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Case Report

Eosinophilic pneumonia associated with use of flecainide

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Short Title: eosinophilic pneumonia and flecainide

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Established Facts and Novel Insights

Established Facts
· Drug-induced interstitial lung diseases are rare causes of acute or chronic pulmonary toxicity

Novel Insights
· Flecainide and other antiarythmic drugs are rare causes of eosinophilic pulmonary reactions. Observations are limited and mostly ancient. This case reports draws the attention on a possible cause of rapid drug-induced pulmonary toxicity

Abstract

Drug-induced interstitial lung disease may be observed during the use of a large panel of drugs, some of them in the form of a rapidly progressing acute eosinophilic reaction. This case report describes the occurrence of an acute eosinophilic pneumonia shortly after the introduction of flecainide, an oral class I antiarythmic drug. Rapid diagnostic evaluation, cessation of the causative drug and temporary steroid treatment reversed the clinical course.

Introduction

Drug-induced pulmonary reactions may be observed after the use of a large panel of drugs, under the form of interstitial or eosinophilic reactions. Some forms may progress rapidly to a stage of respiratory failure, if not diagnosed rapidly and managed appropriately

Case Report/Case Presentation

A 66-year old non-smoking, previously healthy swiss male physician was treated for persistent atrial fibrillation with amiodarone (unsuccessful), then by electrical defibrillation with success and received flecainide 2 x 100 mg/day as prevention after conversion. During the following weeks, he developed progressive dyspnea and fatigue with persistent cough. The pulmonary auscultation revealed diffuse inspiratory crackles. The chest X-ray demonstrated diffuse interstitial infiltration. The spirometry was normal, but with a loss of 450 ml of the vital capacity compared with a routine measurement performed one year before. The laboratory tests showed an increase of the C-reactive protein at 57 mg/l, ESR at 56 mm and 10% eosinophils in the complete blood count. The thorax CT demonstrated multiple ground-glass infiltrations in the upper fields and some dense opacities in the middle and lower fields (Fig 1 and 2). A bronchoscopy was performed, which showed a diffuse hyperemia of the bronchial mucosa. The broncho-alveolar lavage revealed 5% eosinophils, 5% lymphocytes, 10% neutrophils and 70% alveolar macrophages. A diagnosis of drug-induced eosinophilic pneumonia was suspected.

The treatment of flecainide was interrupted and replaced by propafenone and prednisone was added (initially 50 mg/day, rapidly tapered to 20 mg). The cough and dyspnea improved within 3 days and were absent after 3 weeks. After 8 weeks, the patient was symptom-free, the chest-X-ray was normal, the eosinophil count dropped to 0 and prednisone was stopped. No recurrence occured during the next months (follow-up 5 years).

Discussion

Eosinophilic pneumonia (EP), first described in 1989 (1), is a rare interstitial lung disease, characterized by the presence of eosinophils in the broncho-alveolar lavage and, usually, also in peripheral blood (2). It can occur spontaneously or be induced by parasitic infections or drugs. The presentation can be acute, within days or weeks after the beginning of the intake of the responsible drug, or chronic, with slowly progressive symptoms over several months. In the acute form, the predominant symptoms are a dry cough with dyspnea, chest pain and fever which can rapidly progress to acute respiratory distress or drug rash with eosinophilia and systemic symptoms (DRESS). The radiological presentation of both acute and chronic form of EP is characterized by bilateral patchy reticular and interstitial infiltration. A diffuse ground-glass infiltration seems to be observed only in acute EP. The etiology is unknown but most cases seem to be related to the intake of a large panel of drugs, most commonly antibiotics, antiinflammatory drugs, antidepressants, immunomodulating drugs or class III antiarythmics, mainly amiodarone. Recently, novel therapeutic drugs like monoclonal antibodies and biologicals against neoplastic and rheumatological diseases have been increasingly reported as a possible cause of interstitial lung disease (3). In a report of 196 cases of EP published in 2018, no case was attributed to flecainide, a class I antiarythmic drug (4).

Isolated cases of EP attributed to flecainide have been published (5, 6). The mechanism is attributed to a hypersensitivity reaction to flecainide, favoured by the tissue accumulation of the drug. The site pneumotox reports 6 cases of acute pneumonitis or pulmonary fibrosis attributed to the use of flecainide (https://www.pneumotox.com/drug/view) and 3 cases attributed to tocainide, a related class I antiarythmic withdrawn from the market.

