

CHALLENGES IN THE MANAGEMENT OF LONG-TERM CORTICOTHERAPY TREATMENT AT SMOKER PATIENT WITH SEVERE ASTHMA

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Rezumat

Astmul reprezintă o boală cronică obstructivă care, în pofida metodelor moderne de diagnostic și tratament, rămâne o patologie cu morbiditate și mortalitate crescută. Corticoterapia orală a reprezentat pentru aproape un secol principala terapie indicată în astmul sever, crescând calitatea vieții pacientului prin scăderea severității și frecvenței crizelor astmatice. Dezavantajele administrării corticoterapiei sistemice pe termen lung rezidă din prevalența crescută a efectelor adverse. În ultimii ani asistăm la o creștere a administrării terapiilor biologice țintite și în acest context ne întrebăm care este rolul actual al corticoterapiei în managementul astmului sever.

Prezentăm cazul unei paciente în vârstă de 49 ani, fumătoare (25PA), care a fost diagnosticată în urmă cu 20 de ani, clinic, biologic și spirometric cu astm, pentru care a urmat tratament cu prednison 10 mg/zi. Scopul lucrării actuale este de a demonstra impactul potențialelor efecte pe termen lung ale administrării corticoterapiei la o pacientă fumătoare astmatică care prezintă criterii clare de inițiere a unei terapii biologice.

Cuvinte cheie: astm bronșic, corticoterapie, terapie biologică, reacții adverse.

Abstract

Asthma is a chronic obstructive disease with high morbidity and mortality despite modern diagnostic and treatment methods. Oral corticosteroid therapy has been the mainstay treatment for severe asthma for almost a century, improving the patient's quality of life by reducing the severity and frequency of asthma attacks. However, long-term systemic corticosteroid administration has disadvantages owing to the increased prevalence of adverse effects. In recent years, the use of targeted biological therapies has increased, prompting us to question the current role of corticosteroid therapy in the management of severe eosinophilic asthma. We present the case of a 49-year-old female patient, who smoked (25 pack-years) and was diagnosed with asthma 20 years ago based on clinical, biological, and spirometric criteria. The patient was treated with prednisone (10 mg/day). This study aimed to demonstrate the potential long-term effects of corticosteroid administration in smokers with severe asthma who had clear criteria for initiating biological therapy.

Keywords: asthma, corticosteroid therapy, biological therapy, side effects



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Introduction

Asthma is defined as a chronic obstructive condition that causes airflow limitation with reversible clinical and functional characteristics, both spontaneously and under bronchodilator therapy. The key element of asthma is inflammation triggered by contact of the airways with an allergenic substance, resulting in the sudden onset of typical symptoms such as dyspnea, chest tightness, cough, and wheezing. Substances contained in conventional cigarettes contribute to the inflammatory cascade by disrupting the balance between antioxidant and pro-oxidant agents.

Diagnosis was confirmed through a comprehensive medical history, focusing on symptoms, comorbidities, and potential allergens, along with laboratory tests and respiratory function evaluations. Determining the allergen agent often represents a challenging process that requires collaboration between the pulmonologist and the allergist. Inhaled corticosteroid therapy currently represents the most effective treatment for managing asthma symptoms, and emphasis on understanding the correct administration technique prevents unnecessary escalation of treatment. A small percentage of patients experience frequent severe attacks that cannot be controlled despite efforts to administer maximum inhalation therapy with

repeated technique checks and the use of antihistamines, resulting in the addition of systemic oral corticosteroid therapy. Until recently, oral corticosteroid therapy was the only treatment modality for uncontrolled severe asthma, and we now have new therapies that promise to improve the quality of life of asthmatic patients with a reduced frequency of adverse effects.

In this article, we describe the case of a 49-year-old female patient, a smoker, with documented multiple allergies (aspirin, NSAIDs), no exposure to occupational hazards, and diagnosed with severe allergic asthma in 2002, who presented at the hospital during an asthma attack. The particularity of this case is the long-term impact of oral corticosteroid therapy instituted in a 26-year-old patient with asthma, along with additional risk factors for smoking.

