Case Report

Methylphenidate causes chronic eosinophilic pneumonia

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Abstract:

A man who is 38 years old and diagnosed with attention-deficit hyperactivity disorder was prescribed methylphenidate. Three weeks later, he began experiencing progressive shortness of breath and coughing. Imaging of his chest showed patchy bilateral ground-glass opacities, and bronchoscopy revealed a 15% eosinophil count in his bronchoalveolar lavage. A transbronchial biopsy confirmed a diagnosis of eosinophilic pneumonia. The patient's condition improved when he was given steroids and stopped taking methylphenidate. However, he developed the same symptoms again a few days after restarting the medication, along with a skin rash. This strongly suggests that methylphenidate was the cause of his eosinophilic pneumonia.

Keywords:

Allergy, chronic eosinophilic pneumonia, drug-induced lung injury, methylphenidate

Methylphenidate is classified as a central nervous system (CNS) stimulant and is utilized in the management of attention-deficit hyperactivity disorder (ADHD) symptoms in both children and adults. In addition, it is prescribed for narcolepsy, a sleep disorder characterized by excessive daytime sleepiness and sudden sleep attacks. However, this medication can have various adverse effects on different body systems.[1-4] Some respiratory system-related side effects include emphysema, pulmonary talcosis, and pneumothorax.[2-4] Nevertheless, we have not come across any reported instances of eosinophilic pneumonia associated with methylphenidate.

Case Report

The patient is a 38-year-old male with a medical history of bronchial asthma, which is controlled with as-needed (budesonide/formoterol [symbicort]), glucose-6-phosphate dehydrogenase deficiency, and chronic sinusitis. He underwent sinus surgery in August 2022. Recently, he was diagnosed with ADHD and started taking methylphenidate 3 weeks before his presentation to the pulmonary clinic. His primary complaint was worsening shortness of breath on exertion over the last 3 weeks, interfering with his daily activities. He also reported experiencing a dry cough. There was no history of fever, night sweats, upper respiratory tract infections, chest pain, orthopnea, or paroxysmal nocturnal dyspnea. He occasionally vaped but stopped 2 months ago and had no contact with animals or birds. He works as an IT technician in a closed office and denies any environmental exposure history. No symptoms suggest connective tissue disease, skin allergies, or allergic rhinitis. He is not taking any long-term medications, and his presentation was on methylphenidate 36 mg.

On clinical examination, the patient was alert and conscious with stable hemodynamics. Room air saturation was maintained at 98%. Chest examination revealed no wheezing or crackles, normal heart sounds, normal

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jugular venous pressure, no lower limb edema, no signs of connective tissue disease, and no skin rash. The patient underwent a 6-min walk test and was desaturated from 95% to 87% at 300 m. Pulmonary function tests were normal, with a forced expiratory volume in 1 s (FEV1) of 4.06 L (105% predictive, with a predictive value of 3.85 L), forced vital capacity (FVC) of 4.58 L (98% predictive, with a predictive value of 4.46 L), FEV/FVC ratio of 88.7%, total lung capacity (TLC) of 5.3 L (78% predictive, with a predictive value of 6.74 L), residual volume (RV) of 1.19 L (63% predictive, with a predictive value of 1.87 L), RV/TLC ratio of 78%, and expiratory reserve volume of 2.94 L (205% predictive, with a predictive value of 1.43 L). The patient's serum laboratory results showed a normal complete blood count with a white blood cell count of 8.5 (reference range 4–11 × 10^9/L) and normal differentials, kidney function, liver function, negative sputum culture, and normal urinalysis with no casts. Nasopharyngeal viral multiplex polymerase chain reaction (PCR) was negative, and serology for connective tissue disease and anti-nutrophilic cytoplasmic antibodies (ANCA) were negative. HIV, hepatitis C virus, and hepatitis B virus were also negative. The erythrocyte sedimentation rate was 120. The patient's stool is negative for parasitic and helminths, and the toxicology screen was negative.

The chest X-ray revealed bilateral peripheral airspace opacities without mediastinal enlargement and with a normal cardiac shadow. The computed tomography (CT)/high-resolution CT scan showed multiple bilateral peripheral ground-glass attenuations with thickening of the intra- and interlobular septa. The scan also showed a mild air bronchogram [Figure 1a].

The bronchoscopy showed no gross abnormalities, while the bronchoalveolar lavage fluid had a white blood cell count with prominent macrophages at 66%, neutrophils at 5%, eosinophils at 15%, and lymphocytes at 13%. Bacterial, tuberculosis, and fungal cultures and stains were negative, as were the *Aspergillus* galactomannan and viral PCR tests. The transbronchial biopsy revealed a focal interstitial eosinophilic and histiocytic infiltrate. Furthermore, numerous eosinophils and macrophages, some of which were multinucleated, were observed in the alveolar spaces, strongly suggesting eosinophilic pneumonia [Box 1].

