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Mixed hyperplastic and neoplastic polyp of the colon

An immunohistological study

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Summary. A small colonic polyp which was composed of equal parts of hyperplastic and adenomatous tissue sharing a common basement membrane, displayed a paradoxical distribution of immunohistological markers: In contrast with the neoplastic component, the hyperplastic tissue lacked signs of functional maturity (IgA, secretory component) and displayed markers associated with carcinoma (carcinoembryonic antigen, peanut-agglutinin binding).

Key words: Colonic polyp (mixed) – Cell differentiation – Adenoma – Hyperplasia – Antigens-neoplasm – Immunoenzyme technics

Introduction

Hyperplastic polyps of the colon are deemed to be innocuous, nonneoplastic lesions (Arthur 1968; Estrada and Spjut 1980; Fenoglio and Pascal 1982; Jass et al. 1984a; Kaye et al. 1973; Williams et al. 1980; review: Otto et al. 1976).

In contrast, colonic adenomas are regarded as a form of localized, polypoid, dysplastic and precancerous lesion (Morson 1983). The concept of an adenoma-adenocarcinoma sequence for colon carcinoma has been well established since 1974 (Enterline 1976; Fenoglio and Lane 1974; Morson 1974; review: Otto et al. 1976).

The histogenesis of hyperplastic polyps and adenomas has been studied (Goldman et al. 1970; Hayashi et al. 1974; Kaye et al. 1971; Kaye et al. 1973; Lane et al. 1971; Wiebecke et al. 1974; review: Otto et al. 1976). The hyperplastic polyp is characterized by focally enlarged crypts and by mucus depletion. The enlargement and elongation of the crypts are due to increase in cell numbers (hyperplasia) from a large but normally located proliferation zone. Towards the mouth of the crypt, the epithelium displays increasing amounts of cytoplasm, thus producing a serrated appearance. The adenoma, a benign neoplasm, consists of proliferating epithelia forming tubules and/or villi. It lacks epithelial differentiation and reveals extended proliferation zones transposed to the mucosal surface.

Rarely, colonic polyps may contain mixed hyperplastic and adenomatous tissues (Cooper et al. 1979; Estrada and Spjut 1980; Franzin et al. 1984; Sumner et al. 1981; Urbanski et al. 1984; Williams et al. 1980). We report the immunohistochemical findings in such a mixed colonic polyp.

Material and methods

A sessile, 4 mm polyp, 20 cm above the anus, was removed from the colon of a 66-year-old apparently healthy man. No other polyps were found nor were there signs of inflammation in the large intestine. The patient had no previous history of inflammatory bowel disease, and neither he nor members of his family were known to have gastrointestinal polyposis.

The biopsy specimen was fixed in 10% buffered formalin, and processed routinely. Serial 5-µm sections were stained for secretory component, IgA (alpha chain), carcinoembryonic antigen (CEA), and peanut lectin-binding (PNA) sites by a modified peroxidase-antiperoxidase technique (Sternberger et al. 1970; Gebbers 1981). The reagents were obtained from Dakopatts, Copenhagen.

Results

Histopathology. The polyp revealed intermingled hyperplastic and adenomatous zones (Fig. 1). About half of the polyp was typical hyperplastic tissue with a sawtooth appearance and prominent goblet cells. The other half consisted of closely packed adenomatous tubules made up by cylindrical, basophilic cells with small amounts of mucus, and a hyperchromatic, rod-like nucleus. Epithelial

