

Case Report

Bronchial casts attributed to the use of pegylated interferon and ribavirin*

Molde brônquico devido ao uso de interferon peguilado e ribavirina

Eduardo Garcia, Ângelo Ferreira da Silva Junior, Fabíola Schorr, Milene Hota, Ricardo Gondim Brizzi, André Barreto da Silva

Abstract

We report the case of a 53-year-old male patient with a rare profile: bronchial casts associated with the use of pegylated interferon and ribavirin. The patient sought treatment in a pulmonology clinic with a history of progressive dyspnea for four months that had evolved to progressive cough followed by frequent and abundant elimination of bronchial casts. The patient was initially treated with bronchodilators, as well as with oral and inhaled corticosteroids. Fiberoptic bronchoscopy, bronchoalveolar lavage and sputum analysis were carried out but did not contribute to the elucidation of the diagnosis. The symptoms developed while the patient was receiving pegylated interferon and ribavirin for the treatment of hepatitis C. The symptoms resolved 30 days after the discontinuation of the treatment. To our knowledge, this is the first report of bronchial casts caused by the use of pegylated interferon and ribavirin.

Keywords: Bronchitis; Interferons/adverse effects; Ribavirin/adverse effects.

Resumo

Relatamos o caso de um homem de 53 anos com uma rara associação entre moldes brônquicos e o uso de interferon peguilado e ribavirina. O paciente procurou o serviço de pneumologia por apresentar, há quatro meses, dispneia progressiva que evoluiu com tosse progressiva seguida da expulsão de moldes brônquicos frequentes e abundantes. O paciente foi tratado inicialmente com medicações broncodilatadoras e uso de corticoide oral e inalatório. Foram realizados fibrobroncoscopia, lavado broncoalveolar e análise do escarro, os quais não acrescentaram informações para elucidação diagnóstica. Durante o período sintomático, o paciente fez uso de interferon peguilado e ribavirina para o tratamento de hepatite C. Após 30 dias da interrupção das medicações, o paciente ficou assintomático. Este é o primeiro relato sobre a associação entre molde brônquico e o uso de interferon peguilado e ribavirina.

Descritores: Bronquite; Interferons/efeitos adversos; Ribavirina/efeitos adversos.

Introduction

Plastic bronchitis, also known as fibrinous bronchitis, pseudomembranous bronchitis or bronchial casts, is characterized by bronchial secretion that evolves to the molding of bronchial casts.⁽¹⁾

Bronchial casts are typically associated with disorders such as diffuse bronchial hypersecretion, asthma, bronchiectasis, mucoviscidosis, aspergillosis, pneumonia and heart disease.⁽²⁾

Interferon is an immunomodulatory cytokine used in the treatment of various diseases, including chronic hepatitis C. Side effects

and adverse effects are observed in more than half of the patients treated with this drug. However, pulmonary-related adverse effects are uncommon. Ribavirin is another antiviral drug, typically used in combination with interferon, and there have been no reports of respiratory-related side effects in patients treated with ribavirin as monotherapy.^(3,4)

To date, there have been no reports of interferon or ribavirin being associated with bronchial casts. Here, we report the case of a patient who developed respiratory symptoms and persistent

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elimination of bronchial casts while under treatment with pegylated interferon and ribavirin.

Case report

A 53-year-old single (separated) white male, a sailor from Rio de Janeiro and living in the city of Maringá, with diabetes mellitus, as well as a history of alcoholism, smoking and childhood asthma, was admitted to our hospital after having been under treatment (for chronic hepatitis C) with pegylated interferon and ribavirin for four months. Soon after the initiation of treatment, the patient had developed progressive dyspnea and cough, symptoms that had worsened during the two months preceding his admission to the hospital, during which time he had also presented intermittent fever and had lost weight (4 kg). He stated that the cough had been persistent, with occasional “crises”. In the week prior to admission, he had presented incapacitating dyspnea that would temporarily cease after the elimination of abundant secretion, which contained bronchial casts (Figures 1, 2 and 3). The effort required in order to eliminate the casts was exhaustive and anguishing—so much so that the patient voluntarily remained in the prone position, with his head and thorax inverted (hanging off the bed), in an attempt to facilitate elimination of the casts. Based on the symptoms presented, treatment with bronchodilators and corticosteroids (oral and inhaled) was started. In the physical examination, the patient presented dyspnea preceding the expectoration of the casts, as well as diffuse rhonchi and wheezing in the pulmonary auscultation. The results of laboratory tests, such as blood workup, determination of electrolyte concentrations, blood gas analysis and identification of inflammatory markers, were normal, with the exception of the serum levels of IgE, which were elevated (300 IU/mL). Other complementary tests, such as HIV serology, as well as investigation of fungi and TB in the casts, also were all negative. Fiberoptic bronchoscopy revealed no endobronchial alterations, and the analysis of the bronchoalveolar lavage fluid collected did not further the diagnosis, the direct mycological examination and culture of the bronchial cast being negative. In an attempt of elucidate the case, we performed transbronchial biopsy, the anatomopathological analysis of which revealed chronic inflammation and interstitial fibrosis in the lung parenchyma, with accumulation of foamy alveolar macrophages



