

Death during an asthma exacerbation in an adult with sickle cell disease: An autopsy case study

To the Editor: Children with hemoglobin SS (HbSS) and asthma have a higher rate of sickle cell disease (SCD)-related morbidity and mortality compared to those with HbSS and without asthma [1,2]. Since the preponderance of literature describing asthma as a risk for morbidity and mortality is in children, the objective of this case study is to examine a death due to asthma with supporting autopsy findings in an adult with SCD.

A 51-year-old male with hemoglobin SC (HbSC) developed diffuse pain and difficulty breathing at home. Attempting to go to the hospital, he died in a parking lot next to his car with an albuterol inhaler found nearby. Past medical history was notable for chronic pain, avascular necrosis of the hips as well as poorly controlled asthma requiring frequent hospital admissions and prior treatment with chronic oral corticosteroids. Medications included albuterol, fluticasone/salmeterol (500/50), and montelukast 10 mg. He was a non-smoker. Pulmonary function tests demonstrated a forced expiratory volume in 1 sec (FEV₁) of 2.58 L (80% predicted), a forced vital capacity (FVC) of 3.83 L (95% predicted), FEV₁/FVC was 68%, change in FEV₁ with bronchodilator was 46%, and total lung capacity was 5.68 L (101% predicted), consistent with an obstructive pattern with reversibility upon administration of a bronchodilator. Serum immunoglobulin E (IgE) was 1,334 IU/mL. Notably, aspergillus antibodies to evaluate for allergic bronchopulmonary aspergillosis were negative.

Gross autopsy revealed hyperinflation of the lungs (right lung 290 g; left lung 300 g) along with extensive fibrous adhesions. Cut sections revealed occlusion of the bronchi and bronchioles with thick mucus plugs. Microscopic sections demonstrated mucous plugs containing epithelial cells and numerous eosinophils in the lumina of bronchi and bronchioles. Basement membrane thickening and parabronchial muscular hyperplasia was also noted. There was a predominance of eosinophils within the bronchial wall inflammatory infiltrate and surrounding blood vessels were filled with sickled red blood cells (Fig. 1). Histologic sections of the brain, heart, liver, spleen, and kidneys showed extensive sickling of red blood cells within blood vessels and occasional vascular occlusion. Cause of death was attributed to bronchial asthma.

Symptomatic asthma is less common in adults than children [1,3]. Growth of airways with age and less attendant airway obstruction accounts for clinical improvement in the course of asthma [3]. This case report suggests that although symptomatic asthma is seen less commonly in adults, when present, the risks in adults are similar to those demonstrated in children.

A high prevalence of self-reported respiratory symptoms has been described in adults with SCD [4]. In one retrospective cohort study ($n = 114$), 30% of adults reported recurrent, severe wheezing episodes. This subgroup of patients had a higher rate of painful vaso-occlusive crises (pVOC), acute chest syndrome (ACS), and premature death [4]. In another retrospective cohort study that included adults, the association between wheezing and SCD morbidity was confirmed, providing additional evidence that wheezing is a marker for patients with more severe disease [5]. In both studies there was no relationship between asthma diagnoses and SCD morbidity. The most likely explanation for these findings is that wheezing, not related to an underlying

asthma diagnosis, occurs during pVOC; although, under-diagnosis of asthma, potentially due to the presence of non-atopic asthma, cannot be ruled out.

Unlike the prior studies describing wheezing in the absence of asthma, the patient in this case report had clinical features consistent with asthma. During the fatal event, he had an asthma exacerbation that occurred during a pVOC, similar to reports in children describing that asthma exacerbations promote pVOC [6]. Potentially, regional hypoxia in the lung induced by bronchoconstriction is promoting the formation of sickle erythrocytes and subsequent pVOC. If true, aggressive management of asthma to prevent respiratory symptoms may lead to improved outcomes in patients with SCD. Since only a minority of adults with SCD has symptomatic asthma, however, we do not recommend screening for asthma in asymptomatic adults. Instead, we suggest a targeted approach to thoroughly evaluate those adults with characteristic signs and symptoms of asthma (e.g., wheezing, atopy). When asthma is diagnosed, adults should be managed in collaboration with an asthma specialist in an attempt to prevent poor outcomes such as described in this report.

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Conflict of interest: Nothing to report.

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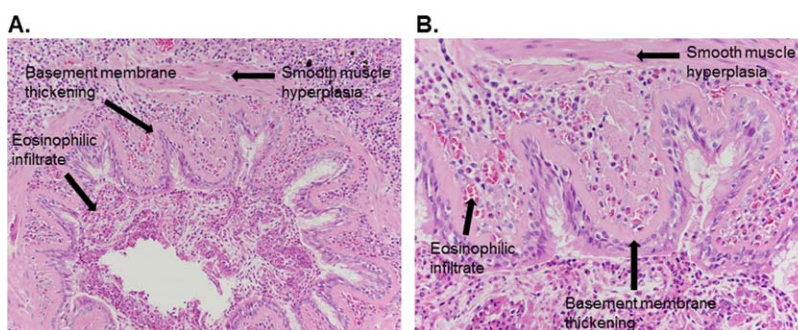


Figure 1. A: Low power of bronchiole with mucus filled lumen, epithelium showing prominent goblet cell hyperplasia, basal membrane thickening, and prominent smooth muscle. B: High power view of mucosal and peribronchial eosinophils. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]