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Case Report

New onset bronchial asthma following oral propranolol for infantile hemangioma

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ABSTRACT

Propranolol, a nonselective adrenergic beta-receptor blocker, is the first-line drug used for the treatment of infantile hemangiomas (IH). However, its use is contraindicated in patients with bronchial asthma. Nevertheless, studies assessing whether propranolol triggers asthma in infants and affects asthma control are limited. Here, we report the case of an infant with IH who developed asthma after starting propranolol. Asthma control was refractory to inhaled corticosteroids and leukotriene receptor antagonists, although it improved remarkably with discontinuation of propranolol. This report suggests that infants with a family history of allergic disorders should be monitored for asthma after propranolol administration.

1. Introduction

Propranolol, a nonselective adrenergic beta-receptor blocker, is the first-line pharmacological treatment of infantile hemangioma (IH) [1]. By contrast, nonselective adrenergic beta-receptor blockers, including propranolol, are generally contraindicated in patients with bronchial asthma. The Japanese Pediatric Guideline for the Treatment and Management of Asthma 2020 recommends avoiding nonselective beta-blockers in patients with asthma because beta-blockers induce acute exacerbations by blocking beta-receptors for endogenous catecholamines [2]. However, because oral propranolol for IH is initiated in early childhood, asthma is rarely diagnosed before the initiation of propranolol treatment. However, the effects of propranolol on the onset and control of asthma remain unclear. We report the case of a boy with no history of wheezing, who developed bronchial asthma while receiving oral propranolol therapy for IH. Asthma control improved after discontinuation of propranolol.

2. Case presentation

The patient was an 8-month-old male infant. He was born at 38 weeks of gestation, weighing 2225 g. His father and sister had bronchial asthma.

At 1 month of age, multiple red spots developed on the body surface. Therefore, the patient was diagnosed with IH. Ultrasonography revealed an intrahepatic hemangioma. Oral propranolol was initiated at 3 months of age and the dose was increased to 2.0 mg/kg/day. The hemangiomas regressed slowly. At 5 months, he began to experience recurrent wheezing attacks, with or without

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respiratory tract infection. His family physician suspected bronchial asthma because the inhalation of a bronchodilator provided symptomatic relief. Inhalation of fluticasone (inhaled corticosteroid [ICS]) 200 μg/day with spacer and oral pranlukast (leukotriene receptor antagonist) were started. However, the patient still experienced recurrent wheezing.

At 8 months of age, the patient was referred to our hospital for further examination and treatment. Auscultation revealed wheezing during exhalation. Blood examination showed eosinophilia (710 eosinophils/μL), and no increase in specific immunoglobulin E inhaled antigens such as house dust mites. Chest radiography revealed no abnormalities. There were no findings suggestive of other causes of the recurrent wheezing, and the modified Asthma Predictive Index (MPI) [3], which predicts future asthma attacks, was positive. Thus, the patient was diagnosed with bronchial asthma. We ensured that the correct inhaler technique using a spacer was performed at all times. Considering that oral propranolol may have affected asthma control, the inhalation of ICS and oral pranlukast was continued at the same dose. The surface and intrahepatic hemangiomas resolved, and propranolol was discontinued. After approximately 1 month, his wheezing disappeared, except during bouts of respiratory tract infections. The frequency of wheezing attacks during bouts of respiratory tract infection gradually decreased with continued treatment (Fig. 1). Wheezing was not observed at 18 months of age. The Japanese Pediatric Asthma Control Program (JPAC) score, which is used to assess the severity and control status of asthma [4], showed improvement from 6/18 before discontinuation of propranolol to 16/18. Furthermore, after discontinuation of propranolol, the hemangioma did not increase in size. Informed consent was obtained from the patient's family for the publication of this report.

3. Discussion

This case demonstrated the potential role of propranolol in the development and exacerbation of asthma, particularly in patients with a family history of allergies. Propranolol is widely used as a first-line treatment for IH; however, its nonselective beta-blocking effect may have adverse effects in patients at risk of developing asthma. The patient had a family history of bronchial asthma, suggesting a genetic predisposition that may have led to airway hyperresponsiveness during propranolol administration.

The improvement in asthma control following the discontinuation of propranolol, without an increase in the ICS dose or additional medication, strongly suggests a potential causal relationship. This observation partially aligns with Shepherd et al.'s report of three cases in which asthma developed after propranolol administration [5]. However, in two of these cases, wheezing persisted even after propranolol discontinuation, and in one case, the patient improved only after an increase in the ICS dose. Therefore, the presence of a causal relationship remains inconclusive. A retrospective analysis by Mei-Zahav et al. did not find a significant increase in wheezing incidence in children treated with propranolol compared to a control group, although this study did not account for a family history of asthma or atopy [6].

In our case, propranolol cessation led to an improvement in asthma control, possibly indicating that beta blockade in patients with genetic susceptibility or subclinical asthma can worsen airway hyperreactivity. This case highlights the importance of monitoring asthma symptoms when administering propranolol to children with a family history of atopy or asthma. Clinicians should be cautious when using propranolol in such patients. Further studies are needed to better understand the interaction between propranolol therapy and asthma development.

CRediT authorship contribution statement

Yuki Yamaguchi: Conceptualization, Data curation, Investigation, Writing – original draft. **Satoshi Horino:** Conceptualization, Supervision, Validation, Writing – review & editing. **Hiroki Miyabayashi:** Writing – review & editing. **Haruka Aki:** Writing – review & editing. **Katsushi Miura:** Writing – review & editing.

Disclosure

The authors declare no conflict of interest.

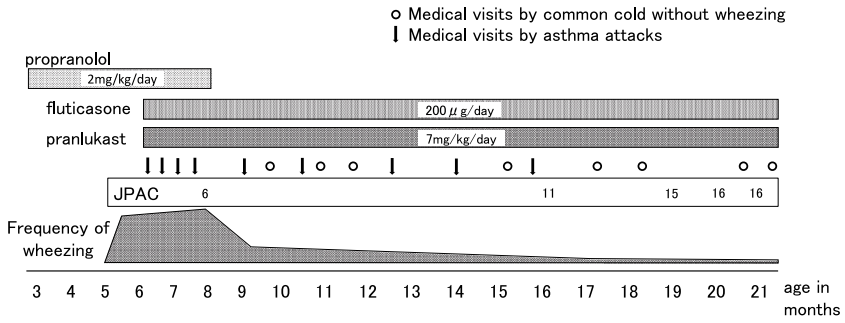

Fig. 1. The clinical course of the patient. The horizontal axis indicates the patient's age in months. The frequency of Wheezing increased from 5 months of age and decreased after oral propranolol was discontinued. JPAC, Japanese Pediatric Asthma Control Program.

Ethics statement

Written informed consent was obtained from the patient's family for the publication of this report.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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