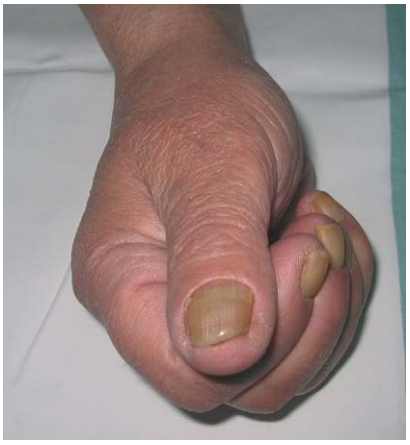
Yellow Nail Syndrome As a Form of Presentation of Pleural Effusion

To the Editor: Yellow nail syndrome is a rare entity characterized by the triad of slow-growing, dystrophic and yellow nails, lymphedema, and pleural effusion of unclear etiology.[1] We report the case of a patient referred for evaluation of pleural effusion associated with yellow nails.

The patient was a 70-year-old male smoker (80 pack-years) who had formerly worked in the construction industry but had no history of asbestos exposure. Aspects of interest in his medical history were mild chronic obstructive pulmonary disease (forced expiratory volume in 1 second, 1.76 L, 71% of predicted), chronic atrial fibrillation, and Graves–Basedow disease being treated with thiamazole. Initial clinical presentation was subacute onset of dyspnea with no other symptoms. Physical examination revealed signs of bilateral pleural effusion and lower limb lymphedema in addition to thickened and slow-growing nails with yellow discoloration on

both hands and feet (figure). A chest radiograph showed bilateral pleural effusion. Erythrocyte sedimentation rate, complete blood count and biochemistry, and levels of antinuclear antibodies, rheumatoid factor, D-dimer levels, immunoglobulins (Ig) including IgG subclasses, and C-reactive protein were normal. The thyrotropin level was 20.75 µU/mL (normal range, 0.4-4 µU/mL) and the free thyroxine level was 0.46 ng/dL (normal range, 0.8-1.8 ng/dL). Thoracentesis yielded a straw-colored lymphocytic exudate with a pH of 7.80. Glucose content was 97 mg/dL; adenosine deaminase, 18.3 U/L; cholesterol, 100 mg/dL; and triglycerides, 22 mg/dL. The results of culture, cytology, and flow cytometry of the pleural fluid were negative as were findings from closed pleural needle biopsy. A computed tomographic scan of the chest revealed bronchiectasis affecting the lingula, small areas of emphysema and subpleural bullae in the upper lobes, and a small bilateral pleural effusion. Echocardiography revealed minimal tricuspid regurgitation but no signs of pulmonary arterial hypertension. No indications of venous thrombosis were detected by venous Doppler ultrasound of the lower extremities. Diuretics were administered although the patient presented no signs of heart failure. Thyroid hormone substitution therapy was started to rule out the possibility that the effusion was due to metabolic imbalance from hypothyroidism caused by antithyroid medication. Neither the diuretics nor the return to normal of thyroid hormone levels had any effect on the pleural effusion. The effusion had been clinically and radiographically stable during the 2 years prior to assessment during which the patient had been attending a respiratory clinic as an outpatient.



Note the dark yellow thickened fingernail.

The association of yellow nails and lymphedema was first described by Samman and White.[1] Emerson[2] later reported the association with recurrent pleural effusion completing the triad that normally characterizes this syndrome. The triad is also found in association with bronchiectasis, sinusitis, bronchitis, and recurrent pneumonia. Yellow nail syndrome has been attributed to an anatomical/functional abnormality of the lymph vessels, an etiology that could explain at least 2 of the 3 common symptoms—lymphedema and pleural effusion.

The nails typically present total or distal yellow discoloration, slow dystrophic growth at a rate of 0.1 to 0.25 mm/week (normal growth, 0.5-2 mm/week), thickening, and cuticle loss of unclear pathogenesis. Onychomycosis is also common. Lymphedema, which is caused by a reduction in lymph flow, tends to be mild and affect mainly the lower extremities. It has classically been attributed to hypoplasia of the lymph vessels demonstrated by peripheral lymphangiography although the fact that the condition is reversible in some cases would suggest a functional rather than an anatomical abnormality.[3]

The pleural fluid is usually an exudate (occasionally only because of its high protein count), with a high percentage of lymphocytes and a low concentration of adenosine deaminase, as in our patient. It may, however, sometimes be chylous. Pleural microscopy reveals dilation of the lymph vessels in both pleurae associated with perilymphatic inflammation.[4] The elevated protein levels found in pleural fluid cannot be explained solely by obstruction of the pleural lymph vessels because the protein concentration in the pleural fluid is substantially lower than in serum.[5] Several authors have hypothesized that protein leakage increases due to microangiopathic lesions in the pleural capilliaries.[6] This would explain why lymphangiographic findings are sometimes normal in these patients. In some cases, serum albumin values are low, secondary to a protein-losing enteropathy caused by the same microvascular abnormalities as those observed in the intestine.

This entity has been reported in association with thyroid diseases, selective immunoglobulin deficit, bronchogenic carcinoma and lymphomas, rheumatoid arthritis, nephrotic syndrome, protein-losing enteropathy, conjunctival abnormalities and, curiously, with obstructive sleep apnea-hypopnea syndrome. A familial association has also been reported. In our patient, it was not possible to establish whether the clinical features were related to any of these diseases.

No specific treatment exists for this syndrome. The following remedial measures have been proposed: repeated thoracentesis, a diet rich in medium-chain triglycerides when the effusion is chylous, somatostatin analogs such as octreotide, implantation of a pleurovenous shunt, and pleurodesis in low-risk patients. Topical vitamin E has been proposed for the treatment of the yellow nails because of its anti-inflammatory effect. Itraconazole is prescribed to patients who present associated onychomycosis.

Xavier Pomares Amigó,
Yosune Ormaza Landabaso,
and Christian Domingo Ribas

Servei de Pneumologia, Corporació Parc Taulí, Sabadell, Barcelona, Spain

1. Samman PD, White WF. The yellow nail syndrome. Br J Dermatol. 1964;76:153-7.
2. Emerson PA. Yellow nails, lymphoedema, and pleural effusions. Thorax. 1966;21: 247-53.
3. Yellow nails. Lancet. 1973;1:1492-3.
4. Solal-Celigny P, Cormier Y, Fournier M. The yellow nail syndrome. Light and electron microscopic aspects of the pleura. Arch Pathol Lab Med. 1983;107:183-5.
5. D'Alessandro A, Muzi G, Monaco A. Yellow nail syndrome: does protein leakage play a role? Eur Respir J. 2001;17:149-52.
6. Miserocchi G, Venturoli D, Negrini D, del Fabbro M. Model of pleural fluid turnover. J Appl Physiol. 1993;75:1798-806.