Classic diseases revisited

Yellow nail syndrome

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Summary

The yellow nail syndrome was defined as a clinical entity in the 1960s. Although nail abnormalities were the first sign to be noticed, this syndrome is now known to involve multiple organ systems and its association with other diseases is well described. A review of the medical literature is provided.

Keywords: yellow nail syndrome

Yellow nail syndrome was first described by Samman and White¹ in 1964. Their original article summarised a series of 13 patients and referred to several other reports from 1927 and the early 1960s (box 1). Most of their patients suffered from ankle oedema and had slow rates of nail growth, ie, less than 0.2 mm per week compared to the normal 0.5–1.2 mm per week. Samman and White were also the first to suggest that an abnormality of lymphatic vessels may explain the pathogenesis of the syndrome. Two years later Emerson described the full triad of slow-growing yellow nails, lymphoedema, and pleural effusions,² while in 1972 Hiller *et al* reported that the presence of two of the three symptoms was sufficient to establish the diagnosis.³ Over the years the features of yellow nail syndrome have been extensively studied, with special emphasis on the involvement of the respiratory tract which is the site of the most distressing symptoms. Recently, it has been proposed that the frequent association of rhinosinusitis with yellow nail syndrome may warrant its recognition as part of the syndrome.⁴

Diagnosis

Yellow nail syndrome is a rare entity and its diagnosis is based on clinical criteria. Characteristically, laboratory findings are within normal limits.⁵ Emerson² defined the syndrome as the presence of the complete triad of dystrophic yellow nails, lymphoedema and pleural effusions but today it is accepted that diagnosis can be made in the presence of just two of these symptoms (box 2). It is noteworthy that yellow nails are found in 89% of cases, lymphoedema in 80% and pleuropulmonary symptoms in 63%.⁵ Yellow nail syndrome may be a diagnostic challenge since all three symptoms are evident in only a minority of patients.⁶

We treated a patient who suffered from long-standing lymphoedema and recurrent pleural effusions but no typical nail changes (box 3). Physical examination of the feet indeed revealed dystrophic nails which are probably not related directly to the syndrome because their colour and shape were not typical. The patient denied that his nails were ever yellow and insisted that they were not slow-growing. In the absence of yellow nails the syndrome is regarded as a diagnosis by exclusion. Therefore, the patient underwent a series of tests in order to exclude infectious, immune-mediated and neoplastic aetiologies of pleural effusion. The clinical findings and the negative laboratory studies supported the diagnosis of yellow nail syndrome.

Clinical features

NAIL ABNORMALITIES

Yellow nail syndrome has been shown to involve multiple organ systems (box 4). Historically, nail changes were the first to be recognised. The slow rate of nail growth may be accompanied by colour changes (pale yellow/green), onycholysis, and occasionally a distinct hump on the nail.¹ As mentioned above, a minority of patients lack nail changes. Moreover, spontaneous clearing of the nail changes has been reported without resolution of the respiratory involvement.⁷ Reversal of nail discolouration has also been noted after treatment of breast cancer.⁸ These cases indicate that the nail changes may be reversible and do not necessarily correlate with other manifestations of the syndrome. They may also be alleviated by local measures; topical use of vitamin E has been shown to improve nail symptoms clinically, with a corresponding increase in nail growth rate.⁹ Likewise, local injections of triamcinolone acetonide has resulted in a partial response.¹⁰

RESPIRATORY TRACT

Pleural effusion is usually the last clinical manifestation of yellow nail syndrome to appear.⁵ Usually it is clear, with a high content of protein, lactate dehydrogenase and white blood cells, predominantly lymphocytes,⁵ although

Yellow nail syndrome: historical aspects

1927–60: reports of 10 cases
1964: Samman and White describe the condition and coin the term 'yellow nails'.¹ This is the first description of a new syndrome of slow-growing nails with a characteristic appearance and oedema, usually affecting the ankles
1966: the syndrome is defined as the presence of a triad of yellow nails, lymphoedema and pleural effusion²
1972: the presence of two of the three symptoms is reported to be sufficient for the diagnosis of yellow nail syndrome
1994: rhinosinusitis may be recognised as part of the syndrome⁴

Box 1

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Yellow nail syndrome: diagnosis

Two of the following criteria:

- slow-growing nails (<0.5 mm/week)
- pleural effusion
- lymphoedema

Box 2**Yellow nail syndrome: features***Nails*

- discolouration (pale yellow/green)
- slow growth
- onycholysis

Respiratory tract

- pleural effusion
- restrictive/obstructive defects
- bronchiectasis
- rhinosinusitis

Oedema

- upper/lower limbs
- eyelids

Others

- chylous ascites
- pericardial effusion

Box 4**Case report**

A 58-year-old man was re-admitted several times to the day care service because of recurrent episodes of shortness of breath of about a year's duration. He had no history of malignancy or liver or renal disease nor of pulmonary disease prior to the past year. The patient complained of swelling of his legs for the last 30 years.

