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Bucillamine-induced yellow nail syndrome

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A 74-year-old Japanese woman with chronic sinusitis and rheumatoid arthritis (RA), for which she has been on bucillamine (300 mg daily) and prednisolone (2.5 mg daily) for 12 years, presented with unilateral pleural effusion that appeared 2 years ago (Figure 1A). On examination, she had pitting edema of her extremities (Figure 1B). Additionally, her fingernails and toenails were distorted and yellow (Figure 1C-D), although there was no evidence of fungal nail infection on the potassium hydroxide preparation test. Laboratory test results, including thyroid function, were normal. Examination of the pleural effusion fluid showed that it was transudative with mostly lymphocytes (66.5%). Although a pleural biopsy was not done, results of the smear, culture, and polymerase chain reaction of the pleural effusion were negative for tuberculosis. Additionally, the adenosine deaminase level in the pleural effusion was not elevated (16.7 U/L). Evidence of malignancy in the cytologic diagnosis of pleural effusion was not confirmed. The echocardiogram was normal.

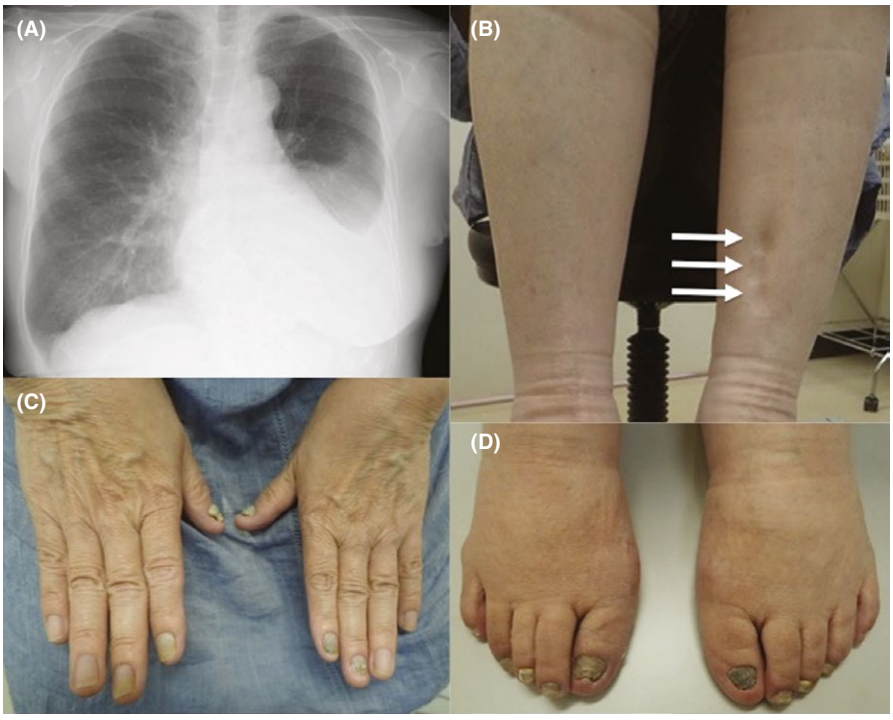

FIGURE 1 Radiograph showing unilateral pleural effusion lasting 2 years (A). Photographs showing edema of the lower extremities (arrows) (B) and yellow nails on the patient's fingers (C) and toes (D)

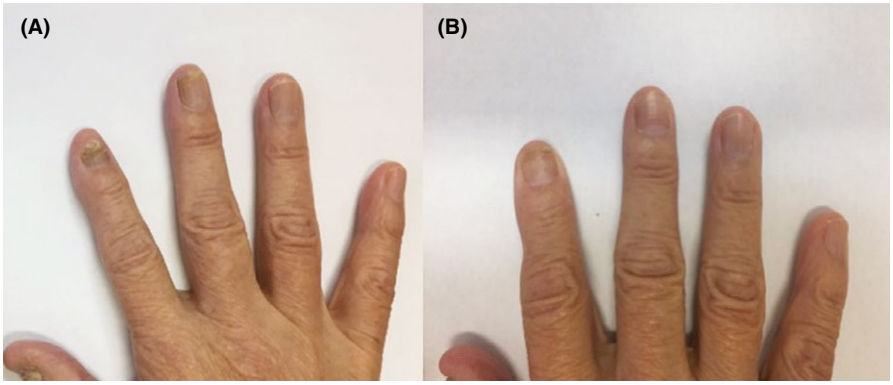

FIGURE 2 Photographs of the patient's fingernails on her right hand before (A) and 9 months after (B) stopping bucillamine treatment

As we suspected bucillamine-induced yellow nail syndrome (YNS), we changed bucillamine to methotrexate. At the follow-up examination 9 months after discontinuing bucillamine therapy, new fingernails were growing (Figure 2A-B). Bucillamine-induced YNS was diagnosed because of lymphedema, chronic pleural effusion, and improvement in yellow nails after discontinuing bucillamine therapy at 9 months, although edema of the lower extremities and pleural effusion remain.

YNS is a rare disease characterized by a yellow nail associated with lymphedema and/or various chronic respiratory manifestations (e.g, pleural effusion, bronchiectasis, and sinusitis),[1] of which the exact pathogenesis is still unclear. RA is one of the common underlying conditions of YNS, and it may have a causal association with spontaneous YNS.[2] In addition, bucillamine (thiol compounds), which is an analogue of D-penicillamine approved for treating RA in Japan, is implicated as the most common cause of drug-induced YNS in patients with RA.[3] Discontinuation of bucillamine results in improvement in yellow nails in 90% of patients; therefore, thiol compounds should be discontinued if YNS newly emerges. However, lymphedema and respiratory manifestations are frequently irreversible,[3] as in this patient.

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CONFLICT OF INTEREST

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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