Case Report

Case of Sudden Fatal Asthma – The Forensic Perspective

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Abstract

Asthma, a chronic lung disease affecting people of all ages[1], is a major global health challenge[2] common among younger individuals[3]. The mortality rates of asthma vary highly across countries, age and ethnic groups[4]. Asthma remains an under-diagnosed and under-treated disease, particularly in low- and middle-income countries[1].Hence, preventable asthma deaths do occur, especially in relation to inadequate treatment. Thus, it is critical for forensic experts to identify various phenomenological and morphological features seen in asthma deaths and understand the associated pathogenetic mechanisms to determine correct manner of death[5], aiding in prevention of future mortality. India lacks data which elaborately investigates on various aspects of asthma and sudden death due to this chronic disease[6] along with the medicolegal issues concerning asthma deaths. Hence, it is important for our national forensic experts to generate database evidence on asthma, as preventable deaths occur due to inadequate treatment. With this intention, we present a case report of a 40-years old male asthmatic (previously untreated), who is brought dead to Shri Atal Bihari Vajpayee Medical College and Research Institute for post-mortem [PM] examination. Internal PM examination reveals hyperinflated lungs with thick tenacious mucus in the airway passages. Microscopically, chronic inflammatory infiltrate with numerous eosinophils is seen around the bronchi, with thickening of its basement membrane. With this case report, we explore the different internal and external PM findings along with the histopathological examination finding to add to the limited pool of database on sudden death due to bronchial asthma.

***Keywords**:* Chronic lung disease; Asthma; bronchi; mortality

Introduction:

Bronchial asthma is a major noncommunicable disease, affecting both children and adults. Most common chronic disease among children, this condition is caused by inflammation leading to bronchial hyperactivity[7] and narrowing of small airways, presenting with any combination of symptoms of cough, wheeze, shortness of breath and chest tightness[1].

According to WHO, roughly 250,000 people die prematurely every year due to asthma globally[1]. Asthma is diagnosed based on the clinical history, physical examination, and pulmonary function tests, including reversibility testing and measurement of bronchial reactivity[7]. Long-term treatment with inhaled corticosteroid medications along with avoidance of asthma triggers and patient education can help to control and reduce asthma symptoms allowing

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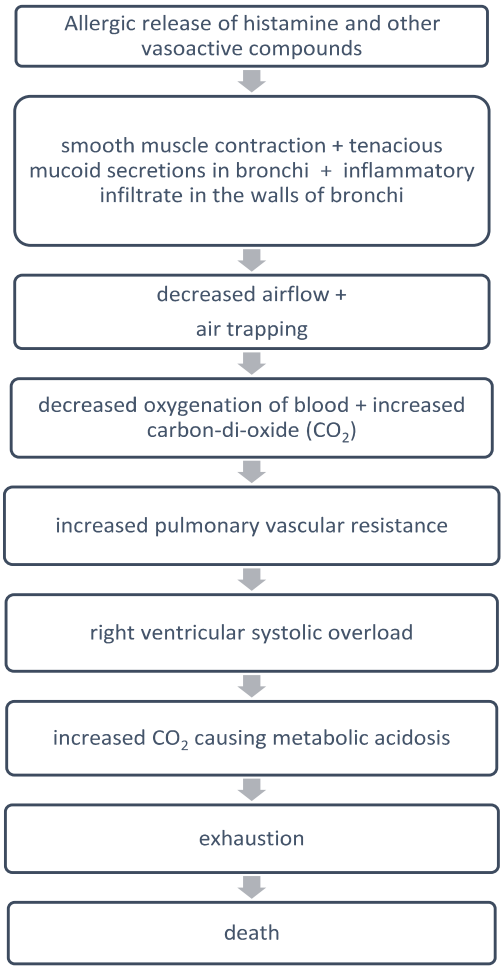
asthmatics to lead a normal, healthy and active life.