Physical examination showed a patient in a generally good condition with signs of mild jaundice. He had tachypnoea of 28/min with a blood pressure of 140/80 mmHg, pulse rate of 100 beats/min and normal temperature. The most prominent findings on physical examination were a massive pleural effusion at the base of the left lung and oedema of all four extremities. The oedema of the legs was most impressive, with an elephantiasis-like appearance, grey nails and lesions resembling Kaposi's sarcoma.

Laboratory studies revealed haemoglobin 18.9 g/dl, haematocrit 60.8%. Pleural puncture yielded 1200 ml of a clear fluid with 49 g/l protein, 23 g/l albumin, 381 U/l of lactate dehydrogenase and 7.9 mMol glucose. The fluid contained numerous lymphocytes, polymorphonuclears and mesotheliocytes but no malignant cells, and cultures of the fluid were sterile. Ziehl–Nielsen staining and mycobacterium cultures of the pleural effusion and of a gastric aspirate were negative. Spirometry tests showed an obstruction of small and large airways with poor response to bronchodilators. Repeated punch biopsies of the lesions on the calf skin were consistent with stasis dermatitis and not Kaposi's sarcoma, as suspected clinically.

Box 3

empyema has also been described.¹¹ No specific treatment has been devised to control the recurrent effusions. Usually a 'mechanical' approach is preferred, such as pleurodesis,¹² pleurectomy,¹³ or pleuroperitoneal shunting.¹⁴ Yellow nail syndrome may involve not only the pleura but also other serosal membranes. Pericardial effusion¹⁵ and chylous ascites with intestinal lymphangiectasia¹⁶ have rarely been reported.

Respiratory tract involvement in this syndrome may also include disease such as rhinosinusitis^{4,17–19} and bronchiectasis.^{17,20} Pulmonary function tests carried out in a series of patients have shown a combined restrictive and obstructive pattern.^{3,21} It is interesting to note that other cases have been described in which respiratory function tests were consistent with small airway disease with an irreversible obstructive defect,²² as in our patient.

LYMPHOEDEMA

Lymphoedema is the initial symptom in one-third of cases.⁵ It usually affects the upper or lower limbs (one report describes lymphoedema of the eyelids²³). It is advisable to care for the limbs using bandages, elevation and intensive treatment of infections. Recently, total resolution of yellow nails and lymphoedema was observed following oral zinc supplementation for two years and this may prove to be a specific treatment.²⁴ Diuretics have been found to have only a modest effect, insufficient to justify their use in most cases.^{3,21} It is also important to remember that, in the presence of lymphoedema, the administration of diuretics may result in severe intravascular volume depletion. Our patient had received diuretics prior to his arrival at the hospital and this was most probably the cause of his severe haemo-concentration, which was rapidly corrected by fluid replacement.

Association with other diseases

Yellow nail syndrome may be associated with a number of systemic diseases such as rheumatoid arthritis,²⁵ acquired immunodeficiency syndrome,^{26,27} tuberculosis,²⁸ immunologic disorders,^{6,15,29} malignancies such as carcinomas of the breast⁸ and gall bladder,¹⁷ and mycosis fungoides.³⁰ Yellow nail syndrome secondary to penicillamine use has also been described.³¹ There is some evidence that yellow nail syndrome may represent a premalignant disorder.⁶ Follow-up is especially important in patients whose diagnosis is made by exclusion.

1 Samman PD, White WF. The 'yellow nail syndrome'. *Br J Dermatol* 1964; 76: 153–7.

2 Emerson PA. Yellow nails, lymphedema and pleural effusion. *Thorax* 1966; 21: 247–53.

3 Hiller E, Rosenow EC III, Olsen AM. Pulmonary manifestations of the yellow nail syndrome. *Chest* 1972; 61: 452–8.

4 Varney VA, Cumberworth V, Sudderick R, Durham SR, Mackay IS. Rhinitis, sinusitis and the yellow nail syndrome: a review of symptoms and response to treatment in 17 patients. *Clin Otolaryngol* 1994; 19: 237–40.

5 Norkild P, Kroman-Andersen H, Struve-Christensen E. Yellow nail syndrome – the triad of yellow nails, lymphedema and pleural effusion. *Acta Med Scand* 1986; 219: 221–7.

