Introduction

The lung is a major target for inhaled agents and toxicants. Many inhaled chemicals are not hazardous as such, but are biotransformed to reactive intermediates [1]. Acute and chronic parenchymal lung injuries as a result of the inhalation of illicit drugs are not uncommon complications in habitual drug users. A variety of interstitial and other lung diseases may occur in such cases with diverse clinical presentations.

Case history

A 22-years old male presented with dyspnea, non-productive cough, myalgia and fever. These symptoms started 4 days prior to admission. His medical history was unremarkable. He smoked tobacco for a few years. Finally, he admitted alcohol abuse, heavy marijuana and cocaine smoking in the last months. Physical examination revealed some crackles at auscultation, he had a high number of polymorphonuclear neutrophils (PMNs; 32.4% of the total cell count with 53.8% alveolar macrophages (AMs), 11.2% lymphocytes (Lyms), 2.0% eosinophils (Eos) and 0.2% mast cells (MC). Moreover, some ‘foamy’ AMs and a few reactive pneumocytes type II (PII cells) were seen (figure 3). No intracellular micro-organisms were seen. Moreover, cultures remained sterile. Serology for HIV infection was negative, as well as the urinary test for Legionella pneumonia and Streptococcus pneumoniae. Serology for common virus, and mycoplasma, ricketsiae and chlamydiae was negative. No underlying immunosuppressive condition was evident. Additionally, relevant CYP450 polymorphisms were profiled. This revealed that he appeared to be a CYP2C19 intermediate metabolizer (*1/*2). The clinical consequences obtained from the software package www.genemedx.com are summarized in table 1.

<table>
<thead>
<tr>
<th>Affected drugs</th>
<th>Change</th>
<th>Causative agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>cocaine</td>
<td>≥ 150%</td>
<td>resveratrol*</td>
</tr>
<tr>
<td>azotrimycin</td>
<td>150%</td>
<td>resveratrol</td>
</tr>
<tr>
<td>bezopiridol</td>
<td>0-25%</td>
<td>resveratrol</td>
</tr>
</tbody>
</table>

*resveratrol: red wine component

Conclusion

This patient was tested as having a heterozygote CYP2C19 variant allele. This means that he is an intermediate metabolizer of the inhaled agent is the most suspected [3].

Several different xenobiotic-metabolizing CYP450 and phase II enzymes (i.e. conjugation enzymes including several transferases) are present in the human lung and lung-derived cell lines, possibly contributing to in situ activation and metabolism of cocaine. CYP2C19 belongs to the largest CYP2C family and together with other members like CYP2D6, and CYP2C9 metabolizes, to varying amounts, more than half of all frequently prescribed drugs [4]. It has also a significant role in the detoxification of many xenotobiotics such as alcohol [5] or marijuana and its metabolites [6].

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Treatment and clinical course

The patient was initially treated with a broad-spectrum antibiotic, moxifloxacine intravenously, aiming to cover the majority of common and atypical microbes. Because of high suspicion of a ‘drug’-induced interstitial lung disease (DI-ILD) and the absence of features of any infectious cause, corticosteroids were started (40mg daily, i.v.) and continued for two weeks. Thereafter, the corticosteroids were tapered gradually. His clinical condition improved within 2 weeks. Dyspnea and cough disappeared, follow-up chest radiograph abnormalities cleared (figure 4) and the PaO2 became within normal limits (11.9 kPa; on room air at rest).

Discussion

A variety of interstitial lung damage due to cocaine or marijuana inhalation, ranging from acute pulmonary haemorrhage to chronic eosinophilic infiltrates have been described [1,2]. To date, the mechanism of lung injury is not fully understood and a direct toxic effect in a dose dependent pattern of the inhaled agent is the most suspected [3].

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