Figure 1 - Bronchial cast.

and chronic inflammation of the bronchiolar wall. Considering the hypothesis that there is an association between pegylated interferon and bronchial casts, the hepatology team, responsible for the treatment of the liver disease, was encouraged to discontinue the treatment with interferon. No consensus was reached, and the patient therefore continued to receive the treatment until the end of the prescribed period. At 30 days after of the discontinuation of the treatment with interferon and ribavirin, the respiratory symptoms resolved.

Discussion

In plastic bronchitis, the casts can be analyzed after being exteriorized through coughing, bronchoscopy or surgery.⁽⁵⁾ The format of the mucoid bronchial casts can be segmental, lobar or, in rare cases, pulmonary.⁽⁶⁾

Bronchial casts are typically associated with disorders such as diffuse bronchial hypersecretion, asthma, bronchiectasis, mucoviscidosis, aspergillosis, pneumonia, heart disease, sickle

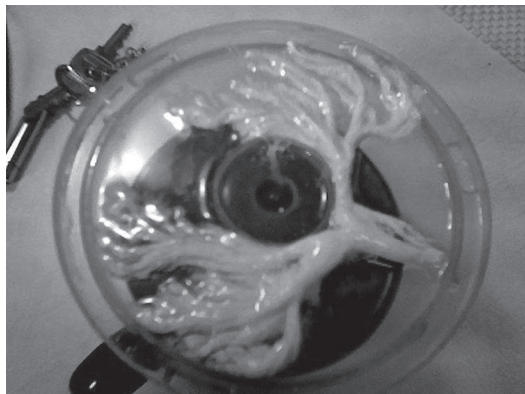


Figure 2 - Bronchial cast in the form of the bronchial tree, including the distal trachea.



Figure 3 – Bronchial cast submerged in water.

cell anemia, lymphangiomyomatosis, pulmonary eosinophilia and TB, as well as with aerosol administration of tissue plasminogen activator and with inhalation of toluene. Bronchial casts are often self-limiting or responsive to symptomatic treatment and have a good prognosis.^(3,6,7)

Interferon is an immunomodulatory cytokine used in the treatment of various diseases, including chronic hepatitis C. Pegylated interferon is a new form of interferon, developed in order to increase the half-life of the drug. Adverse effects—especially leukopenia, anemia and thrombocytopenia—are observed in half of all patients treated, resulting in high rates of temporary or permanent discontinuation of the treatment.⁽⁸⁾ Pulmonary-related adverse effects are rare and include interstitial pneumonia, pulmonary hypertension, pseudosarcoidosis, bronchospasm and pleural effusion. To date, there have been no reports of an association between interferon and bronchial casts.^(5,8) Ribavirin is another antiviral drug, typically used in combination with interferon, and there have been no reports of respiratory-related side effects in patients treated with ribavirin as monotherapy.^(3,4) Nor have there been any reports of cases in which bronchial casts were found to be associated with the use of ribavirin. Monotherapy with ribavirin is not efficacious against the hepatitis C virus, and ribavirin is typically used in combination with pegylated interferon. Therefore, the pulmonary symptoms described in the literature as being attributable to ribavirin are similar to the respiratory-related side effects attributed to the use of pegylated interferon.^(1,9-11)

Treatment of plastic bronchitis consists in controlling the pathologies that cause the bronchial casts. Symptomatic treatment has the

objective of stimulating the elimination of the casts. Medications that have proven useful for promoting the expectoration of bronchial casts include beta-agonists, theophylline, corticosteroids, N-acetylcysteine and aerosolized urokinase. Measures such as respiratory therapy and bronchoscopy also are of value for dislodging bronchial casts.^(4,12)

The case presented here illustrates a potential cause of bronchial casts, as yet unreported in the literature: use of the pegylated interferon-ribavirin combination. Additional reports or studies are needed in order to lend credence to that supposition.

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