Conclusions :

The patient decribed suffered from an acute EP very probably due to the intake of flecainide with moderately elevated eosinophil counts in peripheral blood and BAL. The clinical symptoms, the eosinophilia and radiological signs rapidly improved after the cessation of the drug and a short course of steroid, without recurrence of sequelae 5 years after the acute episode.

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Statement

Statement of Ethics

Study approval statement: no ethical approval was requested for this clinical observation

Consent to publish statement: The patient has given written consent to the publication of this case report in July 2024

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

JPZ made the clinical observation, studied the literature and drafted the report. SS contributed to the observation and preparation of the report

Data Availability Statement

The clinical data are kept in the files of the Centre de Pneumologie.

Figure

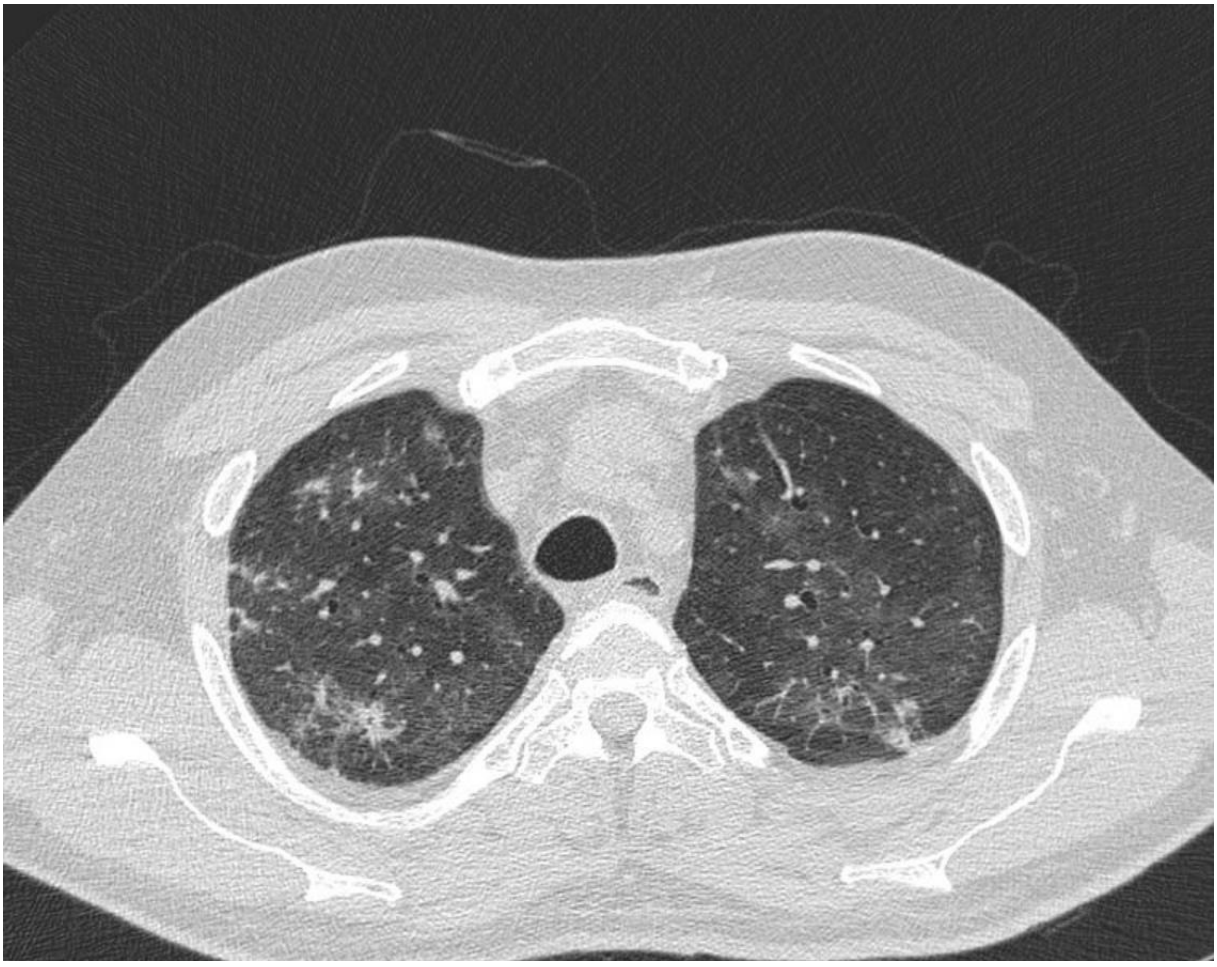

Fig. 1. Chest CT. Multiple ground-glass opacities in the upper fields

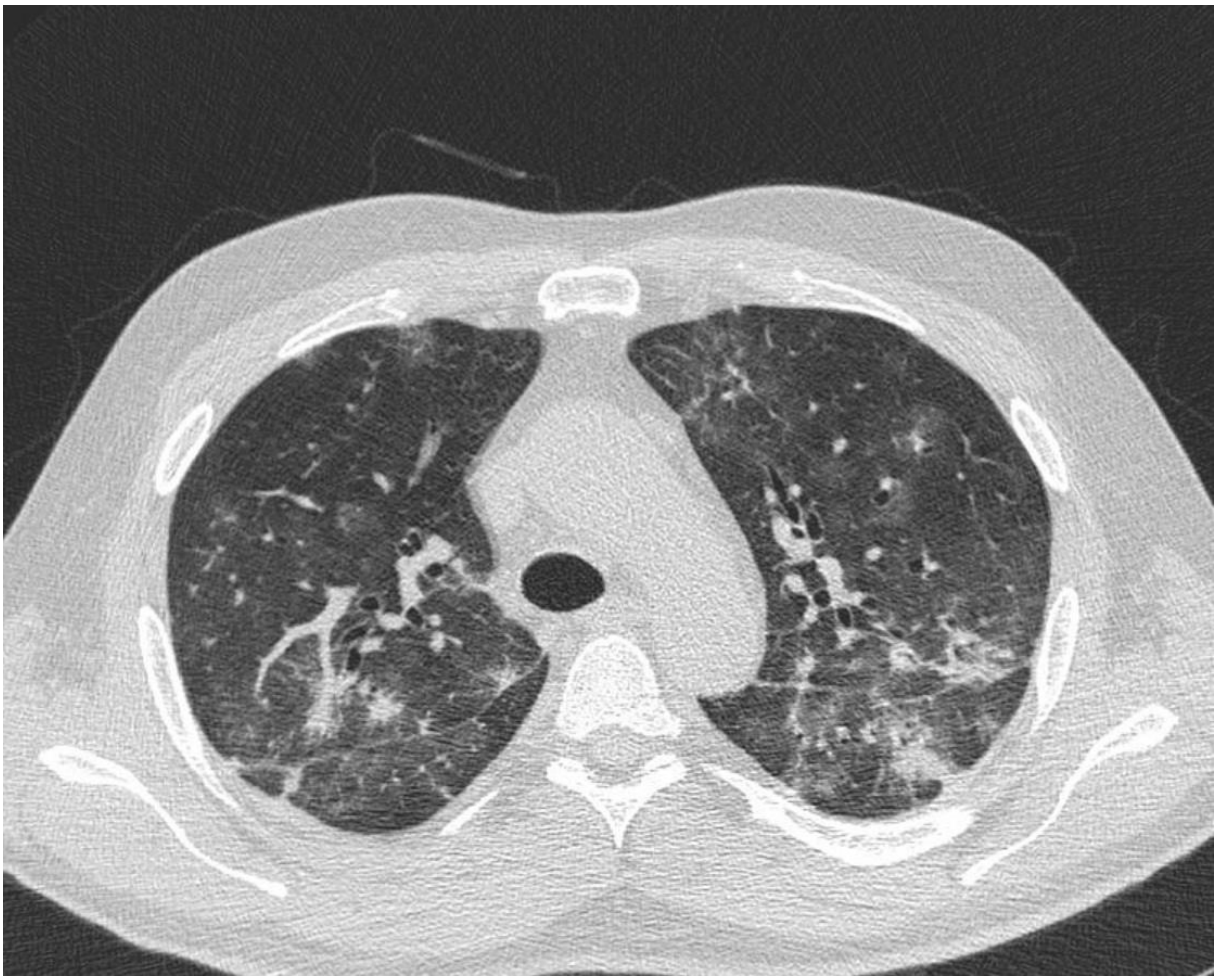

Fig. 2. Chest CT. ground-glass opacities and infiltrations in the middle fields