Institute of Experimental Morphology and Anthropology

Acta morphologica et anthropologica, 9
Sofia • 2004

Morphological Changes in Lungs in Bronchial Asthma (Based on Forensic Material)

J. Petev, D. Radoinova**, E. Softova****

** Militarymedical Academy – Naval Hospital – Varna*
*** Medical University – Varna, Department of Forensic Medicine*
**** Medical University – Varna, Department of General and Clinical Pathology*

With the aim to study the light microscopy findings in the lungs in the case of asthma an autopsy material was examined from 20 cadavers aged 22 to 61, 10 of them with diagnosed bronchial asthma, and 10 controls (traumas, car accidents) with no data pointing to pulmonary diseases. The materials were treated by the standard paraffin method and were stained by haematoxylin-eosin, AZAN (Kruchaj), PAS (McManus) and toluidin blau. There is established strongly manifested thickening of the basement membrane (from 12.5 to 22.5 μm) with its getting bared along a great length. Only basal cells of the epithelium were reserved. The smooth muscular cells of the wall of the bronchi are with hypertrophy, and in some places with atrophy, replaced by connective tissue. In the submucosa and among the epithelial cells were seen infiltrations of plasmocytes, lymphocytes, mastocytes and eosinophilic leukocytes (only in half of the cases). The established changes show that the asthmatic inflammation provokes permanent modifications in the respiratory tubes, evident in the desquamation of the bronchial epithelium and the excessive thickening of the basement membrane.

Keywords: asthma, morphology, basement membrane.

Introduction

The bronchial asthma has been defined as a chronic inflammatory disease in the basic national and international consensus [4, 5, 7, 14]. The use only of the methods in the monitoring and the detailed study of asthma practically proved to be insufficient as a result and as a precision. The reason is the lack of good correlation between specificity and sensitivity during this type of examinations [6, 8, 13] and the secondariness of the functional phenomena in relation to the morphological changes.

As a consequence during the last decade a great number of leading scientists [1, 2, 3, 6, 8, 9, 10, 11, 12, 13], using necropsy and biopsy material, discovered some of the basic pathomorphological changes in the respiratory tubes of people suffering from asthma.

The pathomorphological changes in the bronchial epithelium, manifested in destruction and desquamation, inflammatory cell infiltrations in the submucosa, composed of eosinophiles, neutrophiles, mastocytes, macrophages and lymphocytes in vari-

ous ratios [1, 10, 11], as well as the impressive thickening of the basement membrane even with young, newly-diagnosed asthmatics [2, 6, 8, 13], became basic vectors in the study of the characteristics of the bronchial asthma.

With the wide use of the endobronchial biopsy as a method of examination it became possible to use the so-called in vivo examination of the morphological picture of asthma and the connected with the asthmatic inflammation immunological phenomena. Unfortunately the endobronchial biopsy has one fundamental drawback – the small quantity of material. This makes difficult the interpretation of the morphological changes and some alterations even become disputable (e.g. the desquamation of the bronchial epithelium in pinch biopsy according to some authors is due to artifact of the crushing of the tissue [12].

The alternatives include the so-called expanded pinch biopsy, the open pulmonary biopsy or the examination of autopsy material in diagnosed asthma. The first two alternatives are practically rejected by the volunteers because of their invasiveness.

Due to this the examination of autopsy material from forensic cases, diagnosed with asthma while alive, could give valuable additional information, regarding the study of the characteristics of the asthmatic inflammation.

In this connection we set before ourselves ***the aim*** of studying the light microscopy morphological findings in autopsied forensic cases of individuals, diagnosed with bronchial asthma, belonging to various age groups.

Material and Methods

Material from the lungs of 20 individuals within the age range of 22 to 61 was examined. The cases studied were divided in two groups: first group – 10 cases of individuals, who had had bronchial asthma and died a sudden death; second group – controls – 10 cases with no evidence of any pulmonary diseases (car accidents, hangings, other traumas).

The materials from the lungs were fixed in 10% formalin and processed by the paraffin method. On sections 5μm thick were applied colourings by haematoxylin-eosin, PAS-reaction of McManus with the Schiff's reactive for proving the existence of neutral glycoproteins, by toluidin blue with pH 2,0 for acidic glycosaminglicans and mastocytes, colouring with AZAN according to Krutchay for revealing connective tissue.

Results

First group – with proved bronchial asthma

During hystological study of the lungs the following changes were discovered: the bronchi are with dilated or unevenly lined lumens. The explicit thickening of the basement membrane attracts attention, too. Its thickness varies from 12.5μm (the thinnest measured among all the cases) to 22.5μm (the thickest), or an average of 15.33μm the norm being up to 5μm.