* Dedicated to Prof. Dr. med. G. Seifert, on the occasion of his 65th birthday

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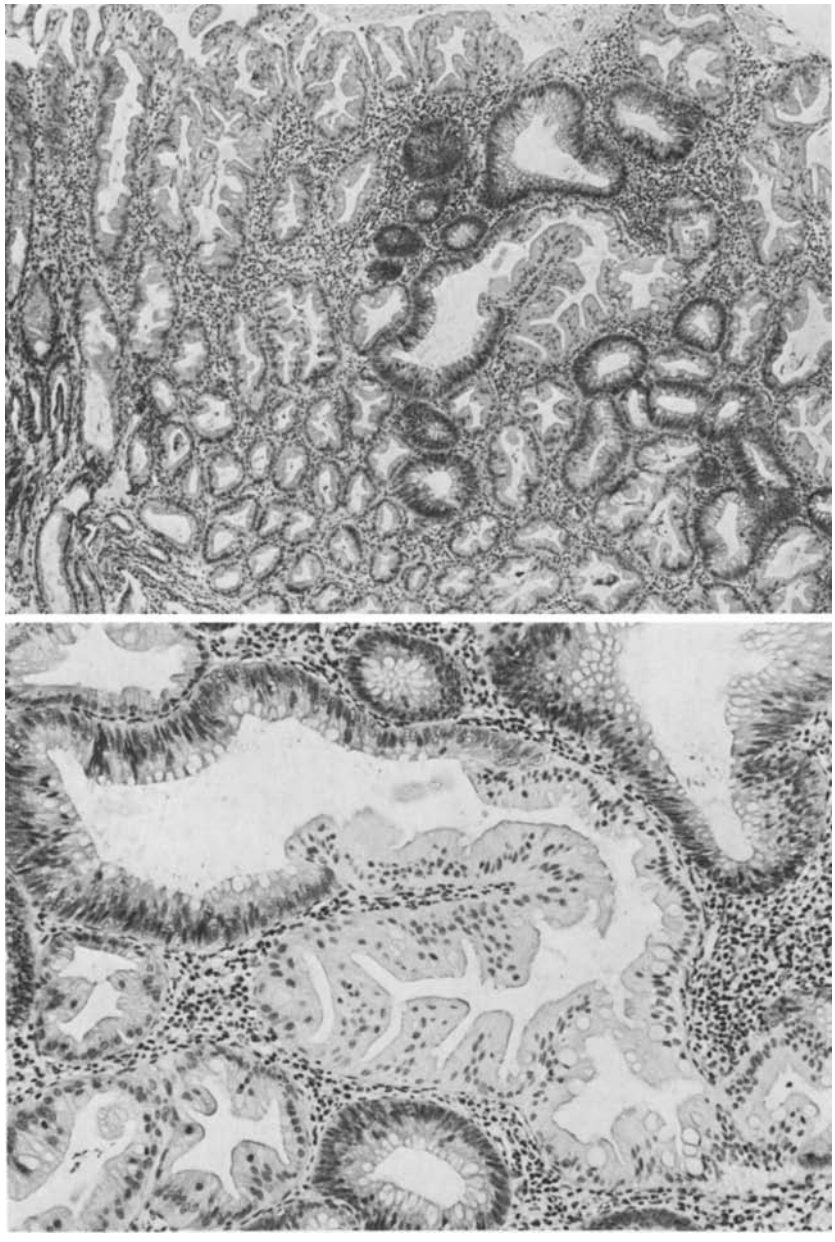

Fig. 1. Mixed hyperplastic and neoplastic polyp of the colon.
Top: Hyperplastic tissue (*left*) intermingles with tubular adenomatous tissue (*right*). HE ×50.
Bottom: Adenomatous (neoplastic) epithelium with hyperchromatic rod-like nuclei (*top*) shares the basement membrane with contiguous hyperplastic epithelium. HE ×100

Table 1. Trends of the main immunohistochemical markers of epithelial hyperplasia/neoplasia in the colon

	Normal epithelium	Polyp		Adenocarcinoma
		hyperplastic	adenomatous	
Mucus formation	+	+/(+)	(+)	+/(+)
IgA	++	−	++	−/(+)
SC	++	−/(+)	++	−/(+)
CEA	(+)	++	(+)	++
PNA	−	++	−	++

− negative; (+) slightly positive; + moderately positive; ++ marked positivity; −/+ variable

