Virchows Arch [Pathol Anat] (1982) 397:1–6

Virchows Archiv A

Immunohistochemical Study of the Immunoglobulin Classes of the Plasma Cells in Papillary Syringadenoma

Nobby C. Mambo

Department of Pathology, College of Medicine, University of Saskatchewan, Saskatoon, Saskatchewan, Canada S7N OXO

Summary. Twenty-one papillary syringadenomas were studied using immunohistochemical methods to characterise the immunoglobulin classes associated with the plasma cell infiltrates characteristically seen in these neoplasms.

It was found that the majority of the plasma cells produce IgG (65.2%). Plasma cells associated with IgA and IgM production constituted 30.4% and 4.4% respectively of the enumerated cells.

These findings confirm the long-presumed inflammatory nature of these infiltrates.

Key words: Papillary syringadenoma – Immunohistochemistry – Immunoglobulins

Papillary syringadenoma (syringocystadenoma papilliferum) is a sweat gland neoplasm whose clinical and pathologic features have been well documented (Pinkus 1954; Helwig and Hackney 1955; Brownstein and Shapiro 1975; Mehregan and Rahbari 1978). The neoplasm typically occurs in the head and neck region, particularly on the scalp, although it has been observed in other sites (Helwig and Hackney 1955; Rostan and Waller 1976). Their histogenesis is still far from settled but there is data to support both apocrine and eccrine origins (Helwig and Hackney 1955; Pinkus and Mehregan (1981); Hashimoto 1972; Landry and Winkelmann 1972).

The histopathologic features of this neoplasm, although variable, are quite distinctive and diagnostic and have been well documented. One of the characteristic features of these neoplasms is the infiltration of the papillary fronds by plasma cells, some of which may be immature. The cause, and particularly the nature, of this plasma cell infiltrate is not known.

The purpose of this study was to characterise the immunoglobulin classes of these plasma cell infiltrates present in papillary syringadenomas by immunohistochemical means and determine their nature.

Offprint requests to: N.C. Mambo at the above address

0340-1227/82/0397/0001/$01.20

Materials and Methods

Thirty-one papillary syringadenomas, fulfilling the accepted histologic criteria, (Pinkus 1954; Helwig and Hackney 1955) were identified during a recent review of the 280 benign sweat gland neoplasms available in the surgical pathology files of our and two affiliated institutions.

The paraffin embedded tissue blocks were retrieved in all cases and further haematoxylin and eosin histologic sections (4 per block) prepared; these and the original ones were studied to detect those lesions in which there was ulceration or disruption of the tumor epithelium, direct exposure of the stroma to luminal secretions and the presence of acute inflammatory exudate in the cystic cavities, lumina or stroma. Ten lesions were excluded from the study on the basis of the presence of the above features.

Ten cases of chronic tonsillitis and 5 of pilonidal sinus were selected for controls.

The unlabelled antibody method was used as previously described (Sternberger 1978; DeLellis et al. 1979). Briefly the sections were initially treated with 0.1% calcium chloride and 0.1% trypsin in 0.05 M TRIS buffer, pH 7.8 at 37° C for 15 min. Endogenous peroxidase was blocked by 10% hydrogen peroxide in absolute methanol. Non specific background staining was reduced by incubation of the sections with normal sheep serum at a dilution of 1:5 for 10 min.

The sections were then treated with rabbit-anti-human antiserum against IgG, IgA and IgM (Behring), Kappa and Lambda light chains (Dako). Dilutions of 1:500 for IgG, 1:300 for IgA and IgM and of 1:1000 for Lambda and Kappa light chains were used, with minimal background staining.

Sheep anti-rabbit serum (Antibodies Incorporated) was then applied, followed by peroxidase-anti-peroxidase complexes (Dako). Each stage lasted for 30 min and was followed by three washings in TRIS buffered saline. Finally the diaminobenzidine reaction was used to localise the sites of peroxidase. The slides were counter-stained with Harris Haematoxylin. Appropriate negative and positive controls were applied as previously described (DeLellis et al. 1979).

