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CASE REPORT

Acute respiratory failure due to cutis laxa pulmonary emphysema treated with high-flow nasal cannula

Tommaso PERAZZO [1, 2], Alessandro PERAZZO [1], Gianluca FERRAIOLI [1], Teresa DIAZ DE TERAN [3], Monica GONZALES [3], Paolo BANFI [4], Antonello NICOLINI [1, 4] *

[1]Respiratory Diseases Unit, General Hospital, Sestri Levante, Genoa, Italy; [2]Respiratory Diseases and Allergy Clinic, Genoa, Italy; [3]Division of Pulmonology, Hospital Universitario Marqués de Valdecilla, Santander, Spain; [4]Rehabilitation Pulmonology, IRCCS Don Gnocchi Foundation, Milan, Italy

*Corresponding author: Antonello Nicolini, Respiratory Diseases Unit, via Terzi 43, 16039 Sestri Levante (GE), Italy.
E-mail: antonellonicolini@gmail.com

ABSTRACT

Cutis laxa is a rare connective tissue disorder characterized by progressive loosening of the skin, associated with abnormalities of other organs such as the lung. We present a case of this disease with pulmonary emphysema and acute respiratory failure successfully treated with high-flow nasal cannula.

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KEY WORDS: Pulmonary emphysema; Cutis laxa; Respiratory insufficiency; Cannula.

Congenital connective tissue pathologies (Marfan Syndrome, Ehlers-Danlos Syndrome, cutis laxa) are rare causes of pulmonary emphysema. Cutis laxa syndrome (CL) is a group of rare heterogeneous diseases, congenital or acquired, whose common denominator is the disruption of elastic tissue that can cause lesions in any organ containing elastic tissue (skin, lungs, vessels).[1] The early development of emphysema is usually limited to autosomal recessive forms, resulting in death in early childhood.[2] The autosomal dominant form rarely presents with emphysema development, mainly because these are young, non-smoking patients without alpha1-antitrypsin deficiency. Only a few rare cases have been reported in the literature. We describe a case of panlobular emphysema, with greater involvement of the lower lobes, which rapidly progressed to respiratory failure requiring treatment with a high-flow nasal cannula (HFC).

Case report

Clinical history

The 58-year-old patient reported worsening of her usual dyspnea to minimal effort (grade 3 mMRC) for 4 months. She had no significant family history or recurrent pathological data. Until then, the patient had been in good health. The patient was a non-smoker. No high-risk occupation.

The patient has consented to the publication of data relating to her clinical case.

Physical examination

The resting respiratory rate (RR) was 18 breaths per minute and the basal oxygen saturation (SpO_2) was 94%.

At the skin level, there was wrinkled skin as-

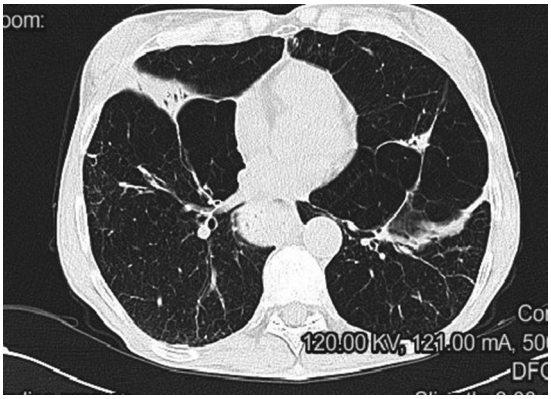

Figure 1.—Typical appearance of the face with cheeks with "mastiff" appearance and excessively wrinkled skin with prematurely aged appearance.

sociated with predominantly flaccid folds in the loose regions of the folds and typical facial features with "mastiff-like" cheeks and excessively wrinkled skin with a prematurely aged appearance (Figure 1).

Physical examination of the chest showed hypersonnant note and a marked reduction of the breath sound mainly at baseline.

Laboratory results

The results of functional laboratory and respiratory tests were as follows: forced vital capacity (FVC) 116% (3.63 L), peak expired volume in 1 second (FEV_1) 56% (1.50 L) FEV_1/FVC% 41, total lung capacity (TLC) 120% (6.37 L) residual volume (RV) 142% (2.73 L), carbon monoxide diffusion test (DLCO) 57.

Chest X-ray and computed axial tomography (CT) showed bullous emphysema mainly involving the lower lobes (Figure 2).

Echocardiography showed mitral prolapse, but pressures remained within normal limits. Dose of al-fa1-antitrisin 187 mg/dL (normal values 90-200 mg/dL).