The patient was diagnosed with eosinophilic pneumonia, most likely caused by methylphenidate. Treatment involved a 14-day course of prednisolone at 40 mg once daily, which gradually tapered over 3 weeks. In addition, the patient stopped taking methylphenidate. At the follow-up appointment 4 weeks later, the patient was doing well with no more dyspnea, and his white blood cell count and eosinophil levels were normal. A repeated chest X-ray and high-resolution CT scan showed normal results [Figure 1b]. The patient also underwent a repeated 6-min walk test, which did not result in desaturation.

The patient resumed using the medication on his own after experiencing a worsening of his ADHD symptoms. Within a few days, he developed a skin rash, itching, and shortness of breath. The patient was evaluated by a psychiatrist, who discontinued methylphenidate and advised him to avoid using it again. The patient was subsequently started on atomoxetine, a selective norepinephrine reuptake inhibitor, which was well-tolerated without any further complications.

Discussion

Methylphenidate is a CNS stimulant that has been associated with adverse effects on multiple body systems, including the cardiovascular, abdominal, psychiatric, and neurological systems.[1] However, it is not currently known to cause lung pathology. Previous case reports have suggested that chronic use of intravenous (IV) methylphenidate (crushed Ritalin tablets) can result in the development of emphysema or pulmonary talcosis.[2,3] These case reports were based on observations after prolonged IV methylphenidate use. In a search of 21 medical records of patients diagnosed with obstructive pulmonary disease related to the use of IV-injected Ritalin, using X-ray and CT scans, all 21 cases demonstrated pulmonary emphysema. The disease distribution was basilar and symmetric, with 14 cases classified as severe.[2]

A single case report has suggested a potential link between chronic oral methylphenidate use and the development of recurrent spontaneous pneumothorax. The case involved a 16-year-old male with ADHD who was started on oral methylphenidate in 2010. In 2011, he experienced his first episode of spontaneous pneumothorax and continued to have recurrent episodes until he was admitted in 2013.[4] After an extensive search, methylphenidate was suspected to be the cause, and the medication was discontinued. Following discontinuation, the patient had no new episodes of pneumothorax.[4] To date, no cases of methylphenidate-associated eosinophilic pneumonia have been reported.[5] However, given that methylphenidate was the only medication started before the onset of symptoms and that ruling out other causes suggested methylphenidate was the most likely cause, particularly as symptoms started immediately after starting the medication. The use of steroids improved the patient's symptoms and radiological findings. Although initially uncertain if methylphenidate was the cause of symptoms or idiopathic eosinophilic pneumonia,[5-7] the recurrence of symptoms and development of skin rash and itching after rechallenging the patient with methylphenidate make it the most likely cause.