Bronchial asthma affects 3% of population in India with a death rate ranging from 1.1% to 7%. Sudden, unexpected death due to an obscure mechanism can be seen in asthmatics without a prolonged attack or status asthmaticus or even an acute attack. 25% deaths from asthma occur within 30 minutes of onset of attack. The frequency of death from asthma is increased at night or in early morning, possibly due to a pronounced diurnal variation in airflow limitation. Mechanism of death in acute asthmatic attacks is explained as below:



Post-mortem findings in death due to asthma include:

(1) Lungs:
   a. Overexpanded, completely occupying chest cavity.
   b. Histopathological examination of lung reveals chronic inflammatory infiltrate with numerous eosinophils around the bronchi

(2) Bronchi:
   a. Full of sticky tenacious white mucus deposit
   b. Histopathological examination of bronchi shows thickened basement membrane of bronchi with wavy appearance.

In chronic cases of asthma, there is protrusion of bronchi above the cut surfaces of lungs.

Case Report:

This is a case of 40-year-old wheatish complexioned male, moderately built and nourished, brought dead to the Bowring and Lady Curzon Hospital, Shri Atal Bihari Vajpayee Medical College and Research Institute at around 10.15 am. Further, this case was referred to the department of Forensic Medicine and Toxicology to perform a detailed autopsy examination to ascertain the cause of death. As per the history furnished by the concerned police, deceased was a driver by profession, unmarried with no history of any previous illness. The previous evening, patient developed nausea and vomiting which ultimately lead to him having fatigue the whole night. With no improvement in the symptoms by next day morning, patient was rushed to Bowring hospital by when he was pulseless and declared dead at around 10.15 a.m. by the in charge medical officer.

On first review of the dead body, rigor mortis was seen in all parts of the body, post-mortem staining was present over the back of the body. Bluish discolouration of lips and tips of all nail beds was noted. On internal examination,

(i) Pleura: right pleura adherent to the chest wall

(ii) Lungs: hyperinflated, surface shows rib markings, congested and adherent at the interlobar fissure. Giant emphysematous bullae are also seen

on the lung surface along with petechial haemorrhages.

(iii) Trachea and Bronchi: presence of thick, tenacious, greyish white, mucus plug

(iv) Heart: sclerosed left anterior descending artery, congested

(v) Liver: fatty, surface shows yellowish discolouration with rounded margins

(vi) All other organs were congested.

Final cause of death was given as: "death is due to respiratory failure as a result of acute on chronic disease of lungs".

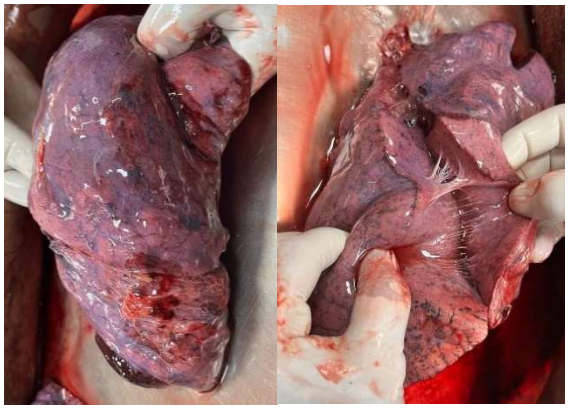


Fig 1. Hyperinflated left lung with emphysematous bullae, petechial haemorrhages, rib markings, and adherent (stripped) pleura. The lung is congested and Adherent interlobar fissure of left lung.

