Case Report

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TANAFFOS

Yellow Nail Syndrome: Report of a Case Successfully Treated with Octreotide

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Yellow nail syndrome (YNS) is an uncommon condition characterized by a triad of yellow nail coloration, lymphedema and respiratory tract involvement. This syndrome typically affects middle-aged persons. Although several etiologies have been described, to date; the exact etiology remains unclear. Different treatment plans have been suggested, but all data available emphasize the fact that treatment is mainly symptomatic and the underlying disease is not targeted. The most reported treatment protocol is chemical pleurodesis combined with alpha-tocopherol (vitamin E). Hereby, we describe a case of YNS in a 34 year-old woman with the onset of symptoms in childhood. The symptoms improved dramatically after treatment with octreotide.

Key words: Yellow nail syndrome, Octreotide, Respiratory tract

INTRODUCTION

Yellow nail syndrome (YNS) is an uncommon entity first described by Samman and White in 1964 (1-5). Classically, it is described as a triad of yellow nail coloration, lymphedema and respiratory tract involvement. Two of the three classical symptoms are required to confirm the diagnosis of YNS (6,3). Almost always, YNS appears in middle-aged persons (7) and has rarely been reported in children (8). It is a very rare clinical condition and only about 100 cases have been reported since 1995. The exact etiology is unknown, yet several hypotheses have been proposed. The most common hypothesis emphasizes on a lymphatic anatomical or functional abnormality and a previously published report considered the capillary involvement as a possible cause (9), suggesting the pathology to be rather acquired than congenital (3). Coincidence with several autoimmune diseases and malignancies has been reported (2), which emphasizes on the importance of diagnostic workup for an underlying disease before starting symptomatic treatment, an approach emphasized by multiple experts. The treatment, although controversial, includes the treatment of the underlying disease (if diagnosed) or it is only symptomatic. The YNS can regress in 7-30% of the cases, spontaneously (2). Different approaches have been suggested for treatment, most of which with a satisfactory success rate. This case report reviews the literature and

describes YNS in a 34 year-old woman, with the onset of symptoms in childhood, which was successfully treated with intravenous (IV) octreotide (10).

CASE SUMMARIES

A 34 year-old woman presented with dyspnea, which had begun progressively in the past two months. She also complained of right leg swelling from childhood, and a tendency of koilonychia was noted when she was 18. She did not complain of weight loss, anorexia, night sweat or malaise. She had no medical or surgical history, and the family history was negative for any disease. She was a non-smoker, denied alcohol consumption and did not use illicit drugs. On physical examination, she was a thin woman (weigh: 45 Kg, BMI: 23) with no malaise. Vital signs included blood pressure of 110/60 mmHg, pulse rate of 80 beats/minute, respiratory rate 16 breaths/minute and body temperature of 36.8°C. There was no lymphadenopathy, ascites or upper extremity edema. Heart sounds were normal. Lung auscultation revealed decreased left side respiratory sounds, accompanied by diminished tactile fremitus and a slight deadened tone in the same region. Yellowish concave nails and right leg edema were noted. Based on these findings, YNS was our first diagnosis, since the patient presented the complete triad of this syndrome. Chest X-ray revealed massive right-sided pleural effusion and mild shift to the left. Consequently, we continued our diagnostic workup with a computed tomography. There was massive right sided pleural effusion, with extension to the azygoesophageal recess and a major fissure leading to passive collapse of the underlying lung, and consequent contralateral shift of the heart and the mediastinum (Figure 1). The aerated lungs were hyper perfused in the context of a probable degree of pulmonary hypertension. Based on these imaging findings, we decided to perform thoracocentesis, with the following results of pleural fluid analysis: protein=8 g/dL, WBC=850/μL, lymphocytes=85%, glucose=124 mg/dL, lactate dehydrogenase (LDH)=162 IU/L, cholesterol=91 mg/dL, triglycerides (TG)=821 mg/dL and albumin=3.8 g/dL. Simultaneous blood analysis showed the following results: erythrocyte sedimentation rate (ESR)=120 mm/h, serum albumin=4.8 g/dL, LDH=253 IU/L, cholesterol=170 mg/dL and TG=65 mg/dL. The cytology of pleural fluid revealed only lymphocytosis and the cultures for bacteria, mycobacterium and fungi were negative. Pleural biopsy was the next step, justified by the dominant exudative lymph pleural fluid aspect, which revealed chronic inflammation. The pathology report ruled out alternative diagnoses like malignant processes – absence of cells with nuclear anomalies, aspergillosis – no visible branching structures, hyphae, absence of caseating or non-caseating granuloma, and the diagnosis of YNS was confirmed. At this stage, we initiated the treatment with pleurodesis with talk powder. However, during the follow up visits, no improvement was seen and repeated thoracocentesis was performed because of refractory fluid buildup in the pleural space. Furthermore, we tried to treat the patient with orally administered medium chain fatty acids and intravenous (IV) octreotide. The administration protocol for octreotide was as follows: IV Octreotide 100 mcg 3 times/day (TID) for 3 days, followed by 50 mcg TID for one week, then 50 mcg daily for 3 weeks (Figure 2), with a 3-month follow-up. After the 3 months, the patient's symptoms improved and there was no visible fluid accumulation on chest roentgenogram.