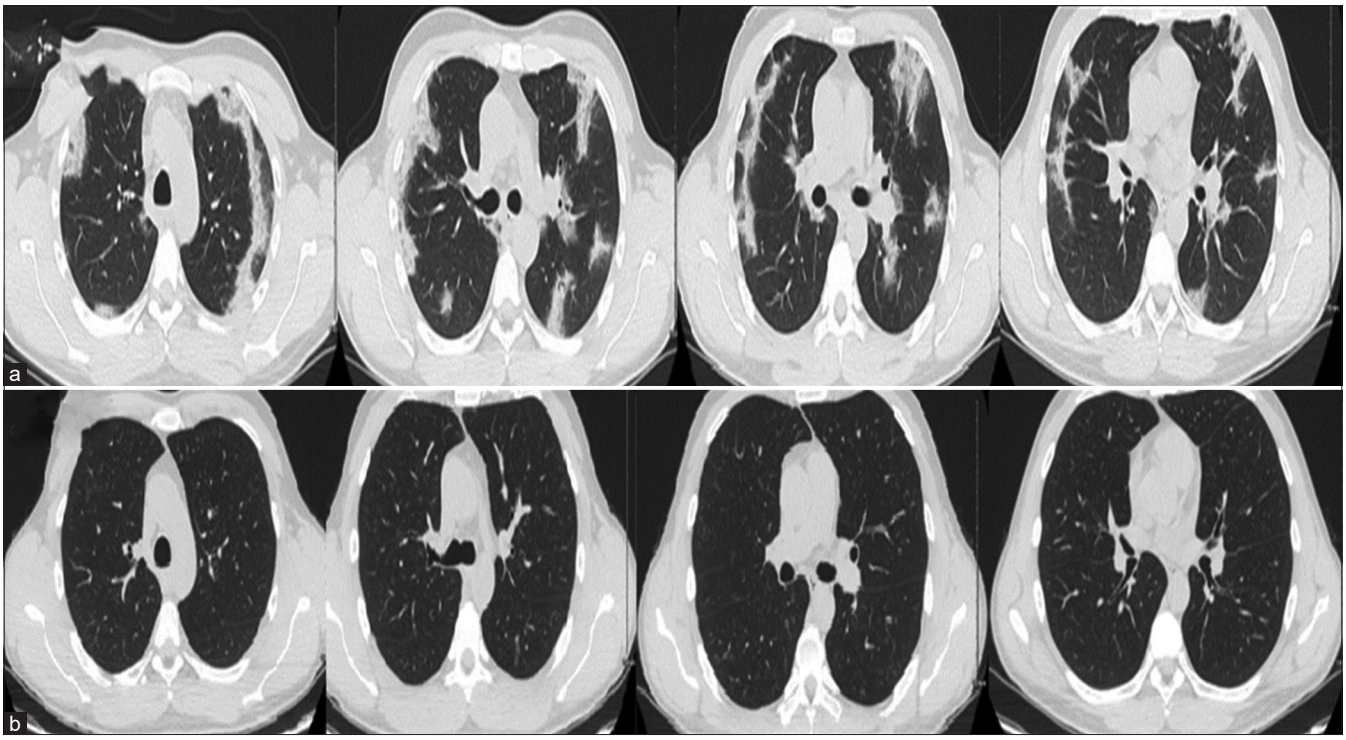
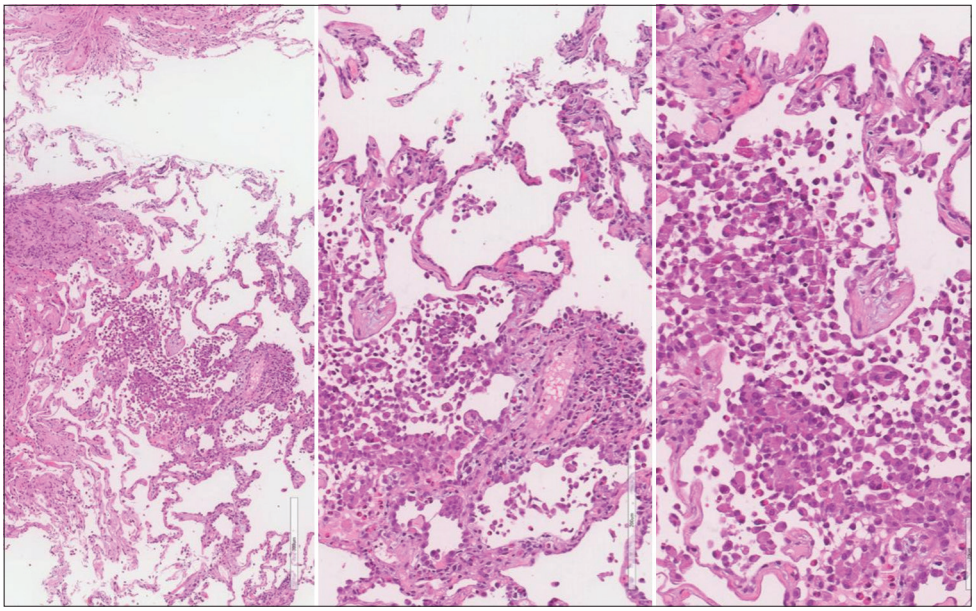


Figure 1: (a) High-resolution computed tomography (HRCT): Peripheral opacities are present in both lungs that are ground-glass attenuation with thickening of the intra- and interlobular septa and associated mild air bronchogram. Some of the opacities demonstrate perilobular and peribronchial vascular distribution. Few small peripheral lung nodules. No enlarged thoracic or axillary lymph nodes. No pleural or pericardial effusion. (b) HRCT: Complete resolution of the lung infiltration



Box 1: Histologic hematoxylin and eosin-stained section from bronchial biopsy shows numerous eosinophils within alveolar spaces and a variable number of macrophages. There is also mixed interstitial infiltrate of eosinophils and lymphocytes. These histologic findings are consistent with chronic eosinophilic pneumonia

Conclusion

To our knowledge, there are no case reports on oral methylphenidate and the development of chronic eosinophilic pneumonia changes such as in the case we have presented. However, the relation of methylphenidate oral or IV form with the development of lung pathology remains unclear. This case and previous case reports should caution clinicians to be aware of possible pulmonary side effects.

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