The enumeration of stained plasma cells was performed as previously described (Green and Fox 1972; Brandtzaeg et al. 1978). At random, 20 high power-fields ($\times 40$ objective) of the stroma were examined and all stained cells scored.

Results

Histopathology

The histomorphologic features of the neoplasms were similar to those already documented. There was some variation in the sizes of the neoplasms, some being very small while others being large.

Briefly the surrounding epidermis was either hyperkeratotic or acanthotic or both. Some neoplasms projected above the skin surface, The neoplasms presented as downward invaginations into the dermis with formation of tubular and cystic spaces; some of these contained secretions. The cystic and tubular structures were initially lined by stratified squamous epithelium which gradually gave way to pseudostratified columnar epithelium and this in turn gave rise to a two cell layered epithelium and this lined most of the cystic and tubular cavities and the papillary fronds that projected into cystic cavities and lumina. This epithelium was made up of tall columnar luminal cell with large nuclei and cuboidal basal cells with smaller dark nuclei; the latter rested on a well-developed basement membrane.

The papillary fronds varied in their size and stroma was infiltrated by varying populations of plasma cells and other mononuclear cells. The stroma around the neoplasms was similarly infiltrated. Most fronds were heavily

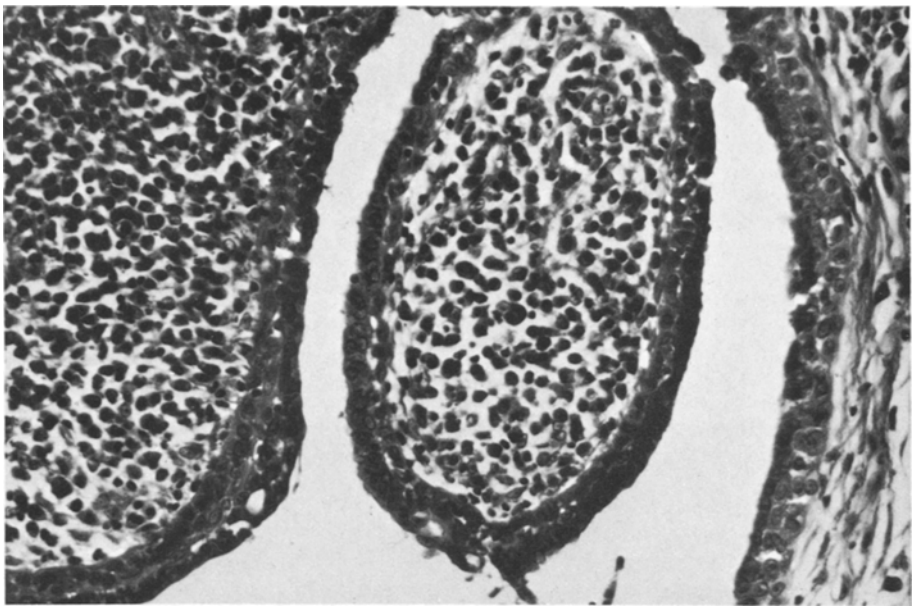

Fig. 1. Papillary fronds heavily infiltrated by plasma cells (H&E ×280)