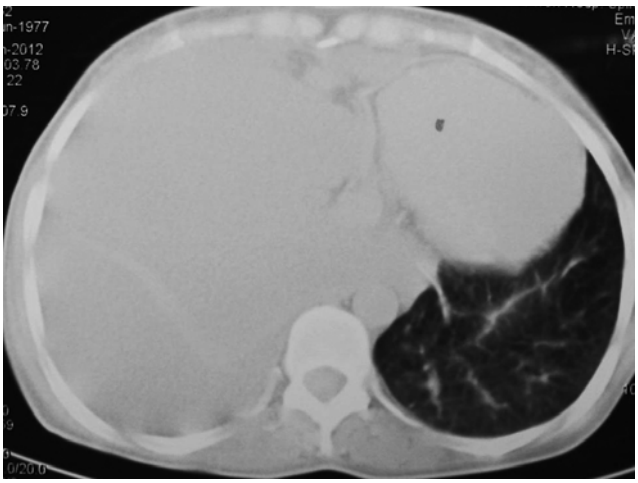

Figure 1. Right-sided massive pleural effusion associated with passive collapse of the underlying lung, and consequent contralateral shift of the heart and the mediastinum.

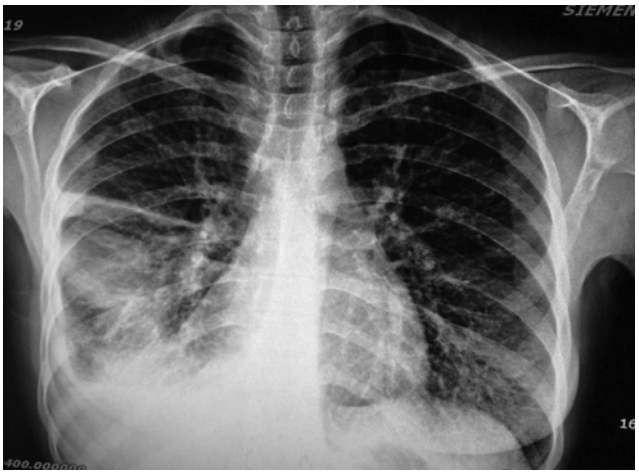

Figure 2. Chest X-ray after treatment with octreotide during hospital admission.

DISCUSSION

The YNS is a rare syndrome characterized by a triad of respiratory involvement, discoloration of nails and lymphedema. Although it often occurs sporadically, several cases may be inherited (11). Diagnosis of YNS is made based on clinical findings, in which two of the three components of the classical triad are adequate for diagnosis. Associations of YNS with the following malignant or autoimmune conditions have been described: autoimmune hypothyroidism (1), membranous glomerulonephritis (2), xanthogranulomatous pyelonephritis (4), minimal change disease (12), carcinoma of the larynx (13), common variable immunodeficiency (CVID) (14), breast cancer (15), arteriovenous fistula in a patient with end stage renal disease (16). Drug induced YNS have been reported as a consequence of treatment with penicillamine (5) and bucillamine in a patient with rheumatoid arthritis (17). Since YNS disappeared after treatment of the underlying disease (12,18) in many cases, the emphasis should be placed on the diagnosis and treatment of the underlying pathology, before starting symptomatic treatment. Respiratory involvement is one of the three manifestations of YNS, with the most frequent presentation being pleural effusion. It is usually bilateral, (1) yet there were previous cases with unilateral involvement (3,4,6,19). Although it is usually an exudative pleural effusion, there are rare cases in which it has the appearance of a frank chylothorax, with lymphocyte predominance. The gross appearance of the fluid is milky (1) or cloudy (2,6,3). The LDH levels of the fluid are often high (2,4) and the protein levels are 4-5 g/dL (1,3,4). The concentrations of cholesterol and triglycerides of the fluid are consistent with chylous ascites (5). Histopathology of pleura is nonspecific, with fibrotic changes (1,2,3,6,7). Other respiratory manifestations include chronic paranasal sinusitis, recurrent respiratory tract infections and bronchiectasis (2). The underlying reasons for development of bronchiectasis are not completely understood (3). Nail discoloration is another manifestation of YNS occurring in one third of patients (yellow-greenish discoloration of nails). Other nail abnormalities include overcurvature, thickening, shrinking, onycholysis, slow growth and loss of lanulae and cuticles, and their mechanisms have yet to be understood (2,3). Lymphedema, as an important manifestation of YNS, is a part of the classic triad and is usually confirmed by lymphangiography (2,3). Edema is observed mostly in the legs and treatment has been based on exercise and use of elastic bandage in the majority of the former cases (2,3). Diuretics have not shown any benefit (2).

Our patient was a 34 year-old woman, with the onset of one symptom in childhood. The patient showed the triad at the time of diagnosis. This is beyond the usual age at which this syndrome presents. Pleural effusion, in this case, was right sided. Other characteristics of the fluid, such as TG level, were similar with the cases previously described in the literature. Lymphedema was right sided and as likely as the pleural effusion. The most common treatment, used for successful treatment of almost all the former cases, is chemical pleurodesis with materials such as picibanil, (20,19) tetracycline (21) and talk powder (22). Other treatment modalities for treatment of YNS available in the literature in order of frequency include: oral and topical alpha-tocopherol (vitamin E) (3, 11, 23-27), enteral azoles (23, 26, 28), systemically administered corticosteroids (most often in cases associated with

underlying autoimmunity, such as rheumatoid arthritis or glomerulonephritis) and topical corticosteroids (2,27). Rarely, fluorouracil (29), vitamin A (26), oral zinc (30), diuretics (23) and dimethyl sulfoxide have been used with different results. However, further trials are necessary to confirm their efficacy. Given the probable etiologies of YNS, it is necessary to find out which treatment approach would be most suitable for the given etiology of YNS in each particular case. However, this task will be very difficult because of the low frequency of YNS. Fortunately, octreotide treatment is relatively safe, with only minimal transitory side effects (gastrointestinal discomfort, vagal inhibition symptoms at the gastrointestinal level, vomiting and sweating) with variable intensities.

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