

Histochemical Nature of Eosinophilic Globules in Pheochromocytoma of Adrenal Medulla

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SUMMARY : Eosinophilic globules were observed in 7 out of 11 cases of pheochromocytoma of the adrenal medulla. All of these globules were present in the cytoplasm, and were round and eosinophilic, measuring 3 μ m to 30 μ m in diameter. These globules were periodic acid Schiff (PAS)-positive with and without diastase predigestion, phosphotungstic acid hematoxylin (PTAH) positive, acid fuchsin positive, and autofluorescent under ultraviolet illumination. These findings were very similar to the eosinophilic globules of yolk sac tumor, hepatocellular carcinoma, Kaposi's sarcoma, and alpha-1-antitrypsin deficiency in light microscopy and histochemistry. They were not stained with Grimelius's method for argyrophil reaction, and Fontana-Masson's method for argentaffin reaction. It might be suggested that eosinophilic globules in pheochromocytoma of the adrenal medulla were not related to the chromaffin secretory granules and these globules were glycoprotein.

INTRODUCTION

Eosinophilic globules have been reported in the adrenal medulla,²⁾⁵⁾ lung carcinoma,³⁾⁶⁾ hepatocellular carcinoma,³⁾⁸⁾¹¹⁾ breast carcinoma,³⁾ yolk sac tumor,⁹⁾¹⁵⁾¹⁶⁾ renal cell carcinoma,¹⁾ Kaposi's sarcoma,¹³⁾ and alpha-1-antitrypsin deficiency.³⁾¹⁰⁾ In the adrenal medulla, these globules were stained with periodic acid Schiff (PAS) with and without diastase predigestion, phosphotungstic acid hematoxylin (PTAH), and autofluorescent with ultraviolet illumination.²⁾⁵⁾ Such globules have been detected rarely in the pheochromocytoma of the adrenal medulla.⁷⁾ Their nature and genesis in pheochromocytoma have not been reported.

The purpose of this report is to present the histochemical characteristics of eosinophilic globules in pheochromocytoma of the adrenal medulla.

MATERIALS AND METHODS

Eleven cases of pheochromocytoma of the adrenal medulla were studied by light microscope. The materials of seven cases were derived from surgical operations in the Nagasaki University Hospital and four other cases were from other hospitals in Nagasaki City.

For light microscopic study, the tissues from the surgical specimen were fixed in 10% formalin, routinely embedded in paraffin. Paraffin-embedded sections were stained with hematoxy-

lin-eosin stain (HE), periodic acid schiff (PAS) stain, PAS with and without diastase predigestion method, phosphotungstic acid hematoxylin (PTAH) method, Mallory's method for collagen fiber, Prussian blue reaction for iron, trichrom method for connective tissue, Mayer's method for mucin, silver impregnation method for reticulum fiber, alcian blue (pH 2.5) stain for acid mucopolysaccharide, Grimelius's method for argyrophil reaction, Fontana-Masson's method for argentaffin reaction, and acid fuchsin method for easy detection of eosinophilic globules.¹⁴⁾ Additionally, unstained and HE stained sections of paraffin-embedded tissues were examined with ultraviolet illumination using fluorescence microscope (Zeiss).

RESULTS

Eosinophilic globules were recognized in seven (63.6%) of 11 cases of pheochromocytoma in the adrenal medulla. In HE sections, all of the eosinophilic globules were present in the cytoplasm, and were round and eosinophilic, measuring about 3 μ m to 30 μ m in diameter (Fig. 1). They usually occurred singularly within cells, but occasionally in groups without fusion.

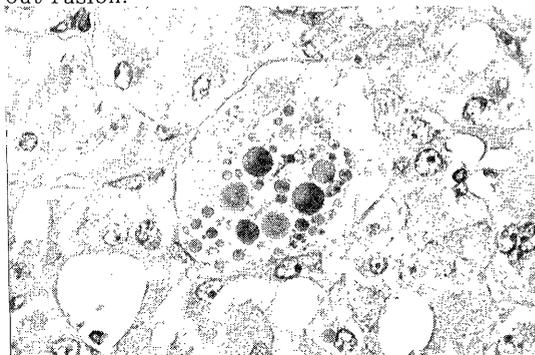


Fig. 1. A cluster of many globules are observed in the cells of pheochromocytoma. (Hematoxylin-eosin, $\times 400$)

The globules were stained with PAS with and without diastase predigestion, phosphotungstic acid hematoxylin (PTAH), and trichrom stain. Mayer's method for mucin, alcian blue (pH 2.5), Prussian blue reaction for iron, and silver impregnation method for reticulum fiber did not stain the globules. They were also

not stained with Grimelius's and Fontana-Masson's methods. They were easily distinguished from red blood cells by using acid fuchsin method (Fig. 2). These globules were autofluorescent intensely in unstained and HE stained sections with ultraviolet illumination by the transmitted fluorescence microscope (Zeiss) (Fig. 3).