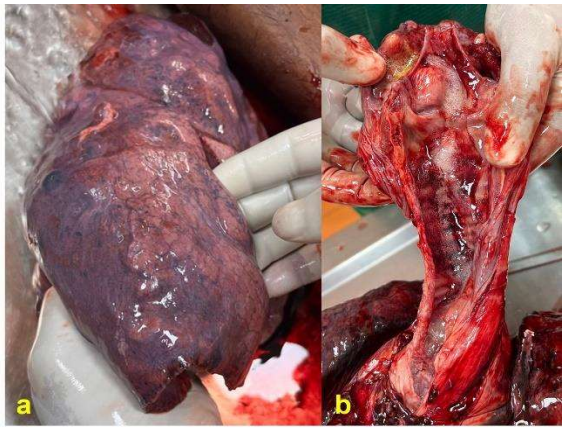


Fig 2: Ballooning of left lung (a) and Mucus in bronchus extending into bronchioles (b)

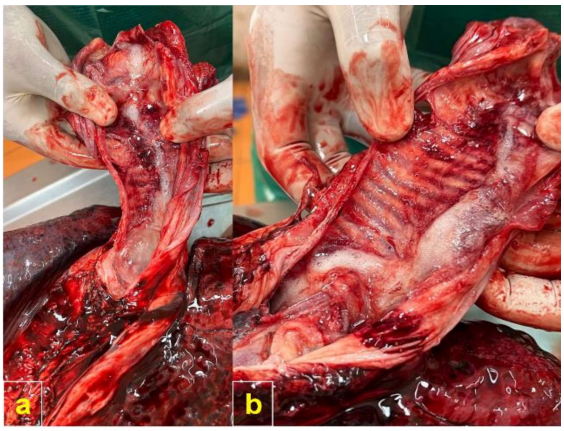


Fig 3: Mucus plug in the trachea (a) and bronchus (b)

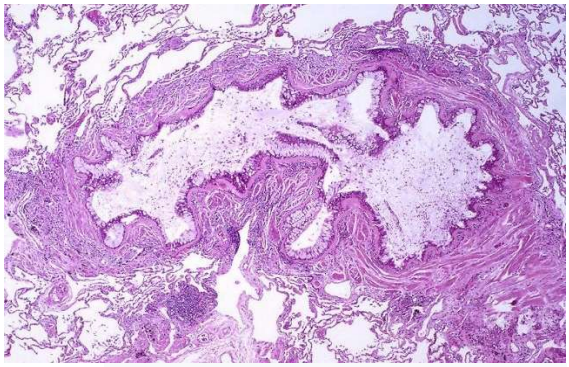


Fig 4: Obstruction of the lumen of the bronchiole by mucoid exudate, goblet cell metaplasia, epithelial basement membrane thickening and severe inflammation of bronchiole

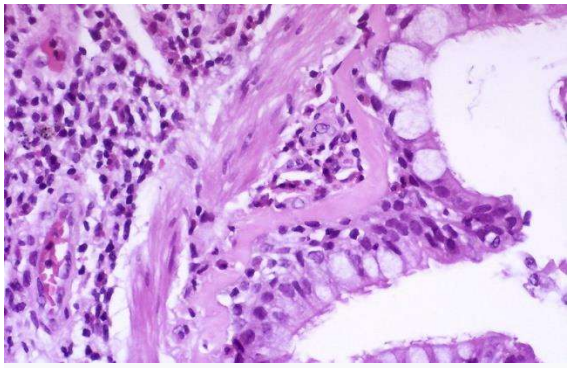


Fig 5: Goblet cell metaplasia, mucoid material in bronchial lumen, epithelial basement membrane thickening, smooth muscle hyperplasia and severe inflammation with predominance of eosinophiles.

Discussion:

Asthma is a heterogenous disease[2] usually characterised by chronic airway inflammation caused due[7] to:

a. Contraction of bronchial smooth muscle
b. Edema of the airway walls
c. Mucous plugging of the bronchioles
d. Irreversible changes in the lungs ("remodeling")

The global burden of the asthma in terms of its incidence and mortality has dropped from 1990 to 2019[2] (figure.1a, figure1b) From 1990 to 2019, the incidence of asthma decreased from 601.20 per 1,00,000 to 477.92 per 1,00,000, and the mortality of asthma decreased from 8.60 per 1,00,000 to 5.96 per 1,00,000. High sociodemographic index (SDI) areas have higher age-standardised asthma incidence and low sociodemographic index areas have higher age-standardised asthma mortality[2].