6 Ben-Yehuda A, Ben-Chetrit E, Eliakim M. Yellow nail syndrome: case report and review of the literature. *Isr J Med Sci* 1986; 22: 117–9.

7 Decoste SD, Imber MJ, Baden HP. Yellow nail syndrome. *J Am Acad Dermatol* 1990; 22: 608–11.

8 Gupta AK, Davies GM, Haberman HF. Yellow nail syndrome. *Cutis* 1986; 37: 371–4.

9 Williams HC, Buffham R, du-Vivier A. Successful use of topical vitamin E solution in the treatment of nail changes in yellow nail syndrome. *Arch Dermatol* 1991; 127: 1023–8.

10 Abell E, Samman PD. Yellow nail syndrome treated by intralesional triamcinolone acetonide. *Br J Dermatol* 1973; 88: 200–1.

11 Lodge JP, Hunter AM, Saunders NR. Yellow nail syndrome associated with empyema. *Clin Exp Dermatol* 1989; 14: 328–9.

- 12 Jiva TM, Poe RH, Kallay MC. Pleural effusion in yellow nail syndrome: chemical plurodesis and its outcome. *Respiration* 1994; **61**: 300–2.
- 13 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.
- 14 Brofman JD, Hall JB, Scott W, Little AG. Yellow nails, lymphedema and pleural effusion. Treatment of chronic pleural effusion with pleuroperitoneal shunting. *Chest* 1990; **97**: 743–5.
- 15 Wakasa M, Imaizumi T, Suyama A, Takeshita A, Nakamura M. Yellow nail syndrome associated with chronic pericardial effusion. *Chest* 1987; **92**: 366–7.
- 16 Duhra PM, Quigley EM, Marsh MN. Chylous ascites, lymphangiectasia and the 'yellow nail' syndrome. *Gut* 1985; **26**: 1266–9.
- 17 Burrows NP, Jones RR. Yellow nail syndrome in association with carcinoma of the gall bladder. *Clin Exp Dermatol* 1991; **16**: 471–3.
- 18 Camilleri AE. Chronic sinusitis and the yellow nail syndrome. *J Laryngol Otol* 1990; **104**: 811–3.
- 19 Miro AM, Vasudevan V, Shah H. Ciliary motility in two patients with yellow nail syndrome and recurrent sinopulmonary infections. *Am Rev Respir Dis* 1990; **142**: 890–1.
- 20 Wiggins J, Strickland B, Chung KF. Detection of bronchiectasis by high-resolution computed tomography in the yellow nail syndrome. *Clin Radiol* 1991; **43**: 377–9.
- 21 Beer DJ, Pereira W, Snider GL. Pleural effusions associated with primary lymphedema: a perspective on the yellow nail syndrome. *Am Rev Respir Dis* 1978; **117**: 595–7.
- 22 Edwards C, Cayton R, Bryan R. Chronic transmural bronchiolitis: a non specific lesion of small airways. *J Clin Pathol* 1992; **45**: 993–8.
- 23 Maisels DO, Korachi AG. Lymphoedema of the eyelids in the yellow nail syndrome. *Br J Plast Surg* 1985; **38**: 93–6.
- 24 Arroyo JF, Cohen ML. Improvement of yellow nail syndrome with oral zinc supplementation. *Clin Exp Dermatol* 1993; **18**: 62–4.
- 25 Ichikawa Y, Shimizu H, Arimori S. Yellow nail syndrome and rheumatoid arthritis. *Tokai J Exp Clin Med* 1991; **16**: 203–9.
- 26 Goodman DS, Teplitz ED, Wishner A, Klein RS. Prevalence of cutaneous disease in patients with acquired immunodeficiency syndrome (AIDS) or AIDS-related complex. *J Am Acad Dermatol* 1987; **17**: 210–20.
- 27 Chernosky ME, Finley VK. Yellow nail syndrome in patients with acquired immunodeficiency disease. *J Am Acad Dermatol* 1985; **13**: 731–6.
- 28 Pang SM. Yellow nail syndrome resolution following treatment of pulmonary tuberculosis. *Int J Dermatol* 1993; **32**: 605–6.
- 29 Govaert P, Leroy JG, Pauwels R, Vanhaesebrouck P. Perinatal manifestations of maternal yellow nail syndrome. *Pediatrics* 1992; **89**: 1016–8.
- 30 Stosiek N, Peters KP, Hiller D, Riedl B, Hornstein OP. Yellow nail syndrome in a patient with mycosis fungoides. *J Am Acad Dermatol* 1993; **28**: 792–4.
- 31 Ilchyshyn A, Vickers CF. Yellow nail syndrome associated with penicillamine therapy. *Acta Derm Venereol Stockh* 1983; **63**: 554–5.