Case presentation

As previously mentioned, we present the case of a female patient, 49 years old, a smoker (25 pack-years) with a history of severe asthma treated with salmeterol/fluticasone propionate (50/500 µg) and prednisone 10 mg/day, with multiple attempts to discontinue oral corticosteroid therapy, chronic rhinosinusitis, and operated nasal polyposis. She presented to the hospital with worsening dyspnea accompanied by wheezing and chest

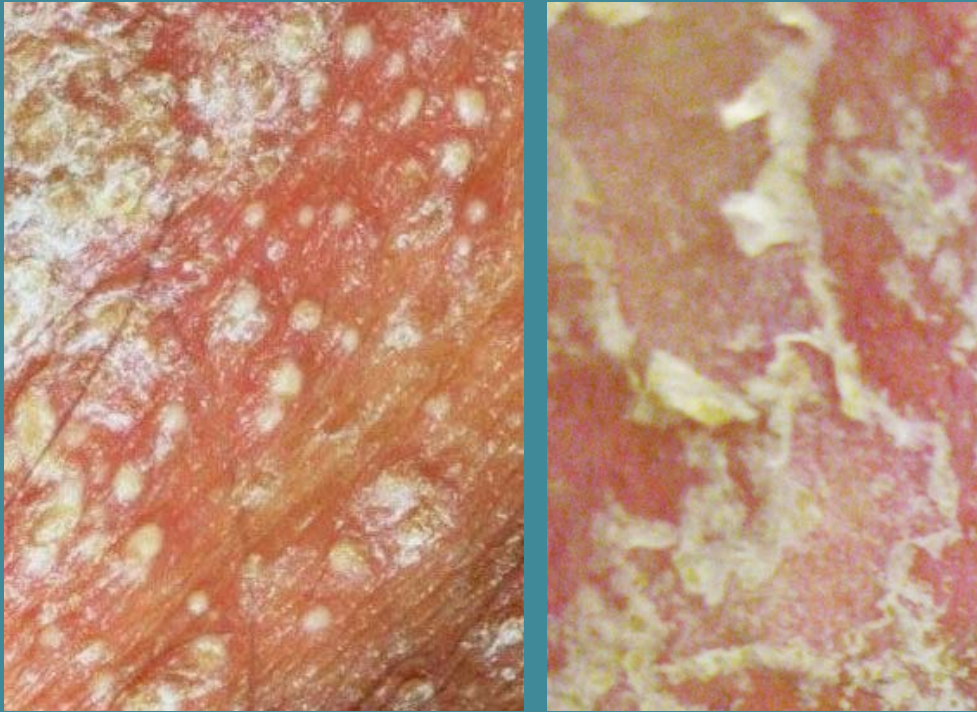


Figure 1. Linear scaly plaques on the thighs and disseminated pustules

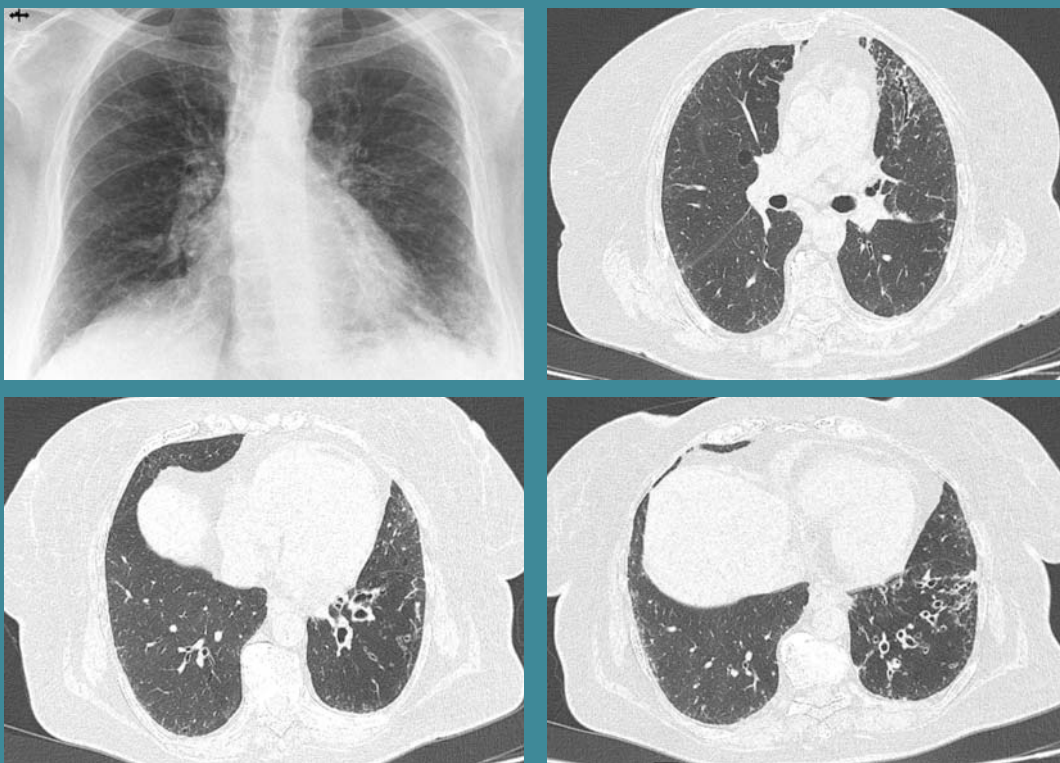


Figure 2. Cylindrical bronchiectasis arranged in clusters



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	2021	2022
FVC	2,3 L (93,1%)	2,18 L (75,4%)
FEV1	1,48 L (70,7%)	1,47 L (59,5%)
FEV1/VC	62,44%	67,4%
PEF	3,66 L (64,9%)	3,57 L (57,9%)
MEF50	0,94 L (25,9%)	1,09 L (25,9%)