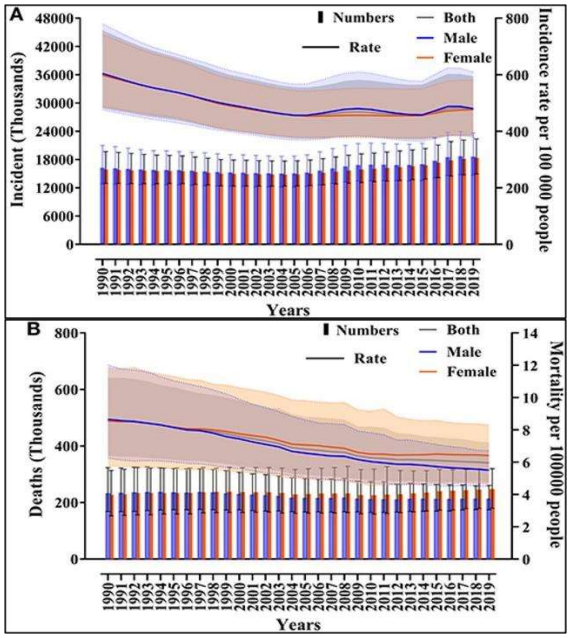


Fig 6: Global asthma incidents, incidence (A), deaths, and mortality (B) from 1990 to 2019[2].

In 1965, Roe was the first to distinguish death following prolonged asthma attack from sudden, unexpected death because of sudden onset asthma attack[8].Asthma-related sudden, expected deaths though rare, may occur in patients with only mild disease in contrast to most asthma related deaths occurring in hospitalised subjects with severe asthma[9]

Sudden- onset asthma attacks occur due to sudden development of airway obstruction while slow-onset asthma attacks usually associated with progressive, slow clinical and functional deterioration[10].In a prospective study on the speed of onset of acute severe asthma attacks, it was noted that 46% of the episodes were rapid (defined as <24 hours) while 13% were less than 1 hour in occurrence[11].

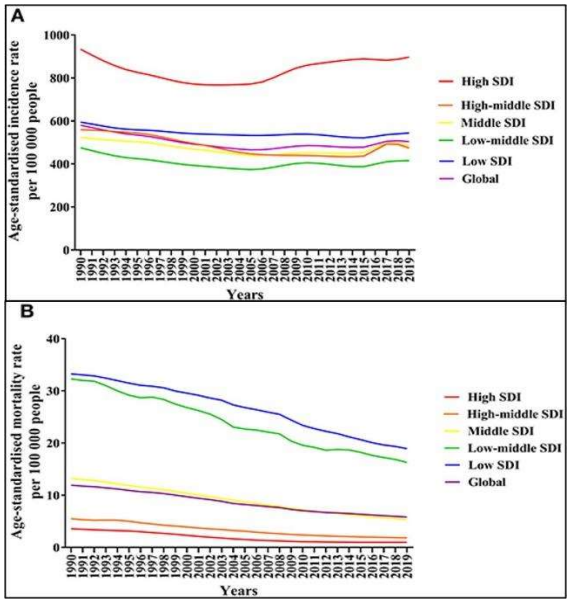


Fig 7: Global age-standardised incidence rate (A) and age-standardised mortality rate (B) of asthma by SDI regions, 1990 to 2019[2].

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Clinically, sudden- onset asthma attacks are defined by a sudden development of airway obstruction with less than 6 hours' duration[12].From a forensic perspective, it is defined as occurrence of death in a specific case within 1 hour of onset of asphyxic asthma attack and fatal slow-onset asthma defined as a fatality in which the time interval between onset of asthma attack and death was longer than 1 hour[13].This distinction is medicolegally important as it tells us if there was a prolonged duration of attack and time frame over which symptoms developed (as reconstructed from witness reports) in an asthma death. This gives us a hint about any mismanagement that might have contributed to the fatal outcome, despite there being enough time to resuscitate and save the patient under attack.

