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An autopsy case of asthmatic death – usefulness of biochemical examination

Uloga biohemijskih analiza u *postmortem* dijagnozi astmatskog napada kao uzroka smrti

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Abstract

Background. Asthma is the one of the major causes of sudden death in Japan. Postmortem diagnosis of asthma has been based on morphological findings in lungs, but it histological evidence, was also reported that the biochemical markers such as total and specific immunoglobulin E (IgE) are useful. **Case report.** We present here a case of fatal asthmatic death. A Japanese male in his thirties, complaining of dyspnea, collapsed suddenly. He was taken by ambulance to hospital, but cardiopulmonary resuscitation was ineffective. From autopsy findings, we concluded that the cause of death was asphyxia due to asthma attack. Biochemical findings indicated that the deceased had a severe asthmatic condition. **Conclusion.** In the presented case, the biochemical examination of the serum obtained at autopsy gave helpful information for the diagnosis that asthmatic attack was a cause of death.

Key words:
asthma; death, sudden; autopsy; blood chemical analysis; immunoglobulin E; interleukin-18

Apstrakt

Uvod. Astma je jedan od čestih uzroka iznenadne smrti u Japanu. *Postmortem* dijagnoza astme bazirala se na morfološkim nalazima pluća, histološkim činjenicama, ali saopšteno je, takođe, da su biohemijski markeri, kao što su ukupni i specifični imunoglobulin E (IgE) od koristi. **Prikaz bolesnika.** Prikazali smo slučaj smrti od astme. Japanac, tridesetih godina, sa dispnejom, kolabirao je iznenada. Ambulantnim kolima prebačen je u bolnicu, ali je kardiopulmonalno oživljavanje bilo bez efekta. Na osnovu nalaza autopsije zaključili smo da je uzrok smrti asfiksija usled napada astme. Rezultati biohemijskih analiza ukazali su na teški oblik astmatskog napada. **Zaključak.** Kod prikazanog bolesnika, biohemijsko ispitivanje seruma na autopsiji pružilo je korisne podatke za dijagnozu astmatičnog napada koji je izazvao smrt.

Ključne reči:
asthma; smrt, iznenadna; autopsija; krv, hemijske analize; IGE; interleukin-18

Introduction

Asthma is the one of the major causes of sudden death. In Japan, approximately 4 000 patients have died annually in the past few years [1]. Postmortem diagnosis of asthma has been based on morphological findings such as overdistention of lung, mucous plugs and histological evidence (loss of the epithelium, hypertrophy of the bronchial smooth muscle, basement membrane thickening and infiltration of eosinophils). It was also reported that the biochemical markers such as total and specific IgE, are useful in the diagnosis of a fatal asthma attack[2]. Here we report an autopsy case of fatal asthma with biochemical examinations.

Case report

The deceased was a Japanese male in his thirties who had suffered from asthma since childhood. For a few years before his death, he had a history of hospital admissions for the treatment of severe asthma attack. On the day of his death, despite not feeling well, he worked until evening. After work, he made his way toward hospital, but complained of dyspnea and collapsed suddenly. He was taken by ambulance to the hospital and was in cardiopulmonary arrest on arrival. Despite the cardiopulmonary resuscitation, his death was confirmed. An autopsy was performed approximately 18 hrs after his death.

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Autopsy findings: the deceased was a Japanese male, 171 cm in height and 61 kg in weight. No external evidence of violence was found. The internal examination revealed that the left and right lung weighed 360 g and 445 g, respectively, and were overdistended (Figure 1a). The bronchi were filled with mucous plugs. Histologically, the lungs were emphysematous and showed occlusion of the airway lumen with secretions, loss of the epithelium, hypertrophy of the bronchial smooth muscle with infiltration of eosinophils (Figure 1b). The heart weighed 325 g, and showed no histologically remarkable findings. The brain weighed 1 525 g and was slightly edematous. There were no notable changes, other than congestion in the other organs.