Table 1. Spirometry 2021 vs 2022

tightness. The patient had periodic follow-ups with the pulmonology department and was referred to the Allergology Service for evaluation, where she underwent multiple assessments that revealed allergies to nonsteroidal anti-inflammatory drugs (NSAIDs) and aspirin, with negative allergy tests for perennial allergens.

In 2015, the patient was diagnosed with psoriasis vulgaris and was treated with topical corticosteroids. Later, in 2021, she was diagnosed with pustular psoriasis, which led to the initiation of methotrexate therapy, which the patient discontinued on her initiative. In 2022, she was diagnosed with psoriatic erythroderma and developed deep vein thrombosis, which was treated with NOAC. On admission, the general physical

examination revealed an obese patient (BMI = 35.2 kg/m²) with facial-truncal obesity and a "moon face" appearance. She had generalized erythema of the skin accompanied by linear scaly plaques on the thighs and disseminated pustules on the posterior and anterior chest and bilateral lower limbs (Figure 1).

Respiratory examination revealed wheezing and scattered wheezing sounds throughout the lung fields, with SpO₂ of 86% in ambient air. Laboratory tests showed the presence of an inflammatory syndrome (ESR, 93 mm/h; fibrinogen, 620 mg/dL; C-reactive protein, 56 mg/dL), leukocytosis with neutrophilia and eosinophilia (leukocytes, 20,000/μL; neutrophils, 18,760/μL; eosinophils, 400/μL), hyperglycemia (blood glucose = 132 mg/dL),

hypercholesterolemia with hypertriglyceridemia (cholesterol = 324 mg/dL, triglycerides = 291 mg/dL), hyponatremia (Na^+ = 132 mmol/L), and hypokalemia (K^+ = 3.1 mmol/L). Arterial blood gas analysis revealed respiratory acidosis without metabolic compensation (pH = 7.26, paO_2 = 57 mmHg; paCO_2 , 51 mmHg, HCO_3^- = 26 mmol/L). Standard chest radiography did not show any acute pathological changes compared to the previous descriptions.

A native and contrast-enhanced chest CT scan was performed, which revealed the presence of cylindrical bronchiectasis arranged in clusters (Fig2) with patent lumens and ruled out a potential acute thromboembolic event. The patient received oxygen therapy via a nasal cannula at a flow rate of 3 L/min, intravenous systemic corticosteroid therapy (hydrocortisone hemisuccinate, 100 mg), and short-acting bronchodilator nebulization (Ventolin), under which the symptoms subsided.

Subsequently, additional investigations were completed with respiratory function tests, which showed a descending pattern of respiratory function compared to previous evaluations, with moderate mixed ventilatory dysfunction, a 49 % reduction in FEV1, and a 25% reduction in FVC at the current presentation compared to mild obstructive ventilatory dysfunction with a 26.8% reduction in FEV1 in a previous evaluation (Table 1).

The patient's condition improved with the described treatment, and she was discharged with recommendations to continue inhalation therapy and reduce the prednisone dose to 7.5 mg, with reassessment of the opportunity to initiate biological therapy. Later, the patient was referred to the dermatology department, where she had been followed up before the current episode.

Discussion

We present the case of a 49-year-old female smoker diagnosed with severe asthma who underwent long-term treatment with oral corticosteroids and presented with associated comorbidities and medication side effects. Asthma is a highly prevalent condition among the general population. In Europe, it is estimated that 8.2% of the adult population is diagnosed with asthma, which is nearly identical to the global prevalence estimate of 9.5%⁽¹⁾. Severe asthma is defined as asthma that cannot be controlled solely by inhaled corticosteroid treatment and often requires the addition of oral corticosteroids to reduce the risk of uncontrolled asthma. Although the prevalence of severe asthma accounts for approximately 10-15% of all asthma cases, this number is concerning considering the reported range of 1.8-38%⁽²⁾.

Currently, approximately 25% of asthmatic patients are smokers, which has a negative impact on prognosis because this group of patients is characterized by a more rapid decline in lung function, more pronounced symptoms, and a poorer response to treatment than non-smokers^(3,4). Studies have shown that patients with asthma have diminished responses to both inhaled and systemic corticosteroid therapy owing to a decreased vasoconstrictor effect.

Surprisingly, both smoking and asthma are independently associated with a decreased response to corticosteroids, suggesting an additive effect of these two factors⁽⁵⁾.