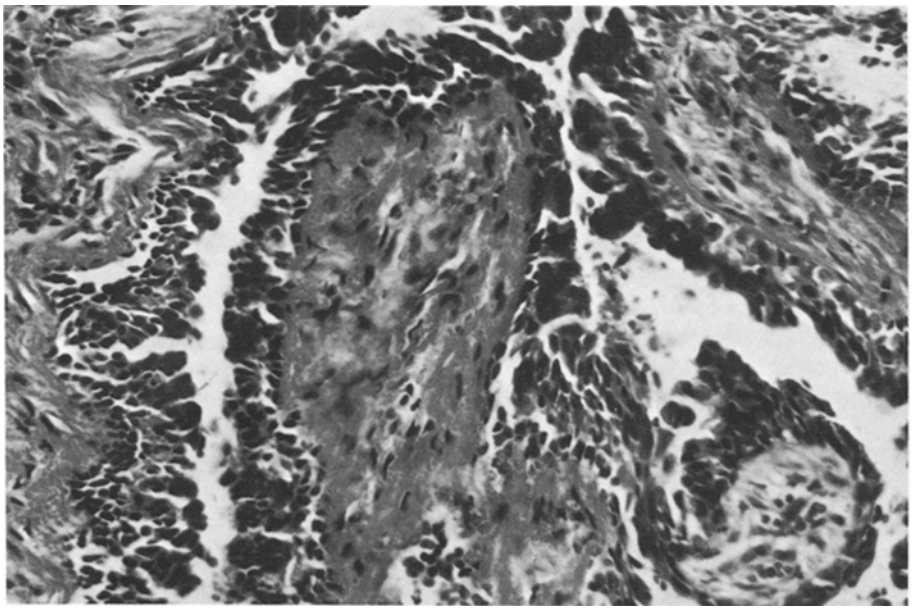

Fig. 2. Papillary fronds with fibrosed stroma and devoid of plasma cells (H&E ×280)

Table 1. Distribution of Immunoglobulin-producing cells in study and control cases

	% IgG cells ±S.D.	% IgA cells ±S.D.	% IgM cells ±S.D.
Papillary syringadenoma ($n=21$)	65.2±12.1	30.4±11.3	4.4±3.0
Chronic tonsillitis ($n=10$)	67.0±11.8	28.4±9.6	4.6±1.8
Pilonidal sinus ($n=5$)	70.5±12.5	25.6±14	3.9±3.4

S.D. = standard deviation; n = number of cases

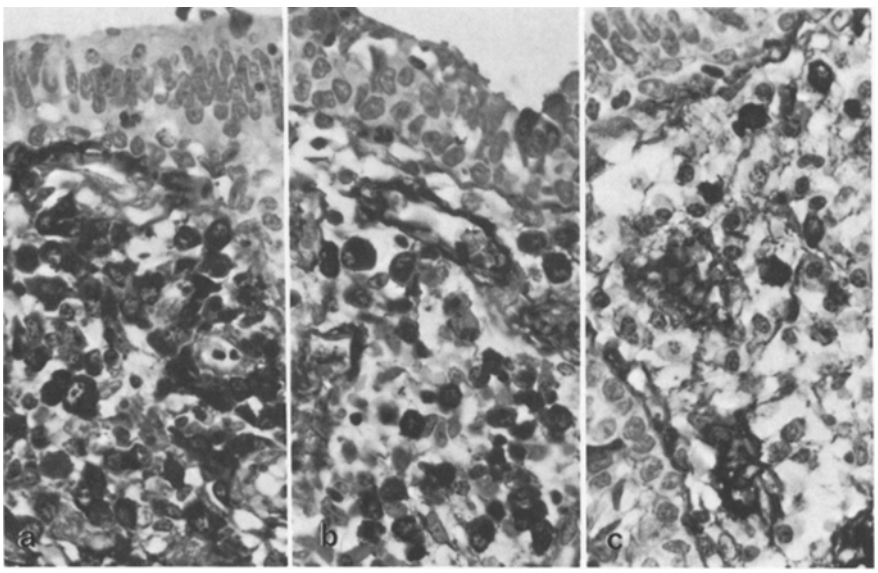

Fig. 3a–c. Immunoglobulin producing cells in papillary fronds in serial sections of same lesion (**a**) IgG cells, (**b**) IgA and (**c**) IgM. Note positive staining of some epithelial cells with IgG and IgA (Peroxidase-anti-peroxidase technic ×400)

infiltrated by plasma cells (Fig. 1) while occasional ones were sparsely or not infiltrated (Fig. 2). The infiltrates tended to be more marked in the large lesions. Occasional mononuclear cells were seen in the lining epithelium. Despite the intensity of plasma cells in some cases, no Russell bodies were seen. Lymphoid germinal centres were also not seen.

Immunoperoxidase Study

The distribution of the classes of immunoglobulins in the study and control cases are summarised in Table 1.

