Yellow Nail Syndrome Associated with Pericarditis and Pericardial Effusion: a Case Report

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Abstract- Yellow nail syndrome (YNS) is an uncommon condition characterized by nail changes, lymphedema, in addition to pulmonary disorders and pleural effusion. Pericarditis and non-cardiac disorders can evolve with pericardial effusions including autoimmune conditions, hypothyroidism, malignancies, tuberculosis, and uremia. A 72-year-old Brazilian woman under treatment for arterial hypertension and hypothyroidism was admitted with pericarditis and pericardial effusion concomitant with yellow nail syndrome. She denied tobacco smoking, alcohol abuse, and similar disorders in her family. Clinical and complementary evaluation ruled out infectious diseases, malignancies, and autoimmune disorders as etiologic factors in this case. Hypothyroidism is a well-known cause of pericardial effusion, the vast majority in the absence of pericarditis, and has been described as an associated condition in some individuals with YNS. Case studies might contribute to better understanding of these causal or casual relationships.

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Introduction

The yellow nail (YNS) syndrome is an uncommon condition of unclear etiology, and about a hundred cases have been described since 1964. YNS is characterized by nail changes, recurrent respiratory disturbances, and lymphedema, and two of the features can indicate this clinical diagnosis (1-8). Chest disorders include asthma, bronchitis, sinusitis, bronchiectasis, pneumonia, and pleural and pericardial effusions. The nail changes may be slow growth, thickening, hardening, excessive convexity, transversal ridging, onycholysis, onychorrhexis, paronychia, deficient cuticles, and absence of lunules (1-8). Pericardial effusion may follow pericarditis and also occur in non-cardiac conditions such as autoimmune disturbances, hypothyroidism, malignancies, tuberculosis, uremia, or iatrogenic effect (9). Hypothyroidism is a known cause of pericardial effusion without pericarditis; moreover, this endocrine disorder can be related to the development of the YNS (1). The mechanisms of the syndrome remain elusive because the respective studies are scarce (4,7). The objective is to report a patient with YNS, hypothyroidism, and pericarditis with effusion. Case studies may contribute to better understanding of the pathogenic mechanisms of YNS.

Case Report

A 72-year-old Brazilian woman under treatment for arterial hypertension and hypothyroidism with losartan 50 mg plus amlodipine 5 mg twice-daily, and levothyroxine 100 mcg once a day, was admitted at Emergency Section claiming of accentuated thoracic pain and breathlessness. She denied tobacco smoking, alcohol abuse, or previous episodes. Physical examination showed Body Mass Index (BMI) 29 kg/m2, temperature 36.7oC, blood pressure 115/ 71 mmHg, heart rate 110 bpm, and respiratory rate 20 ripm. There were signs of left pleural effusion and pitting edema of

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extremities, in addition to ungual dystrophic changes with a yellowish discoloration (Figure 1).

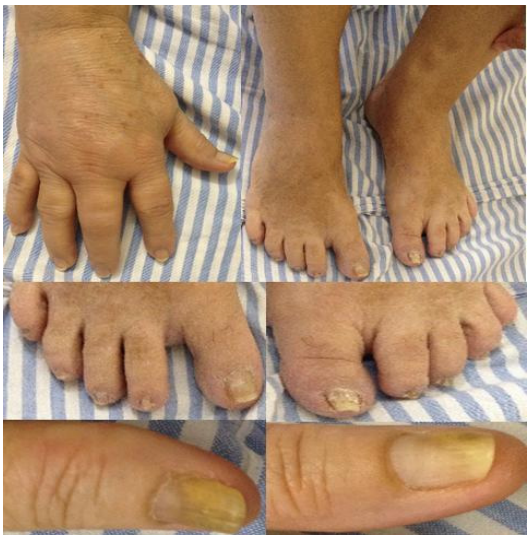

Figure 1. Slight symmetric pitting pretibial, ankle and hand edema; the nails show a yellowish discoloration of distal one-third of the plaque, thickening, and hyperkeratosis, in addition to excessive transverse curvature and onychorrhexis

