LETTER TO EDITOR

Yellow nail syndrome: differentials and prognosis

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We read with much pleasure the article 'Yellow nail syndrome with complete triad' by Kuwahara et al., published in *The Netherlands Journal of Medicine*. The authors have done an excellent job in describing a patient with yellow nails, non-pitting leg edema and bilateral pleural effusions in the background of diffuse parenchymal micronodules.[1] The authors have tried to rule out various conditions including onychomycosis, tuberculosis, cardiac failure, renal failure, liver failure, hypothyroidism; and exposure to medications such as bucillamine and D-penicillamine. The reader needs to be aware that various underlying systemic diseases like connective tissue disease, malignancies, endocrine abnormalities, and immunodeficiency states can present with yellow nail. In fact, the most common connective tissue disease presenting with yellow nail syndrome (YNS) is reported to be rheumatoid arthritis.[2] Did the patient give a past history of rheumatoid arthritis? Knowing this is important, as patients with past history of rheumatoid arthritis treated with older disease-modifying agents such as gold, penicillamine, and bucillamine can present with YNS.[2] Even though many of these conditions can mimic yellow nail, the rate of nail growth in patients with a yellow nail syndrome is very slow compared to normal nail growth. Similarly, the triad of clinical manifestations of YNS is variable over time, and hence the presence of any two of three manifestations in the absence of other contributory cause could prompt the diagnosis of YNS. The authors have appropriately ruled out the presence of heart failure, and it is also prudent to rule out fungal infection of the nail with the help of microscopic visualization and fungal culture of the nail.

We would also like to add that yellow nail, being the most common presentation of YNS, has been reported to be successfully treated with vitamin E, zinc, the azole group of antifungals, and intralesional triamcinolone.[3] YNS secondary to drug treatment, have been reported to improve following withdrawal of offending agents. Pleural effusions have been treated with pleurodesis as mentioned by the authors. The median survival of patients with YNS has been reported to be 132 months, (11 years) and we beg to defer from the authors regarding its prognosis as being poor.[3]

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Response

Dear Dr. Paul van Daele, *Editor-in-Chief,*
Dear Dr. Mishra and colleagues,

Thank you for your constructive suggestions. As the authors described in 'Letter to Editor', the most important consideration when diagnosing yellow nail syndrome (YNS) is to rule out other possibilities that cause yellow-coloured nails. In our case, the patient did not have any symptoms which indicates connective tissue disease and had no past medical history of rheumatoid arthritis. His serological tumour markers were also

negative and multiple cytopathologic examinations of pleural fluid showed no malignancy. The rate of nail growth is also useful to diagnose YNS, since nail growth rate among patients with YNS is very slow compared to other differential diagnoses of yellow nails such as tinea unguium, pachyonychia, tetracycline, and hypothyroidism.[1] We agree with the authors that biopsies from his nails may rule out fungal infections, however, we failed to obtain his consent for such testing. As an alternative, we started antifungal agents, but the discoloration of his nail did not alter.

The authors also provided important insight into the treatment for YNS. We agree that several reports stated that vitamin E, clarithromycin, and azole antifungals were effective for the treatment of yellow nails accompanied with YNS, and that clarithromycin, in particular, may reduce lymphoedema and promote nail growth;[2] however, it is also true that a well-established treatment strategy still does not exist. But we do agree that consideration of these medications may reduce symptoms and lead to a true diagnosis.

The authors described prognosis of YNS on the basis of same references we cited, but we still believe that median diagnosed age of 61 years with median survival length of 132 months is still not enough to be considered long-term.[3] We appreciate the time and effort Dr. Mishra and colleagues have dedicated to provide us with insightful feedback on ways to strengthen our manuscript and to advance medicine for rare disorders.

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