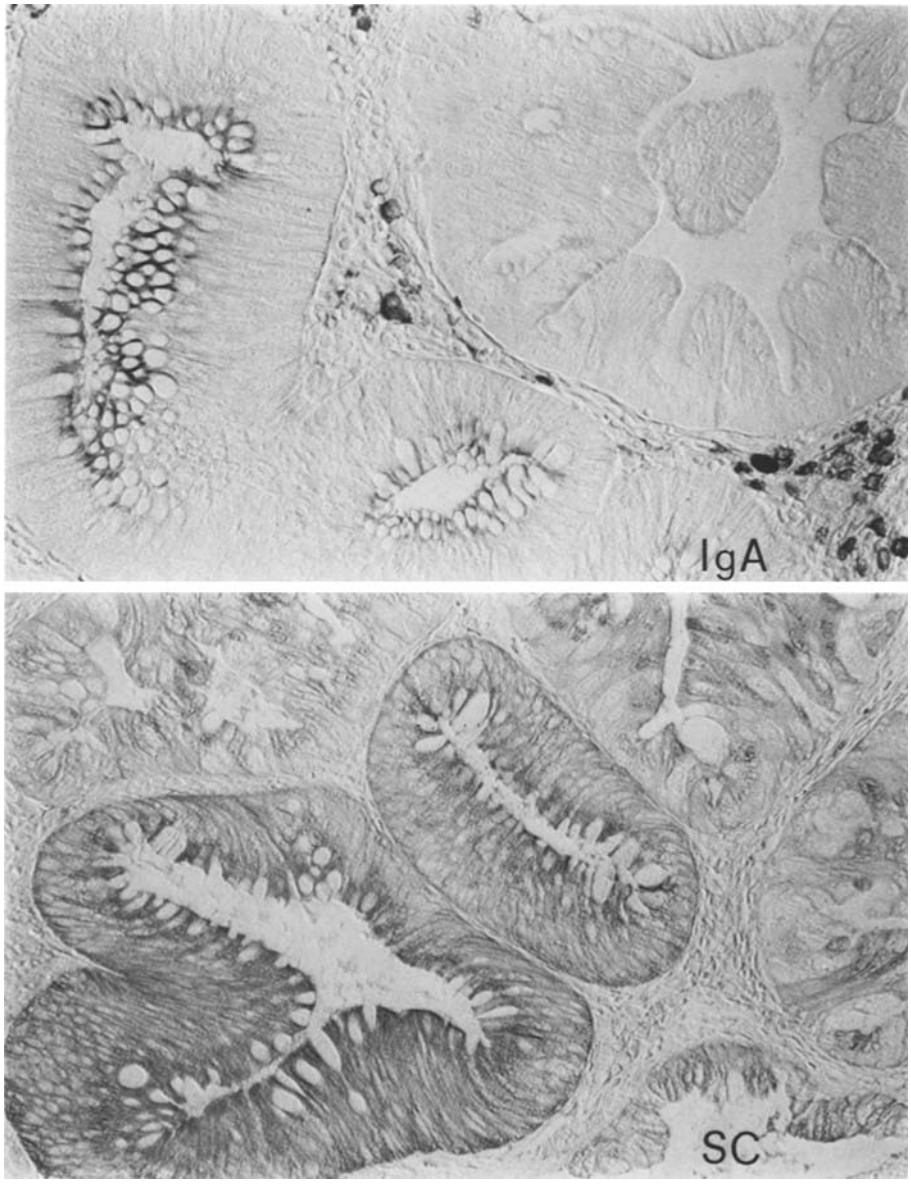

Fig. 2. Marked staining for IgA (*top*) and secretory component (*SC*) (*bottom*) in the neoplastic epithelium, but no staining for IgA or less staining for SC in the surrounding hyperplastic tissue. Immunoperoxidase (*PAP*) technique, no counterstain, Nomarski interference-contrast optics. ×950

stratification occurred. More mitotic figures were present than in the hyperplastic component. Hyper- and neoplastic epithelial cells were contiguous on the same basement membrane (Fig. 1).

Immunohistochemistry. IgA was evident in the apical region of adenomatous cells and in stromal plasma cells, but not in hyperplastic cells (Fig. 2). Secretory component (SC), present in neoplastic cells, was barely recognizable in the supranuclear region of hyperplastic cells (Fig. 2).