Death scene:

a. Occurs mostly outside the hospital, often in the absence of any witness
b. Seen in mostly younger age group
c. Such deaths occur mostly during night-time or in the early morning than during daytime[14-19], possibly because of diurnal airflow limitation variation[20-23].
d. Doors and/or windows might be open at the scene where deceased is found, explained by affected individual's attempt to get better oxygen supply during acute asphyxic attack[22].
e. Scene could be in a state of disorder as the individual tried to search for antihistaminic drugs/inhaler during the attack and same may be found in the hand, close to the deceased or somewhere else at the death scene[24].

Gross pathology:

1. Hyperinflated lungs which are overexpanded, appearing ballooned and occupying the whole thoracic cavity.
2. Giant emphysematous lung bullae are not uncommon.
3. Pneumothorax and pneumomediastinum due to rupture of these bullae may be seen
4. Rib markings/indentations on pleural surfaces of ballooned lungs.
5. Petechial haemorrhages beneath visceral pleura (Tardieu's spots) may be seen.
6. Sharply outlined margins of lobes of lungs showing loss of parenchymal retraction due to hyperinflation.
7. Greyish-whitish mucous plugs occluding the airways completely, involving airways of all sizes till terminal bronchiole. Mucus is relatively dry, tenacious, adherent to mucosal surface of airways.
8. Bronchial wall thickening may be seen on cut surface of lungs.
9. Rarely laryngeal edema with total or near-total obstruction of larynx.
10. Atelectasis and bronchiectasis indicate chronic airway occlusion as a sequel of chronic persistent asthma.

Histopathology[42]:

1. Mucus plugs in airway lumen, edema and inflammation of airway walls
2. Thickening of airway walls
3. Subbasement membrane fibrosis (due to deposition of type I and III collagen)
4. Increased vascularity (vascular congestion)
5. An increase in the size of submucosal glands and number of airway goblet cells (goblet cell hyperplasia)
6. Hypertrophy and/or hyperplasia of bronchial wall muscle

Medicolegal aspects of fatal asthma:

1. Accuracy of death certification is questioned repeatedly over decades as there is no enough database to elaborate the various findings seen in a case of sudden death due to acute asthma in our country. Looking at the western research reports, three studies can be highlighted:

a. 31% false-negative rate for death certificate was reported in the 0- to 64- years of age group in a study conducted by Wright and co-workers who reviewed asthma deaths in Norther Ireland registered between 1981 and 1984[25].
b. Among 235 patients dying in mainland Scotland between 1994 and 1996, Bucknall and co-workers reviewed general practice and hospital records to find out that only 95(40%) deaths were confirmed as being due to asthma[26].
c. In another Danish study by Sidenius and co-workers who coded 218 death certificates as that due to asthma, a group of pulmonologists later concluded that among there, only 9% (16) deaths were due to asthma, while asthma could be a probable cause of death in another 12 (7%) , 109 suffered or died from COPD and 14 from heart diseases[27].

Hence accuracy of death certificate in asthma deaths is poor and more forensic studies with deeper insights are necessary to differentiate true asthma deaths from the others.