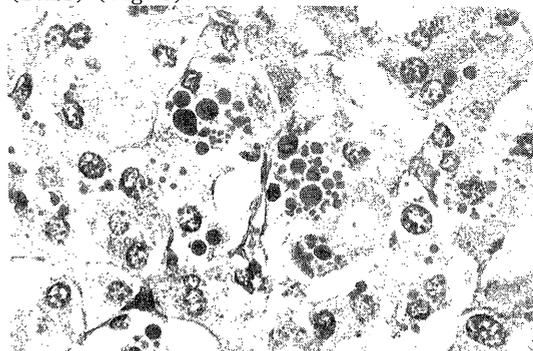


Fig. 2. Differently sized round eosinophilic globules are seen in the cells of pheochromocytoma. (Acid fuchsin method, $\times 400$)

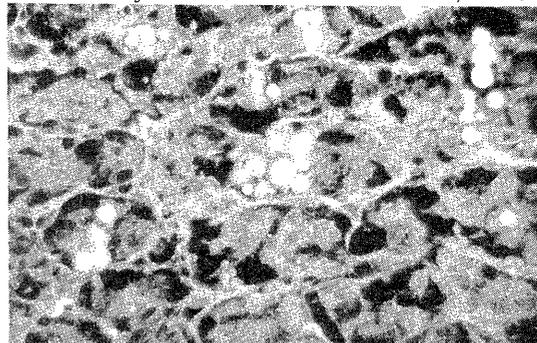


Fig. 3. Eosinophilic globules are autofluorescent under ultraviolet illumination with BP 450-490 and FT 510 filters. ($\times 400$)

COMMENT

The eosinophilic globules were recognized in seven of 11 (63.6%) pheochromocytoma of the adrenal medulla. This incidence is higher than in other neoplasms.¹³⁾ Light microscopically, these globules were similar to the globular bodies found in yolk sac tumor,⁹⁾¹⁵⁾¹⁶⁾ Kaposi's sarcoma,¹³⁾ alpha-1-antitrypsin deficiency,³⁾⁹⁾ hepatocellular carcinoma,³⁾⁸⁾¹¹⁾ lung carcinoma,³⁾⁶⁾ breast carcinoma,³⁾ renal cell carcinoma,¹⁾ and adrenal medulla.²⁾⁵⁾ They also have similar histochemical properties, such as PAS, with and without diastase predigestion, phospho-

tungstic acid hematoxylin (PTAH), and auto-fluorescence positive (Table 1). Some of these globules were stained positively by immunohistochemical techniques for alpha-1-antitrypsin, alpha-fetoprotein, and beta-subunit of human gonadotropin, or human albumin.⁹⁾¹⁰⁾¹⁵⁾ 16) Hart described that eosinophilic globules in the adrenal medulla had a possible relation to infections and certain neurologic disease such as multiple sclerosis and Parkinson's disease.⁵⁾ Dekker suggested that hyaline globules in the adrenal medulla were similar to lipofuscin pigments and had a relationship to products of lipid peroxidation.³⁾ But we could not confirm these findings in our cases of pheochromocytoma. Eosinophilic globules are certainly different from lipofuscin pigments in the light microscopic and histochemical properties. Lipofuscin pigments are brown, PTAH negative and yellow-orange autofluorescent under ultraviolet illumination. These globules in pheochromocytoma of the adrenal medulla were not stained with argyrophil and argentaffin reactions. These histochemical findings suggested to us that eosinophilic globules of pheochromocytoma of the adrenal medulla were not related to the chromaffin granules and were glycoprotein.

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Table 1. Characterization of eosinophilic globules

Globules	PAS	D-PAS	Trichrom	PTAH	Auto - fluorescence	Authors
Pheochromocytoma	+	+	Red	+	+	Present cases
Yolk sac tumor	+	+	ND	ND	ND	Wold et al., 1984
Kaposi's sarcoma	+	+	Red	+	+	Senba et al., 1986
Alpha-1-antitrypsin deficiency	+	+	Red	+	+	De Lellis et al., 1972
Hepatocellular carcinoma	+	+	ND	+	+	Dekker et al., 1973
Lung carcinoma	+	+	ND	+	+	Dekker et al., 1973
Breast carcinoma	+	+	ND	+	+	Dekker et al., 1973
Renal cell carcinoma	+	+	ND	+	+	Datta, 1977
Adrenal medulla	+	+	ND	+	+	Dekker et al., 1971

PAS : periodic acid Schiff, D-PAS : periodic acid Schiff reagent after diastase predigestion, PTAH : phosphotungstic acid hematoxylin, ND : not done, + : positive.

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