Diuretic resistant oedema: nailing the diagnosis

Howard Fine¹, Xun Zhou¹, Colm Magee¹,² and Mark Denton¹,²

¹Harvard Medical School and ²Renal Division, Brigham and Women’s Hospital, Boston, Massachusetts, USA

Keywords: peripheral oedema; pleural effusion; Yellow Nail Syndrome

Introduction

Peripheral oedema is a commonly encountered clinical problem. Although it has many causes, its pathophysiology ultimately involves two processes: altered capillary haemodynamics and renal salt and water retention. A minority of cases are resistant to diuretic treatment; causes of such resistance include excessive sodium intake, poor diuretic drug absorption, reduced secretion of free diuretic into urine (for example, in nephrotic syndrome, renal failure, and heart failure), and lymphatic obstruction. We present a case of diuretic-resistant oedema associated with pleural and pericardial effusions. Only after extensive ‘negative’ investigations and subsequent careful clinical examination was the diagnosis of Yellow Nail Syndrome (YNS) made. This case highlights the importance of considering a broad differential diagnosis when managing peripheral oedema, particularly in the setting of diuretic resistance.

Case report

A 70-year-old woman with diabetes mellitus and hypertension presented with progressive dyspnoea and lower limb oedema. The oedema had been present for 15 years and was refractory to combined loop and thiazide diuretic therapy. Prior outpatient investigations had demonstrated normal cardiac function by echocardiography and patent lower limb deep veins by duplex ultrasound. One month prior to admission she had presented to another hospital with dyspnoea and was found to have bilateral pleural and pericardial effusions. The pleural effusions were drained with symptomatic relief and a pericardial window was created.

The patient denied cough, sputum production, or chest pain. She was a non-smoker. Medications were torsemide, metolazone, potassium chloride, metoprolol, metformin, and famotidine. The patient was afebrile, tachypnoeic (30 min); pulse was 80 min, and blood pressure 140/80 mmHg lying, 120/70 mmHg standing. The jugular venous pressure was not raised. Examination was further notable for stony dullness to percussion at the bases and marked pitting oedema of the lower limbs (see below).

Laboratory tests showed a plasma creatinine of 140 µmol/l, albumin 47 g/l, and a normal full blood count. She had a metabolic alkalosis secondary to diuretic therapy. Urinalysis was negative for protein. Chest radiograph revealed a normal cardiothoracic ratio and large bilateral pleural effusions (see below). Pleurocentesis yielded 1.1 and 0.6 litres of straw-coloured exudative fluid from the right and left lung bases, respectively (total protein 54 g/l, LDH 127 U/l, amylase 53 U/l, glucose 7.9 mmol/l, triglycerides 0.7 mmol/l, pH 7.64). Cytology, Gram stain and culture of the pleural fluid were negative. Histological examination of the pericardial tissue removed during the prior hospitalization showed proliferating mesothelial cells but no evidence of malignancy or infection. Repeat echocardiography showed a small pericardial effusion. Constrictive pericardial disease was excluded by cardiac catheterization.

The renal service was then consulted regarding management of diuretic-resistant oedema. On further inspection, the patient was found to have yellow, ridged, dystrophic nails, lacking lunulae. Specific questioning revealed that the fingernails and toenails had been extremely slow growing and had had a yellow discolouration for many years.

A diagnosis of YNS was made. The pleural effusions were drained and chemical pleurodesis performed.
The patient's dyspnoea subsequently improved. Her diuretics were reduced with correction of postural hypotension and metabolic alkalosis. She was advised to wear pressure support stockings.

Discussion

YNS was originally described in 1964 by Samman and White who observed in 13 patients the curious association of yellow, slowly-growing, dystrophic nails with recurrent peripheral oedema [1]. Subsequent authors have noted that exudative pleural effusions, pericardial effusion, bronchiectasis, and/or rhinosinusitis may also be associated with the syndrome. Organ-specific manifestations of the syndrome frequently present at different times; indeed all components of this syndrome rarely co-exist. Age of disease onset may vary from birth to late adult life. The precise aetiology remains unknown. Several authors posit that YNS is primarily due to a congenital structural deficit in lymphatic vessels. However, the recurrent nature of the oedema and the clinical and lymphoscintigraphic differences between YNS and classical lymphoedema argue against this hypothesis [2]. YNS has been associated with malignancy, thyroid disease, rheumatoid arthritis, immunodeficiencies including AIDS, and with the use of certain drugs, including penicillamine [3].

Pleurodesis with chemical irritants such as talc or tetracycline can be an effective therapy for the recurrent pleural effusions seen in YNS [4]. Pleuro-peritoneal shunts have also been used. Topical vitamin E and oral zinc supplementation have been successfully used for treating the nail disease, perhaps via anti-oxidant effects [5]. Unfortunately, the recurrent peripheral oedema of YNS remains a difficult problem, as it is often refractory to diuretics. Recognition of this fact is important since excessive diuresis may result in intravascular volume depletion and metabolic alkalosis as seen in this case.

Teaching points

(i) The diagnosis of YNS relies predominantly on clinical criteria alone: the key features, as here, being slowly growing yellow nails, peripheral oedema, and exudative pleural effusions.

(ii) Early diagnosis of YNS is important to minimize the morbidity and costs associated with excessive investigation and inappropriate treatment.

(iii) Lymphoedema, including that due to YNS, should be considered in the differential diagnosis of diuretic resistant oedema.

References


Fig. 1. Top panel shows fingernails with characteristic yellow discoloration, thickening, exaggerated longitudinal curvature, transverse ridging, and absence of lunulae and cuticles. Middle panel shows marked leg oedema. Lower panel (CXR) demonstrates bilateral pleural effusions.