The reaction for carcinoembryonic antigen (CEA) was strongly positive in the apical zone and glycocalyx of hyperplastic cells, but faint in neoplastic epithelia (Fig. 3). Peanut-lectin binding (PNA) was marked in the supranuclear region of hyperplastic, but not in neoplastic cells (Fig. 3).

Discussion

True mixed hyperplastic/adenomatous polyps of the colon are rare. They occurred in 0.6% of 554, or in 2.3% of 173 hyperplastic polyps respectively (Williams et al. 1980; Franzin et al. 1984). However, 13% among 171 hyperplastic polyps exhibited adenomatous changes (Estrada and Spjut 1980). Few case reports have been published on mixed colonic polyps (Cooper et al. 1979; Sumner et al. 1981; Urbanski et al. 1984).

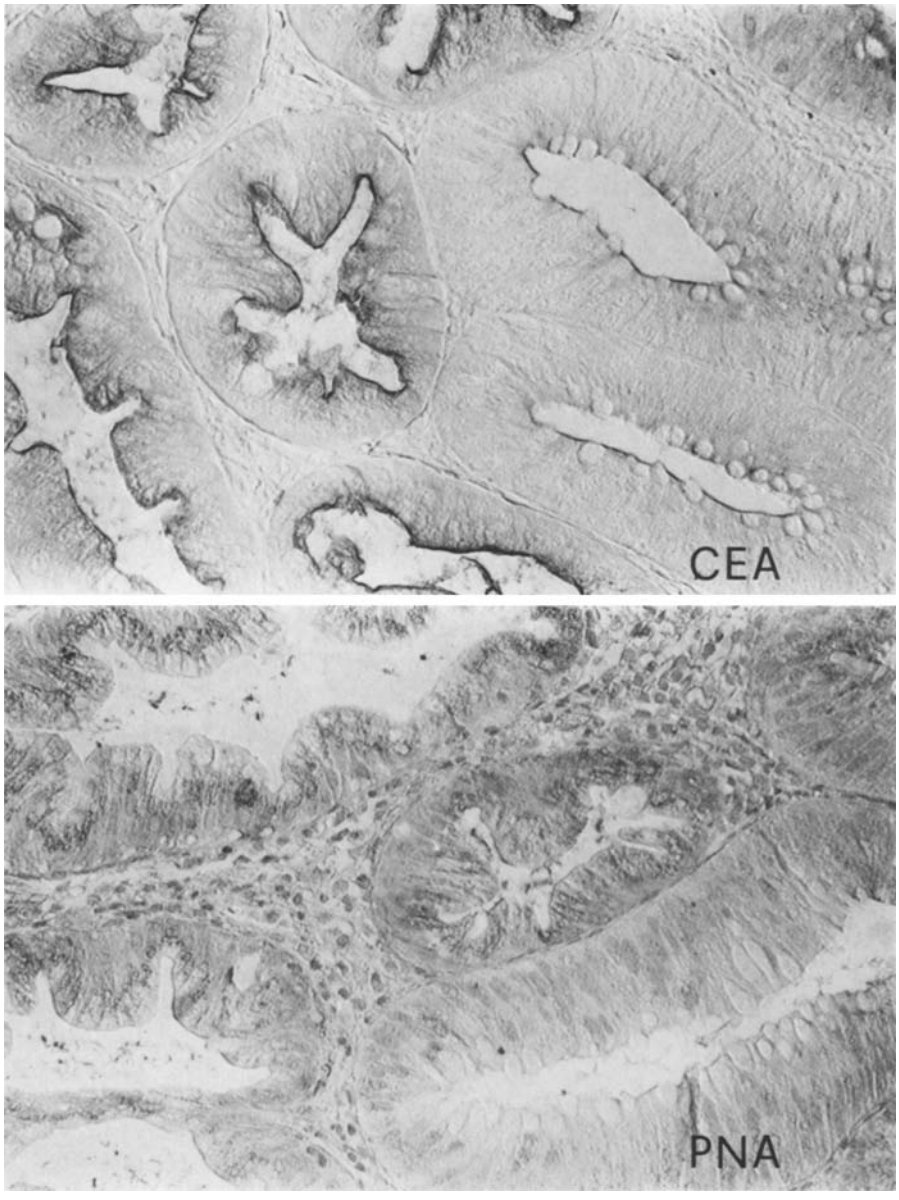

Fig. 3. Increased expression of carcinoembryonic antigen (*CEA*) in the hyperplastic epithelium and "normal" CEA expression by the neoplastic cells (*top*). Peanut agglutinin (*PNA*) binding in the supranuclear region of the hyperplastic cells, but not in the neoplastic cells (*bottom*). Immunoperoxidase (*PAP*) technique, no counterstain, Nomarski interference-contrast optics. ×950