An association between bronchiectasis and asthma is common in the general population. Although there are limited studies regarding the influence of these associations on prognosis, the estimated prevalence ranges from 2.7% to 42%. Asthma is believed to increase the risk of bronchiectasis



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superinfection, leading to an accelerated decline in lung function rates⁽⁶⁾. Another identified risk factor for asthma-bronchiectasis overlap syndrome (ABOS) is smoking, which has been shown to have an impact on the development of bronchiectasis, especially in patients with more than 10 pack-years, increasing the risk of respiratory infections⁽⁷⁾.

ABOS represents a distinct syndrome in which studies have demonstrated a common pathogenesis between asthma and bronchiectasis, including predominantly cellular involvement in inflammation, altered immune response, mucus hypersecretion, and altered airway microbiota⁽¹⁰⁾. Asthma and bronchiectasis share common symptoms, and recommendations for patients with severe asthma, the elderly, and those with altered medication responses involve performing a chest CT scan to investigate potential associations⁽¹¹⁾.

The impact of bronchiectasis on quality of life and respiratory function tests is significant in patients with other obstructive lung diseases⁽⁸⁾. Psoriasis is a chronic immune-mediated inflammatory disease that affects approximately 2-3% of the world's population. The association between asthma and psoriasis has been reported in the literature, with studies estimating a prevalence of 9.2%⁽¹²⁾. Asthmatic patients diagnosed in childhood or young adulthood are predisposed to developing psoriasis during their lifetime because these two entities share common

pathophysiological mechanisms. In general, the main interleukins studied in asthma are IL-4 and IL-5/IL-13, which are pharmacological targets used to block the specific inflammatory cascade of eosinophilic asthma. However, studies have demonstrated the involvement of IL-17 in the pathogenesis of severe asthma, and the relevance of the association between asthma and psoriasis lies in the favorable response of psoriasis patients to IL-17A inhibitors^(13,14).

The use of systemic corticosteroids may be indicated for short courses during asthma attacks or for long periods in cases of severe asthma. High-dose long-term oral corticosteroid therapy (prednisone >5 mg/day) is associated with an increased risk of infections, cardiovascular and metabolic disorders, and osteoarticular complications compared with short courses of treatment.

In the present case, the patient had grade II obesity with facial-truncal disposition, indicating Cushingoid syndrome caused by long-term oral glucocorticoid treatment. Adverse effects associated with corticosteroid therapy are frequently reported, with a recent estimate indicating a prevalence of > 90%, with weight gain being the most common side effect⁽¹⁵⁾. Oral corticosteroids do not cause venous thromboembolism. In the present patient, we noted the presence of multiple risk factors associated with the development of deep vein thrombosis, including immobi-

lization due to systemic pain associated with psoriatic erythroderma, smoking, and obesity. A study conducted in 2021 on a sample of 4,956 patients who experienced a first episode of deep vein thrombosis demonstrated an increased risk of thrombotic events from 2.53 before initiating oral corticosteroid therapy to 5.28 one week after initiation⁽¹⁶⁾. Psoriatic erythroderma is a severe, rare subtype of psoriasis that accounts for approximately 1-2.25% of all cases. It is frequently associated with a history of psoriasis, prolonged use of systemic and topical corticosteroids, and abrupt discontinuation of methotrexate therapy⁽¹⁹⁾.

Characteristically, it presents as erythematous plaques affecting more than 75% of the body surface area, accompanied by severe desquamation and disseminated pustules. Psoriatic erythroderma is a potentially life-threatening condition due to electrolyte disturbances and frequent associated infections^(17,18).

In the present case, initiation of biological therapy was indicated because the patient met the following criteria: severe asthma, eosinophil count > 400/ μ L, nasal polyposis, frequent severe exacerbations (≥ 2 exacerbations per year), reduced lung function values, and the use of oral corticosteroids⁽⁹⁾.

Conclusions

This study aimed to draw attention to the cascade of events that can occur in a young patient with severe asthma who had no other associated comorbidities at that time. Despite the multiple adverse reactions patients face, oral corticosteroid therapy remains a treatment that improves the quality of life for asthma patients as long as the indication of the treating physician is respected. However, we must not forget about the current

biological therapies and continually evaluate the potential opportunities to initiate such treatment. The burden of adverse effects caused by long-term oral corticosteroid therapy, especially in young patients, should not be neglected and the possibility of dose reduction should be considered. Asthma remains a prevalent condition in the general population and, despite innovations in diagnosis and treatment, continues to be a challenge in terms of patient management and correct treatment administration. Although initiating treatment and potential escalation of therapy based on current guidelines may seem easy, they largely depend on the patient's adherence to treatment, which can be difficult to achieve in young adults who are not aware that they have a chronic disease that requires treatment.

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