In all cases studied the basement membrane is bared either thoroughly or just in separate regions, or upholstered with single-layer epithelium – one line of basement cells most of which are slightly rounded, with nuclei arranged like "segments of rosary". Sections, covered with normal multiple-layer epithelium, are visible too. Foci with basement hyperplasia are observed as well and here the cells are with oblong, oriented perpendicularly to the basement membrane nuclei.

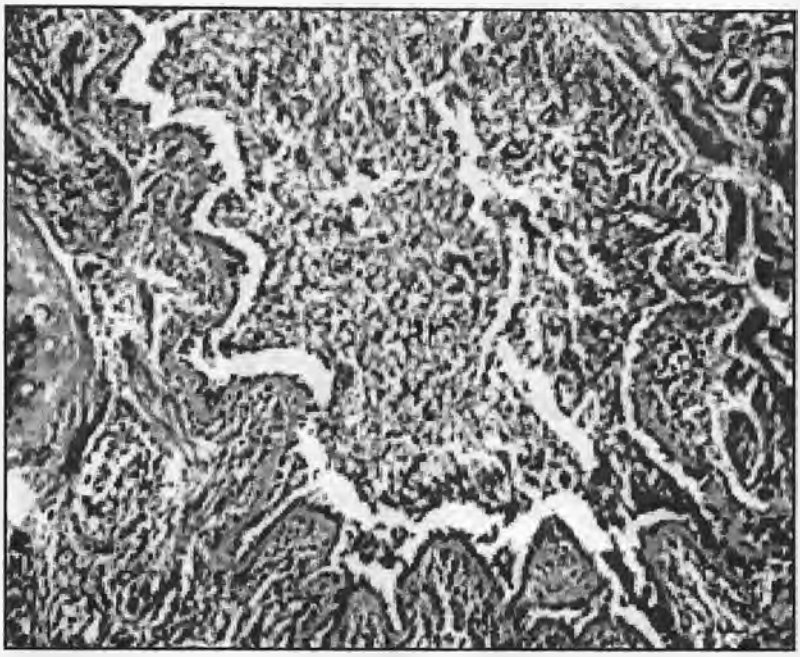

Fig. 1. Part of the bronchial wall with greatly thickened basement membrane, which in many places is bared, stained by HE (Microphoto × 200)

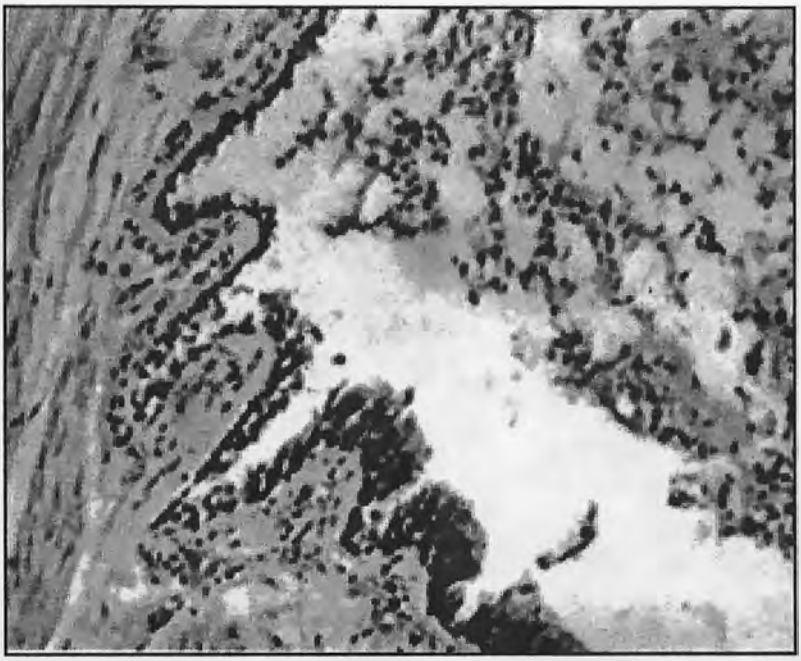

Fig. 2. Part of bronchial wall with thickened basement membrane; foci with multiple-line epithelium; stained by TB (Microphoto × 200)