Laboratorial determinations showed white cells 13.59 x 109/mm3, red cells 4.18 x 1012/mm3, hematocrit 37.8%, hemoglobin 12.9 g/dL, and platelets 420 x 109/ mm3, urea nitrogen 25.8 mg/dL, creatinine 0.8 mg/dL, albumin 3.11 g/dL, globulins 3.8 g/dL, calcium 1.19 mmol/L, sodium 140 mmol/L, potassium 4.4 mmol/L, magnesium 1.8 mEq/L, glucose 97 mg/dL, ALT 91 U/L, AST 13.4 U/L, alkaline phosphatase 99.2 U/L, prothrombin activity 82%, INR 1.13, TTPA 0.637, gamma-GT 280 U/L, ESR 39 mm/h; C-reactive protein 14.6 mg/dL, TSH 0.84 µIU/mL, free T4 1.63 ng/dL, procalcitonin 0.036 ng/mL, troponin T 0.008 ng/L, CKMB 0.325 ng/L, pro-BNP 501.5 pg/mL, C3 complement 162.81 mg/dL, C4 complement 40.36 mg/dL, rheumatoid factor 21.1 IU/mL, anti-citrullinated protein antibody negative, and ANA 1:160 IU/mL with nuclear dense fine speckled pattern on HEp-2 cells (cytoplasmic and nucleolar negative, and metaphase chromatin positive). The levels of tumor markers were unremarkable CA 15.3: 10.35 IU/mL, CA 19.9: 16.79 IU/mL, CA 125: 15.49 IU/mL, alfa-fetoprotein: 0.693 IU/mL, and carcinoembrionic antigen (CEA): 1.03 ng/mL. The intradermal Mantoux test (PPD) was negative. The chest radiography revealed the pleural effusion. The EKG changes were not suggestive of pericardial effusion, which was further confirmed by transthoracic echocardiogram (Figure 2).

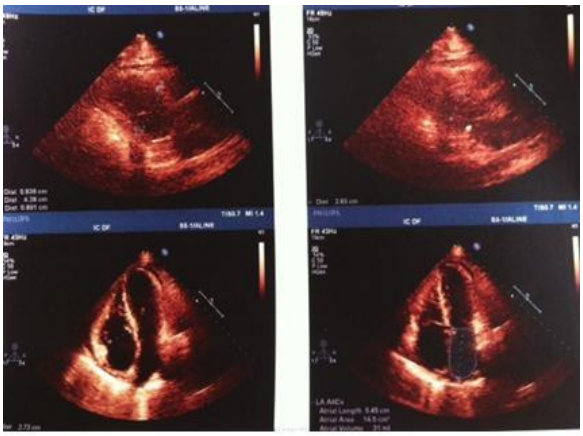

Figure 2. Images of the transthoracic echocardiogram showing thickened pericardium and pericardial effusion

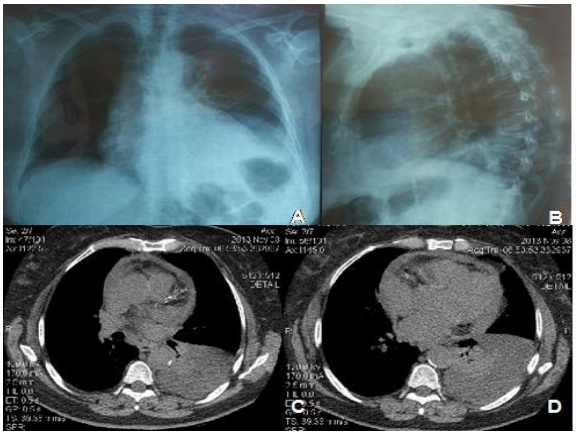

Figure 3. A and B: Chest radiography on admission, showing enlarged heart silhouette, elevation of the left diaphragmatic dome and left pleural effusion; **C and D**: CT of the thorax revealing pericardial thickening and effusion, in addition to partial left lung atelectasis associated with pleural effusion

