Pathology Image of the Month

Fatality Following Acute Onset of Shortness of Breath

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A 30-year-old Caucasian man became unresponsive following acute onset of extreme shortness of breath. Emergency services were dispatched and, despite aggressive efforts, resuscitation was unsuccessful, and the patient was pronounced dead. Medical history was unknown at the time. Full, unrestricted autopsy permission was granted under coroner authorization.

Postmortem laboratories were significant only for a total serum IgE of 316 IU/mL (normal < 100 IU/mL). Complete blood, urine and vitreous toxicology was negative. The right lung weighed 340 gm (663 ± 239) and the left was 290 gm (583 ± 216). No significant pleural fluid was noted; no pulmonary thromboemboli were present. Gross and microscopic images from the lungs can be seen on pages 235 and 236, respectively. No other pathologic findings were identified on complete postmortem examination.

What is the cause of death in this case?

Explication is on p. 236
DIAGNOSIS: Fatal, status asthmaticus

DISCUSSION

Asthma is a chronic inflammatory disorder of the airways characterized by recurrent and largely reversible episodes of wheezing, dyspnea, and cough. Classically, asthma has been categorized in two major categories: the more common extrinsic (allergic, atopic) type resulting from an inhaled allergen and the rarer, intrinsic (idiopathic, nonatopic) type believed to arise independent of atopy. Current thinking, however, suggests that asthma is, rather, a heterogenous group of disorders that share some common features such as reversible airflow obstruction and variable airway inflammation but that can also be subdivided into several distinct subtypes or subphenotypes.

Severe, acute asthma attacks clinically known as status asthmaticus describe the uncommon exacerbations that can persist for up to days and even weeks wherein airflow obstruction reaches such an extreme that it frequently warrants intensive care hospital admissions, including mechanical ventilation. Risk factors for status asthmaticus include patients who have had prior hospitalizations, particularly those wherein endotracheal intubation was required. Additional independent risk factors include concomitant viral upper respiratory tract infections in up to 50% of cases; medical nonadherence or insufficient use of prescribed corticosteroids; strong and constant allergen exposures, especially to pets in severely atopic individuals; inhalation of irritants such as smoke and paint; and prior reports of exercise-induced bronchoconstriction.

Deaths due to asthma are uncommon, especially among children and young adults. Mortality data document a 26% decrease in asthma fatalities over the years 1999-2009, with a reported 3,388 individuals dying of asthma in the year 2009. The highest asthma-related mortality is observed in black females, and the highest age-adjusted risk occurs in those aged 65 years or older. Predictors of death due to asthma, aside from gender, age, and ethnicity, include prior hospitalizations requiring endotracheal intubation. Deaths due to asthma have been classified into those either following a prolonged slow-onset attack or following an acute, sudden-onset attack as defined by death within one to two hours of the onset of the dyspneic episode. Some studies based on autopsy data have reported that deaths from sudden-onset attacks are more frequently found in younger males and are less likely to be observed in association with a concomitant viral infection as they are to be associated with an immunogenic trigger. Such distinction into prolonged versus acute-onset asthma attack is, furthermore, important for medicolegal purposes in that fatalities due to acute-onset attacks would naturally be cases wherein investigation into inadequate medical management would not be warranted.

Maintaining a high index of suspicion for asthma at the time of autopsy is important for the pathologist in a case where the agonal event is an acute onset of respiratory distress, particularly when there is no known historical evidence to suggest an asthmatic history at the time of the autopsy. The approach at autopsy should include modification of evisceration techniques to evaluate for the diagnostic possibility of a pneumothorax as well, as was done in the current case. When bilateral, diffuse pulmonary hyperinflation and overexpansion is seen, as is clearly depicted in Figure 1, the probable mechanism is air-trapping. The visceral edges of all lobes of the lungs are sharply demarcated, and the medial edges of the upper or middle lobes frequently meet in the midline known as the “kissing sign.” Blood collection, frequently from either the inferior vena cava or the right ventricle should include a serum total IgE, as a strong association between asthma and levels of IgE have been repeatedly suggested.

Following blood collection and removal of the lungs en
bloc, the bronchial tree should be opened longitudinally for detection of the presence of mucus plugs. Mucus material that occludes airways of all sizes is considered a pathologic hallmark of asthma. The plugs are tenacious in quality and can be extracted from the bronchial tree and sent for subsequent histologic examination. The bronchial wall often has a thickened appearance grossly, manifest microscopically as subepithelial basement membrane thickening and hyperplasia of surrounding smooth muscle. Laryngeal edema, though occasionally seen, is more often associated with anaphylaxis-related deaths than with asthma fatalities. Adequate pulmonary tissue should then be retained in formalin, preferably from central and peripheral lung from all five lobes of both lungs, for subsequent histopathologic examination. The pathognomonic microscopic features of asthma are well-depicted in Figure 2 and include intrabronchial mucus, bronchial epithelial inflammation that includes a predominance of eosinophils, subepithelial basement membrane thickening, and hyperplasia of both the surrounding smooth muscle and the surrounding glands. Periodic acid-schiff (PAS) staining best highlights the intrabronchial mucus plugs in their characteristic forms known as Curschmann spirals, which can occlude the airspaces totally and are heterogenous mixtures of mucins, plasma exudates, and inflammatory cells that are primarily eosinophils.

The case presented here is notable for its clinical presentation and for the pathognomonic gross and histologic features. Though the patient’s age, gender, and ethnicity make his inherent asthma-related mortality risk low, retrospective historical questioning of his parents revealed a significant past medical history complicated by multiple prior admissions, many requiring intensive care and endotracheal intubation. Additionally, the patient’s compliance with his prescribed corticosteroid therapeutic regimen was described as incomplete. Finally, considering the rapid onset and death and the postmortem IgE levels detailed in the current case, we can further classify the case as an atopic or extrinsic-subtype asthma fatality following an acute-onset exacerbation, and thus, it warrants no further investigation of medical management.

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REFERENCES