2. Exogenic trigger factors leading to exacerbation of asthma is important to prevent the deaths due to acute asthma attack which are known to be major contributors of the disease. These include:
   a. Allergens including dust mites, atmospheric pollution, nutrition, lifestyle changes, maternal smoking, diesel fumes, geography, the "hygiene hypothesis," etc.
   b. Substances of abuse (exogenic trigger factors) are of medicolegal or forensic interest as these may trigger life-threatening asthma exacerbation, resulting in fatal outcome. E.g. Heroin insufflation, uncontaminated morphine, etc leading to bronchospasm or pulmonary mast cell degranulation[28-33].
   c. Alcohol can trigger asthma[34].
   d. Hormonal variations during menstruation can play an important role in asthma exacerbation in females. Roughly 30-40% female asthmatics complain of worsening of asthma during menstrual and/or premenstrual period[35].
   e. Strenuous exercise can precipitate acute asthma attack[36].
3. Adverse effects of asthma medication:
   a. With regard to deaths, Beasley et al. found evidence showing that high-dose of fenoterol and isoproterenol (beta adrenoceptor agonists commonly used to treat asthma) were associated with increased mortality, being the major causes of the epidemics of asthma mortality observed in some countries[37].
   b. Also, commonly reported adverse effects of inhaled corticosteroids include oropharyngeal and esophageal candidiasis [38,39].
4. The Medical Expert Witness in asthma deaths and issue of medical malpractice may be required in the following scenarios:
   a. the death of an asthmatic who is known to have consulted a physician before death but the correct diagnosis was not made
   b. the death of an asthmatic who had consulted a physician before death (it does not matter whether this was during an acute state of the disease or not) and the correct diagnosis was made but treatment was inadequate or even worsened the attack; or
   c. the sudden, unexpected death of an asthmatic occurring outside the hospital or out of a physician's surveillance, witnessed or unwitnessed, with or without a previous history of asthma.
   d. Burr and co-workers conducted a secret inquiry of 52 deaths where asthma was given as cause of

death; 15 cases were attributed to deficiencies in medical care. The authors established the following demographic characteristics of asthma deaths: (a) nearly all asthma deaths in persons younger than 65 years of age occur outside hospital; (b) in half the cases, the disease is chronic and severe; an acute catastrophic attack occurs in one-third of patients whose disease is moderate or mild; (c) other factors con- tributing to fatal outcome other than the severity of the disease can be identified in 70% of asthma deaths; (d) in 60% of cases, a "patient factor," particularly relating to psychosocial problems and poor compliance with treatment, can be identified; and (e) in 30% of cases, some aspect of the medical care may have contributed to the death, particularly lack of inhaled steroids, inadequate follow up, or contraindicated medication[40].

Asthma deaths may occur due to some non-verifiable causes like poor patient compliance, delay in seeking medical attention, failure to keep appointments or comply with treatment, symptom denial, alcohol or drug abuse, serious self-management errors, etc. It is important to identify and safeguard the health providers against such factors which are dependent solely on patients. Robertson and co-workers conducted a study which represents issues discussed before. This team examined the circumstances surrounding the deaths of 163 patients dying from asthma in the state of Victoria, Australia, over a 12-month period. 13% of the affected individuals had a history of trivial or mild asthma, 22% a history of moderate asthma, and 65% a history of severe asthma. Death occurred outside the hospital in 150 subjects (92%). In the fatal attack, 58% had a sudden onset and collapsed within minutes, 20% were found dead, and 27% had an acute progression of an established attack. 29% deaths were retrospectively assessed as preventable due to factors like inadequate assessment or therapy of prior asthma (35%), poor compliance with therapy (33%), and delay in seeking help (43%). A significant number of subjects in this survey could not be classified as belonging to the "high-risk" patient group[41].

Conclusion:

Asthma bronchiale represents a major health issue and a vital cause of sudden, unexpected death, and will likely remain so for decades. A thorough autopsy is the final word is quintessential in ascertaining a sudden death as due to acute asthma attack. Preventable asthma deaths still occur, particularly in relation to inadequate treatment. With limited national forensic database on the findings obtained in a case of sudden death due to asthma, it is crucial for the forensic doctors and forensic pathologists to identify different phenomenological and morphological features under which asthma deaths may present, as well as the associated pathogenetic mechanisms that may have exacerbated the acute, fatal asthma attack to determine the correct manner of death. In addition, an in-depth medicolegal knowledge of issues raised by asthma deaths is essential for every- one involved in death investigation.

Conflict of Interest:

None

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