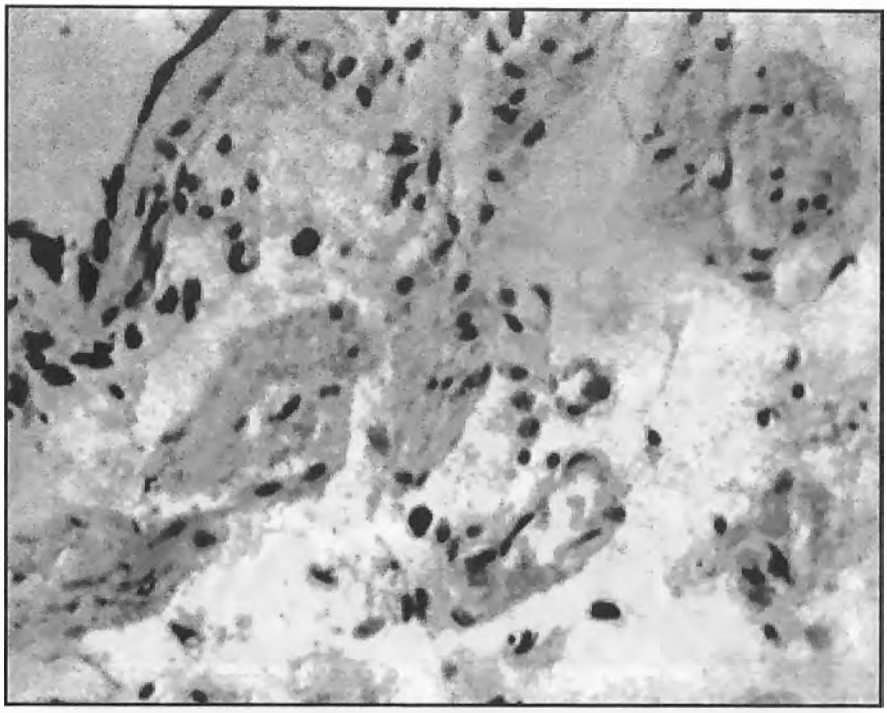

Fig. 3. Presence of scattered mastocytes in the wall of bronchus, stained by TB (Microphoto × 400)

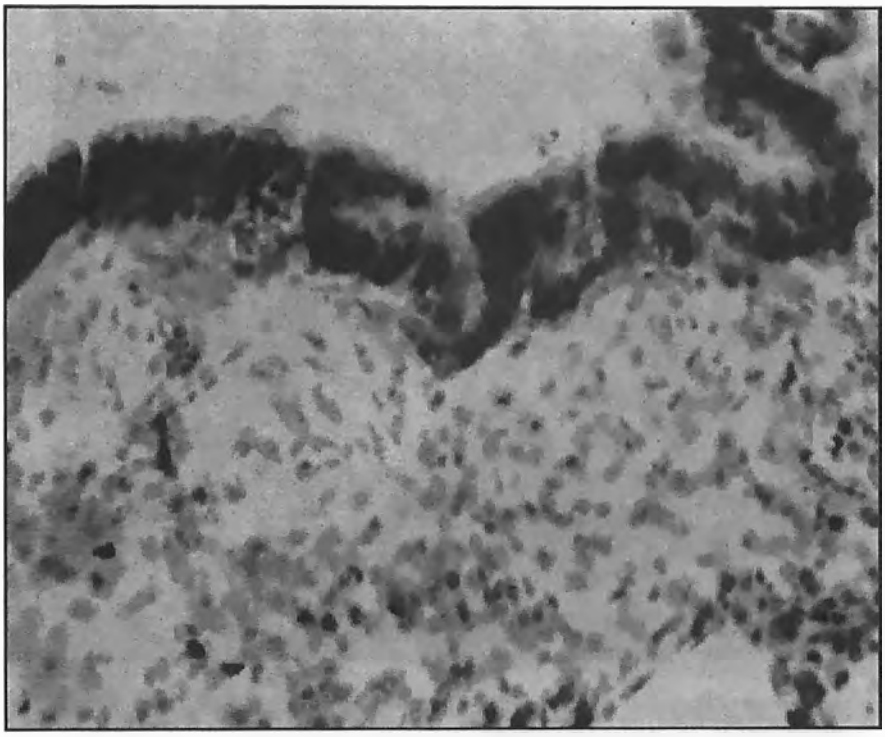

Fig. 4. Part of bronchial wall from a control case, stained by HE (Microphoto × 200)

The flaked epithelium is in the form of stripes or layers and it is found in the lumens of the bronchi, mixed with mucous materials and inflammatory cells (Figs 1, 2).