Evolution

During follow-up the patient presented a sudden worsening of the clinical and functional respiratory picture (FVC 57%, FEV_1 29%, CPT 266%, RV 293% DLCO 36%) as well as gasometrical presenting respiratory insufficiency (PaO_2 55, $paCO_2$ 44, pH 7.37 with FiO_2 0.21) which initially benefited from low flow oxygen therapy (2

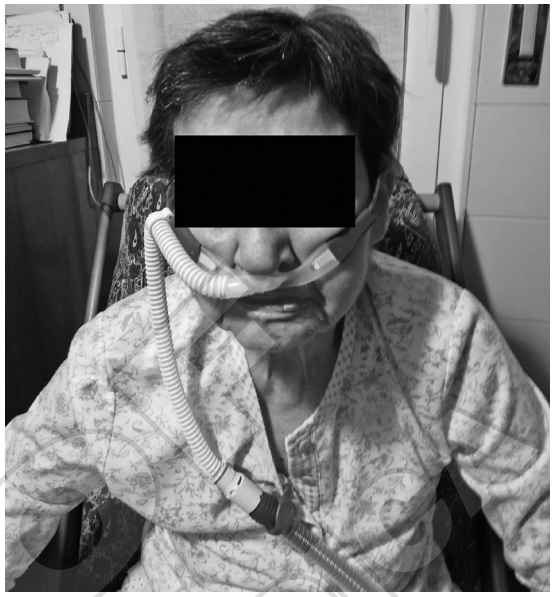

Figure 2.—Chest CT presence of pulmonary emphysema of bullous dystrophic type at the lower lobes.

L at rest, 6 L during exercise). About 2 months later, new worsening with an episode of acute respiratory failure (PaO_2 34, $PaCO_2$ 53 pH 7.35, PaO_2/FiO_2 166) and tachypnoea (RR around 28 bpm), initially treated with oxygen therapy with Venturi mask 60%, but with little improvement in PaO_2. In this situation, it was decided to start non-invasive ventilation (NIV) in bi-level mode (positive inspiratory airway pressure — IPAP 10 cmH_2O and positive expiratory airway pressure — EPAP 4 cmH_2O and FiO_2 60%) with an initial improvement in gas exchange, although this had to be discontinued due to poor tolerance on the part of the patient. It was then decided to start treatment with high-flow nasal cannula (HFNC) (FiO_2 100%) which, together with maximum optimization of medical treatment, led to a final improvement in the patient's oxygenation (PaO_2/FiO_2 [P/F] 240 in constant improvement until reaching P/F 300 after 48 hours). The patient is currently on HFNC at home with a reduction of FiO_2 to 70%.

Discussion

Lower lobe emphysema is a pathology rarely found in non-smoking patients without alpha1-antitrypsin deficiency. In the case that came to

our attention, it was associated with a clinical diagnosis of cutis laxa. CL groups together a series of clinically and genetically heterogeneous conditions, characterized by cutaneous hyperlaxity, with abnormally elastic and flaccid skin in the presence of numerous folds and wrinkles that give the skin a wrinkled appearance, predominantly in the regions free of the folds and in the facial features with a prematurely aged appearance. This characteristic semiological appearance is the result of various connective tissue abnormalities that may be congenital or acquired. Inherited forms include autosomal dominant CL (ADCL), autosomal recessive CL (ARCL), Urban-Rifkin-Davis syndrome (URDS), macrocephaly-alopecia-CL-scoliosis syndrome (MACS), arterial tortuosity syndrome (ATS) and X-linked CL (CLLX)1. Among the modes of transmission, the autosomal recessive form is characterized by more severe clinical manifestations. This form usually involves cardiopulmonary involvement, especially emphysema, diaphragmatic abnormalities, arterial malformations and aneurysms.[1, 3-5] Joint laxity and muscle hypotonia are also observed. Patients often die of pulmonary or cardiac complications in early childhood.[5-7] In the autosomal dominant form, skin involvement can occur from birth or later in early adulthood.[7, 8] They present with flaccid, inelastic and redundant skin that often worsens with age. Previously, the autosomal dominant form of CL was considered a benign skin disorder with few systemic lesions.[8] However, subsequent research has shown that emphysema and aortic aneurysms[5] are part of the phenotypic profile of this syndrome and can lead to significant morbidity and mortality. Approximately 30% of patients with the dominant form of CL have a new mutation. The genetic abnormality responsible for this form is a genetic mutation affecting the elastin gene ELN.[1, 5] The mechanism of development of emphysema in ADCL involves elastic fibers, which are extracellular matrix (ECM) structures composed essentially of fibrillin and elastin microfibrils that provide structural and mechanical support to different tissues.[9-12] In addition, they are necessary for the regulation of the bioavailability of several growth factors, such as transforming growth factor beta (TGFB).[13] The most common molecular abnormalities of the autosomal dominant form of CL are frameshift mutations found in exons 30, 32 and 33 at the 3 end of the ELN gene. These mutations are responsible for the production of elastin in a normal amount but whose function is altered.[14] In addition to impaired ventilatory mechanics, mutant elastin expression is also associated with increased TGFB signaling and, consequently, activation of cell apoptosis. Several studies have shown that these mechanisms are strongly implicated in the development of emphysema.[2, 14, 15] A better understanding of these mechanisms could lead to specific treatments for emphysematous disease in the context of lax skin and the more common forms of emphysema typical of chronic obstructive pulmonary disease.

Conclusions

Cutis laxa syndrome is represented by a group of rare elastic tissue diseases, which can be acquired or inherited, characterized by cutaneous hyperelasticity associated with variable systemic manifestations. Early diagnosis allows for better patient management. This management has four components: investigation, monitoring and treatment of the associated systemic manifestations, identification of modes of transmission that may allow genetic counselling, psychological support for the patient and family, and plastic surgery to correct the cutaneous manifestations. Respiratory symptoms are often present and require early and thorough pneumological evaluations.

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