IgG producing plasma cells formed the majority of the immunoglobulin producing cells, constituting 65.2% (range 48–85%) of all enumerated plasma

cells in the study cases (Fig. 3a) with the IgA and IgM plasma producing plasma cells constituting 30.4% (range 26.8–45%) and 4.4% (range 0–16.4%) respectively (Fig. 3b and Fig. 3c). The stained plasma cells were evenly distributed in the papillary fronds and the surronding stroma. The Kappa and Lambda chains were also evenly distributed in each neoplasm. Some individual epithelial cells, usually the luminal ones, stained strongly for IgG and IgA and not for IgM. IgG and IgA were also detected in the secretions.

The tonsillar and pilonidal sinus tissues showed a similar predominance of IgG producing plasma cells, 67.0% and 70.5% respectively. Their content of IgA and IgM producing plasma cells was comparable to that of the study cases.

Discussion

Two findings in this study indicate that the mononuclear cell infiltrates in papillary syringadenomas are reactive in nature and are not an integral component of the neoplastic process.

The first is that there was marked variation in the amounts of plasma and other mononuclear cells among the papillary syringadenomas. The stroma of some papillary fronds did not contain any plasma cells while those of others were heavily infiltrated. Related to this was the observation that smaller lesions were not as heavily infiltrated as larger ones. This observation seems to suggest that the plasma cell infiltrates are a function of time.

The second is the striking preponderance of IgG producing plasma cells over the plasma cells producing the other two immunoglobulins. The distribution pattern was similar to that seen in the 2 control groups where chronic inflammation is known to be the antigenic stimulus. Results quite similar to those seen in the study cases have been reported by others in tonsillar tissue. Brandtzaeg et al. (1978) found that in tonsillar tissue IgG producing plasma cells constituted 65.2%, IgA producing plasma cells 30.1% and IgM producing plasma cells 30.1% and IgM producing plasma cells 3.5% with IgD producing plasma cells constituting the remaining 1.2%. This compares favourably with the results of the present study.

If the plasma cells were an integral part of the neoplastic process, one would expect to see a distribution of the immunoglobulin producing cells different from that typically seen in inflammatory processes or a predominance of 1 of the 2 light chains of the immunoglobulin chain.

In *summary*, the mononuclear cells that are seen in papillary syringadenomas are reactive in nature to some unidentified stimulus which would either be bacterial, viral or degenerating components of the neoplasm itself. The results of this study militate against their being an integral part of the neoplastic process and do not give an insight into the nature of the antigenic stimulus.

References

Brandtzaeg P, Surjan L, Berdal P (1978) Immunoglobulin systems of human tonsils. I. Control subjects of various ages, tonsillar morphometry and serum Ig concentrations. Clin Exp Immunol 31:367–381

Brownstein MH, Shapiro L (1975) The sweat gland adenomas. Int J Dermatol 14:397–411

DeLellis RA, Sternberger LA, Mann RB, Banks PM, Nakane PK (1979) Immunoperoxidase technics in diagnostic pathology. Am J Clin Pathol 71:483–488

Green FHY, Fox H (1972) An immunofluorescent study of the distribution of immunoglobulin-containing cells in the normal and the inflamed gallbladder. Gut 13:379–384

Hashimoto K (1972) Syringocystadenoma papilliferum. An electron microscopic study. Arch Dermatol Forsch 245:353–369

Helwig EB, Hackney VC (1955) Syringadenoma papilliferum. Lesions with and without naevus sebaceous and basal cell carcinoma. Arch Dermatol 71:361–372

Landry M, Winkelmann RK (1972) An unusual tubular apocrine adenoma. Arch Dermatol 105:869–879

Mehregan AH, Rahbari H (1978) Benign epithelial tumors of the skin. IV. Benign apocrine gland tumors. Cutis 21:53–56

Pinkus H (1954) Life history of naevus syringadenomatosus papilliferus. Arch Dermatol Syphilol 69:305–322

Pinkus H, Mehregan AH (1981) A Guide to dermatohistopathology. 3rd edn, Appleton-Century-Crofts, New York, p 444

Rostan SE, Waller JD (1976) Syringocystadenoma papilliferum in an unusual location. Report of a case. Arch Dermatol 112:835–836

Sternberger LA (1978) Immunocytochemistry. Prentice-Hall Inc, Englewood Cliffs, NJ

Accepted April 7, 1982