Few immunohistochemical studies of hyperplastic (Cooper and Reuter 1983; Jass 1983; Jass et al. 1984a; Jass and Faludy 1985; Rognum et al. 1982a) or neoplastic colonic polyps (Isaacson 1982; Isaacson and Le Vann 1976; Rognum et al. 1982a, b; Skinner and Whitehead 1981; review: Jass et al. 1984b) are available. We are not aware of similar studies of combined lesions. Results from the literature quoted below and own results are compiled in the Table 1.

Faint staining for secretory component (SC) and lack of epithelial IgA (Fig. 2) characterize hyperplastic polyps (Jass 1983; Jass and Faludy 1985) and colorectal carcinoma (Rognum et al. 1982c). Conversely, the neoplastic cells of this polyp stain strongly for IgA and SC (Fig. 2). It has been shown that increasing dysplasia in adenoma is accompanied by reduced staining for SC and epithelial IgA (Isaacson 1982; Rognum et al. 1982a). This reduction accompanies the loss of mucus production, and presumably reflects diminished cell differentiation.

Conversely, the hyperplastic cells express more CEA than neoplastic epithelia (Fig. 3). This is in keeping with previous findings (Jass 1983; Jass et al. 1984a; Rognum et al. 1982a). The normal location of CEA in the apical cytoplasm and luminal border, however, is maintained. In contrast, the neoplastic tissue appears to express as much CEA as normal colorectal epithelium does (Geb-

bers and Laissue 1983; Ahnen et al. 1982). In severe dysplasia, akin to "carcinoma-in-situ", marked CEA staining may be seen (O'Brien et al. 1981; Isaacson and Le Vann 1976). Enhanced CEA expression thus seems to accompany the process of malignant transformation (Ahnen et al. 1982; Huitric et al. 1976).

The hyperplastic cells bind lectins (PNA) in the supranuclear (Golgi) zone, whereas the neoplastic cells do not (Fig. 3); PNA does not bind to normal colorectal goblet cell mucus, but to mucins of colorectal carcinoma (Boland et al. 1982; Cooper 1982). However, the normal Golgi zone binds PNA. Prolonged sialidase digestion results in a positive reaction of normal goblet cell mucus for PNA (Cooper 1982). This suggest that PNA detects incomplete mucins lacking the terminal sialic acid moiety. All hyperplastic polyps bind PNA (Cooper and Reuter 1983) but only 2% of the glands in small tubular adenomas do so. With increasing size and dysplasia, more neoplastic glands become positive, but not to the same extent as in hyperplastic polyps (Boland et al. 1982).

Rarely, carcinomatous change in hyperplastic polyps has been reported (Cooper et al. 1979; Franzin and Novelli 1982; Sumner et al. 1981; Urbanski et al. 1984).

In conclusion, hyperplastic and neoplastic changes can originate at the same site of the colorectal mucosa and form a mixed lesion. This may indicate a similar cause and pathogenesis. Paradoxically, the non-neoplastic tissue of the lesion appears to be functionally less mature than the neoplastic tissue, and displays differentiation markers associated with malignancy. In contrast, the latter are not found in the neoplastic, obviously dysplastic, precancerous component. To explain the functional overlap between hyperplastic polyps and carcinoma, Jass (1983) suggested that in the colon two separate sets of factors lead to the development of adenomas and hyperplastic polyps, and that both sets are required to cause malignant transformation. Hyperplasia may therefore signal a potentially carcinogenic microenvironment. Hence, the identification of factors resulting in formation of hyperplastic polyps could contribute to the prevention of colorectal cancer.

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