Pericardiocentesis with biopsy was then performed and disclosed a chronic fibrinous pericarditis; and the fluid contained red cells 56.550 /mL, protein 4.57 g/dL, DHL 1.175 UI/L, glucose 90 mg/dL, white cells 550 /mL (95% mononuclear). The angio-computed tomography ruled out the hypothesis of pulmonary thromboembolism, and showed pericardial and pleural effusions, in addition to partial collapse affecting the pulmonary lingual and left basal segments (Figure 3). Arterial gasometry showed pH 7.35, pCO2 39.7 mmHg, pO2 70.2 mmHg, HCO3 21.4 mmol/L, total CO2 19.3 mmol/L, base excess -3.3 mmol/L, O2 saturation 91.9%, and anion gap 8.4 mEq/L. The patient evolved with fever and dyspnea, and about 700ml of pleural fluid were drained. Pleural biopsy samples showed chronic inflammatory changes with the absence of granulomas. The search for AAFB and the determination of

adenosine deaminase were negative; moreover, the PPD test was negative; these findings contributed to the exclusion of tuberculosis. The tests for collagen diseases were either inconclusive or negative, and this etiology was also ruled out. The patient improved well with clinical management and was discharged for outpatient follow-up. The association of YNS with chronic pericarditis and pericardial effusion was not well clear.

Discussion

We report the case of a 72-year-old Brazilian female with YNS, pericarditis, and pericardial effusion, and hypothyroidism. Pleural as well as pericardial biopsies and the evaluation of the drained fluids from both cavities ruled out infectious agents, malignancies, and collagen diseases. As herein reported this syndrome has been more often found in middle-aged and elderly females. The etiology of YNS is related to primary or secondary disturbances of lymphatic drainage, which may be permanent or reversible depending upon the nature of associated conditions (1-8). Pericardial effusions are described in some of the individuals with YNS; nevertheless, this manifestation is not a classical component of the triad and did not have merit major emphasis (8). More frequently, pericardial effusion can constitute an additional finding in some patients due to concomitant conditions as polyserositis, hypoalbuminemia, malignancy and hypothyroidism (5). The fluid is frequently a transudate or exudate, but chylous effusions have been reported (2). Malek *et al*., reported the YNS in a young male with pleural and pericardial chylous effusions related to lymphangiectasia, that was controlled by albumin and middle chained triglycerides (2). Jung *et al*., reviewed the etiologies of pericardial effusions in 1612 patients from six countries and reported infection: 2%-69.6%, malignancy: 9.4%-52.6%, idiopathic: 3.4%-48%, iatrogenic: 6%-42%, uremia: 2%-22%, collagen disease: 1%-10%, and hypothyroidism in only 2%-7.8% (9). The pericardial cavity of normal individuals may contain from 10 to 50ml of a transudative fluid. Based on the fluid volume, pericardial effusions are classified as minimal (50-100ml), small (100-250ml), moderate (250-500ml), and those greater than 500ml are considered large (9). Pericardiocentesis is done to control large or symptomatic effusions, with or without tamponade. Transthoracic echocardiography is the gold standard tool for the diagnosis of pericardial effusion, and to guide percutaneous needle procedures to drain fluid or to obtain pericardial specimens (9). In this case study, both fluid and pericardial tissue samples were obtained with diagnostic purpose; however, the results of the respective analysis were unremarkable to establish the etiology. Because the laboratory tests also did not characterize the exact origin of this pericarditis with effusion, no identifiable etiology was found, and it was considered idiopathic (9). The initial concern was about the possible role of hypothyroidism, which can be associated with YNS (1) and is a well-known cause of pericardial effusion of variable volumes (9-12). However, pericardial effusions due to hypothyroidism have decreased from up to 80% to 2-7.8% of cases (9,12), and the exceedingly rare cholesterol pericarditis was not characterized in this case study. In addition to hypothyroidism, this exceptional modality of chronic pericarditis has been reported in association with tuberculosis and rheumatoid arthritis and has distinctive aspects: a fluid with cholesterol level above 70 mg/dL, and tissue samples containing crystals of cholesterol (10). Cholesterol pericarditis results from a chronic granulomatous response of the foreign body type, elicited by longstanding deposits of crystallized LDL-cholesterol in the pericardial membrane (10). Thickened pericardium has a lower absorptive capacity, which leads to pericardial effusion (10). Therefore, this diagnostic hypothesis was ruled out with a base on the complementary evaluation.

In conclusion, idiopathic seems to be the main hypothesis for pericarditis with effusion in this patient because no other etiologic factor could be disclosed during this period of investigation. Notwithstanding, one cannot rule out definitely the possibility of some underestimated causal relationship between pericardial manifestations and the still unclear mechanisms of the YNS.

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