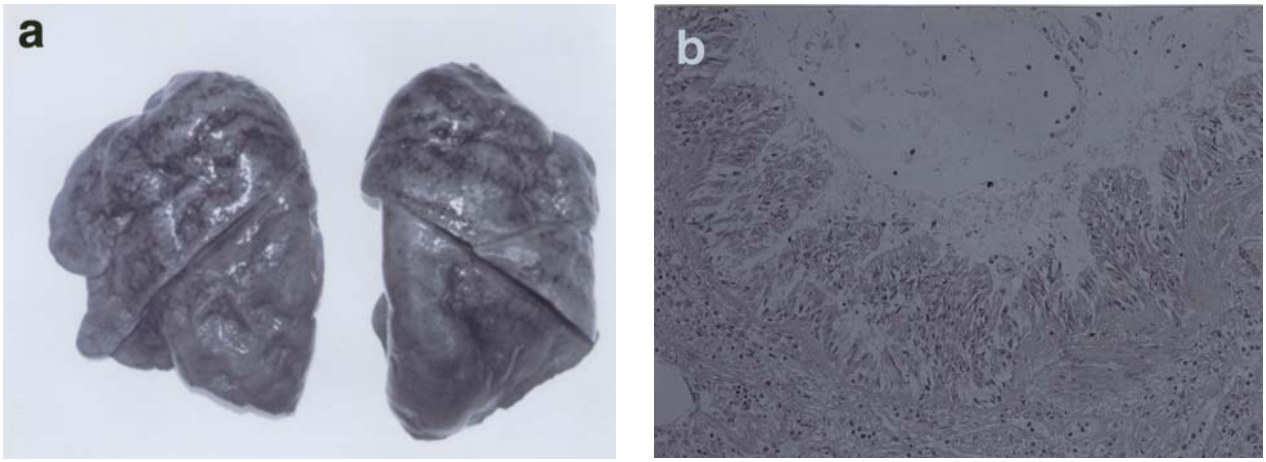

Fig. 1 – Gross appearance of the lung (a), mucous plug and infiltration of eosinophils (b) HE ×20)

Table 1

Mast cell tryptase, total immunoglobulin E (IgE) and interleukin-18 (IL-18) levels in sera

Parameters	Patient's value	Normal value
Tryptase (μg/l)	6.2	< 10
Total IgE (IU/ml)	770	< 173
IL-18 (pg/ml)	1 220	259*

*The mean value+3SD of the serum IL-18 concentration in healthy subjects

Table 2

Allergen-specific immunoglobulin E (IgE) levels

Allergen	IgE (UA/ml)
House dust	92.4
Acarus *(Dermatophagoides pteronyssinus)*	71.7
Candida	39.3
Japanese cedar	10.3
Dactylis glomerata	2.87
Moth	1.57
Cat dander	0.72

Levels less than 0.34 UA/ml are considered negative

Biochemical examination: the femoral blood was collected for subsequent biochemical examination. Quantification of total imunoglobuline E (IgE), specific IgE, mast cell tryptase and serum interleukin-18 (IL-18) were performed. Total IgE and the specific IgE were assayed by commercial fluoroenzyme immunoassay (FEIA) (UniCAP, Phadia, Uppsala, Sweden). Serum mast cell tryptase level was determined using FEIA (UniCAP TRYPTASE; Phadia, Uppsala, Sweden). Serum IL-18 concentration was measured by a sandwich ELISA (MBL, Nagoya, Japan). The levels of mast cell tryptase, total IgE, and IL-18 in sera are shown in Table 1. Specific IgE was found positive for some kinds of allergens, as shown in Table 2.

Toxicological analysis: screening of the urine sample, using a Triage™Drugs of Abuse panel (Biosite Diagnostic Inc. San Diego) was negative. No ethanol was detected in the blood or urine using head-space gas-chromatography.

Discussion

It is well known that asthma is one of the major causes of sudden death[1]. In the present case, we concluded that the cause of death was asthmatic atack, from the macroscopic and histopathological findings such as over distention of

lungs and mucous plugs, loss of the epithelium and infiltration of eosinophils.

There is a strong association between asthma and levels of serum IgE [2, 3]. Together with the above findings, further biochemical examination revealed that high levels of total IgE and seven kinds of specific IgE are considered positive for allergens. According to a previous report, high levels of total IgE and a large number of positive allergens indicate the severity of asthma [2]. Thus, our findings indicated that the deceased had a severe asthmatic condition.

Tryptase, a protease in mast cells, is considered an indicator of anaphylaxis. It is useful for the postmortem diagnosis, as it is stable in serum over a period of days [4–6]. Although asthma may be related to an allergic reaction, tryptase may not be useful in the diagnosis of a fatal asthmatic attack [2]. Anaphylaxis is a systemic disorder of the vasculature, but asthma is a local disorder of the bronchi [7]. This may influence the difference of the serum tryptase level. In the present case, the serum tryptase level was within normal range, which also suggests that the cause of death was asthma.

Histamine is a mediator of allergic responses [8]. As histamine is not stable and its metabolism is very rapid, it is not suitable as a marker of allergic reactions [4]. Most histamine is stored in mast cells and released quickly into the bronchial tissue, and increase of IL-18 production in asthma may be partly stimulated by the histamine release [9]. Interleukin-18, a proinflamatory cytokine, that induces interferon gamma, plays an important role in Th1 cell response [10]. It has been reported that IL-18 may act as a co-inducer of Th1 and Th2 (activated + helper) cytokines [11]. Asthma is a Th2-dominant disease and serum IL-18 levels reflect the activities of asthma exacerbation [9]. In the present case, because the IL-18 level was above the normal range, it is speculated that his condition was poor. However, since there was no data for the stability and influence of IL-18 concentration in the postmortem sample, further studies might be required.

Conclusion

In the present case, the biochemical examination of the serum obtained at autopsy gave helpful information for the diagnosis that asthmatic attack was a cause of death.

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