In all cases there is hyperplasia of the Goblet cells with increased quantity of mucous substances in their cytoplasm. There are changes observed in smooth muscular cells of the wall of the bronchi, manifested in zones with hypertrophy and such with atrophy, and widely spread connective tissue in their place.

The inflammatory infiltration in the submucosa and between the epithelial cells is presented in all cases by lymphocytes, plasmocytes and eosinophilic leukocytes (in one half of the cases). Also observed are scattered mastocytes, some of which are with degranulated cytoplasm.

Around the so altered bronchi in the pulmonary parenchyma are observed emphysema, hemosiderosis, foci or diffusion interstitial fibrosis, hyperemia and oedema.

Second group – controls without evidence of chronic pulmonary disease – missing deviations from the normal structure of the bronchial wall.

Discussion

It was proved with methods, based on the immunohystochemistry and flowcitometry, that the asthmatic inflammation has its own immunological characteristics, different from the other acute and chronic pulmonary diseases. Unfortunately these methods are expensive and labour consuming, due to which their routine use becomes considerably difficult. On the other hand, despite the large number of publications, regarding the light microscopy changes in asthma, at this stage no investigators undertake to define whether the inflammation has a specific morphological picture. Yet an object of particular interest is the great thickening of the basement membrane – a result from the deposition of the extracellular matrix [2, 6, 13]. This thickening can be discovered even at the earliest stages of the disease [6, 10] and is at the base of the so-called remodelling of the respiratory tubes in asthma, leading to alteration of its functional characteristics at the latest stages of the disease [3, 10]. We think that the morphometry of the basement membrane, and especially with in-patients having different duration and severity of the disease could give valuable information about the pathomorphological dynamics of the asthma.

Conclusions

1. In all cases from the first group there is a manifested thickening all along the basement membrane – a fact, which was present in none of the controls.

2. The apparent destruction of the bronchial epithelium with baring of large sectors of the basement membrane is probably not an artifact because it is either missing or discreetly presented (only in small separate sectors) in the controls.

3. The eosinophils are not an unavoidable component in the inflammatory-cell infiltrations in asthma.

4. Irrespective of the functional reversibility of the limits of airflow in asthma, the morphological changes in the respiratory tubes are durable and irreversible. Probably they are the reason for the alteration of the functional characteristics in the last stages in the development of this disease.

References

1. Bousquet, J. Inflammatory processes in asthma. – Internat. Archives of Allergy & Appl. Immun., **94**, 1991, 227-32.
2. Davies, D. E., R. Polosa. The epithelial growth factor receptor and its ligand family: their potential role in repair and remodeling in asthma. – Allergy, **54**, 1999, No 8, 771-783.
3. Enarson, D. Asthma, asthmalike symptoms, CB and bronchial reactivity. – Am. Rev. Resp. Dis., **136**, 1987, 613-74.
4. Global initiative for asthma. Publ. N 95-3091, 1996.
5. Guidelines for the diagnosing and management of asthma. Expert Panel report II, N 97-4051, 1997.
6. Holgate, S. T. Epithelial-mesenchymal interactions in the pathogenesis of asthma. – J. Allergy Clin. Immunol., **105** (2pt1), 2000, 193-204.
7. International report – consensus for diagnosing and treatment of asthma. Bethezda, Publ. N 90-3091, 1992.
8. Jeffery, P. K. Morphology of airway wall in asthma and COPD. – Am. Rev. Resp. Dis., **143**, 1991, 1152-1158.
9. Klark, T. J., H. S. Godfrey, T. H. Lee. ASTHMA. Chapman & Hall medical. Publ. No 044231582 1993.
10. Laitinen, L. A., A. Laitinen. Bronchial biopsy findings in intermittent or early asthma. – J. Clin. Immunol., **98** (5pt2), 1996, 3-6.
11. Ollerenshaw, S. L. Characteristic of the inflammation in biopsies from large airways of subjects with asthma and with COPD. – Am. Rev. Resp. Dis., **145**, 1992, 922-927.
12. Ordonez, C. R., D. Ferrando, M. Hyde, H. H. Wong, G.V. Fahy. Epithelial desquamation in asthma: artifact or pathology? – Am. J. Crit. Care Med., **162** (6), 2000, 2324-2329.
13. Watanabe, K., S. Senju. Thickness of the basement membrane of bronchial epithelial cells in lung disease as determined by transbronchial biopsy. – Respir. Med., **91**, 1997, No 7, 406-410.
14. Национален доклад-консенсус за диагностика и лечение на астмата. София, 2000.