 1234.
4. Maldonado F, Tazelaar H.D, Wang C.W. Yellow nail syndrome: analysis of 41 consecutive patients. *Chest* 2008, Vol. 134, pp. 375-378.
5. Benaixa, J.P, Garcia-Morillo JS, Esteban F, Gonzalez-Perez JM. A syndrome of yellow nails: a case associated with Mycobacterium tuberculosis. *Rev Clin Esp* 2006 Nov;206 (10):536–538.
6. Maldonado F, Tazelaar HD, Wang CW, Ryu JH. Yellow nail syndrome: analysis of 41 consecutive patients. *Chest* 2008 Aug; 134(2):375–381.
7. Letheulle J, Deslée G, Guy T, Lebargy F, Jego P, Delaval P, Desrues B, Jouneau S. The yellow nail syndrome: a series of five cases. *Rev Mal Respir.* 2012 Mar;29(3):419-25.
8. Hiller E, Rosenow EC 3rd, Olsen AM. Pulmonary manifestations of the yellow nail syndrome. *Chest.* 1972 May;61(5):452-8.
9. Nanda S, Dorville F. Clinical Images: Yellow nail syndrome. *CMAJ.* 2009 Oct 27;181(9):614.
10. Tosti A, Piraccini BM, Iorizzo M. Systemic itraconazole in the yellow nail syndrome. *Br J Dermatol.* 2002 Jun;146(6):1064-7.
11. Siakatos A.N. and Munkers K.D. Recent developments in the isolation and properties of autofluorescent lipopigments. Elsevier 1982, pp. 165-187.
12. Müller RP, Peters PE, Echternacht-Happle K, Happle R. Roentgenographic and clinical signs in yellow nail syndrome. *Lymphology.* 1979 Dec;12(4):257-61
13. Iqbal M, Rossoff LJ, Marzouk KA, Steinberg HN. Yellow nail syndrome: resolution of yellow nails after successful treatment of breast cancer. *Chest.* 2000 May;117(5):1516-8.
14. Bokszczanin A, Levinson AI. Coexistent yellow nail syndrome and selective antibody deficiency. *Ann Allergy Asthma Immunol.* 2003 Nov;91(5):496-500.
15. Gubinelli E, Fiorentini S, Cocuroccia B, Girolomoni G. Yellow nail syndrome associated with sleep apnoea. *J Eur Acad Dermatol Venereol.* 2005 Sep;19(5):650-1.