Virchows Arch A (1987) 411:239–243

Virchows Archiv A

Frequency distribution of plasma cells in the medullary cords of tumour-draining axillary and paracolic lymph nodes

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Summary. Five hundred and ninety-seven axillary lymph nodes draining 104 invasive ductal breast cancers, and 94 paracolic lymph nodes draining 30 invasive adenocarcinomas of the large bowel were investigated immunohistologically to determine the frequency distribution of plasma cells (PC) in the medullary cords (MC). The degree of plasmacytic infiltration was calculated semiquantitatively using the 3-grade scale (0/+, ++, +++) of Cottier et al. (1973). Statistical analysis yielded the following results: While a marked reactive plasmacytosis (+++) was seen in 28.7% of the paracolic lymph nodes, only 1.5% of the axillary lymph nodes exhibited a comparable degree of plasmacytic infiltration ($p<0.0001$). Conversely, low PC counts (0/+) were encountered in 51.1% of the paracolic lymph nodes, but in 83.9% of the axillary lymph nodes. A comparison of axillary lymph nodes with and without nodal metastasation revealed no significant differences (nodal-negative cases: 0/+: 83.6%, ++: 14.3%, +++: 2.1%; nodal-positive cases: 0/+: 84.3%, ++: 14.9%, +++: 0.8%). However, significantly more ($p<0.001$) paracolic lymph nodes of the nodal-negative group revealed a marked plasmacytosis, whereas in the nodal-positive group lymph nodes with low PC counts were more frequent (nodal-negative cases: 0/+: 27.7%, ++: 29.7%, +++: 42.6%; nodal-positive cases: 0/+: 74.5%, ++: 10.6%, +++: 14.9%). The degree of plasmacytic reactions in the tumour-regional lymph nodes was not related to the stage of the primary tumour. Moreover, no correlation exists between the PC content of the MC and the amount of PC in metastatic deposits of the same lymph nodes. Altogether, these results do not support the concept that the plasmacytic reactions in the MC of tumour-draining lymph nodes are chiefly determined by effects (stimulating or suppressing) of the primary carcinomas. The topography of the lymph nodes, however, seems to be the main determinant influencing the PC content of MC.

Key words: Plasma cells – Axillary lymph nodes – Paracolic lymph nodes – Medullary cords – Breast cancer – Adenocarcinoma of the large bowel

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Introduction

Plasma cells (PC) in human lymph nodes generally accumulate in the germinal centers and pulp (Lennert and Müller-Hermelink 1975). The pulp of the medullary cords (MC) is the main site of plasmacytogenesis and antibody production. It is generally agreed that not only cellular but also humoral immunity may be involved in host defense against a malignant tumour.But antibody-producing PC can exert both positive and negative effects on the host response to a malignant tumour. A positive reaction can be seen in the cooperation of antibodies and certain effector cells (namely macrophages, lymphocytes, and neutrophils) in triggering the final destruction of an antibody-coated tumour cell (antibody-dependent cellular cytotoxicity). Conversely, immune (antigen-antibody) complexes may also have a negative effect by serving as blocking factors, directly or indirectly inhibiting the effector cells (Theofilopoulos et al. 1977; Bogdanovic et al. 1983).

Since the effectiveness of PC is not necessarily related to close intercellular contact, an analysis

Table 1

a Invasive breast cancers grouped according to the TNM system of classification		b Colorectal carcinomas grouped according to the DUKES' system of classification	
Stage (pT)	Number of cases	Stage	Number of cases
T1	62	DUKES A	8
T2	36	DUKES B	7
T3	2	DUKES C	15
T4	4		

of the frequency distribution of PC in tumour-draining lymph nodes may also contribute to our understanding of immunooncological interactions. While several – often conflicting – studies (Tsakraklides et al. 1973; Byrnes et al. 1983) deal with the prognostic implications of immunomorphological changes in tumour regional lymph nodes, especially concerning reactions of B-follicles ("germinal center hyperplasia"), T-regions ("lymphocyte predominance pattern"), or sinuses ("sinus histiocytosis"), the plasmacytic reactions in MC have not been so intensively analysed. In the present study histological and immunohistological investigations on a large series of tumour-draining axillary and paracolic lymph nodes were performed to determine the PC content of the MC. The aim of the study also was to assess basic data for a planned prognosis-related analysis.

Material and methods

Between February 1983 and April 1985, 104 females (median age: 54 years) with invasive ductal breast cancer and 30 patients (median age: 72 years) with invasive adenocarcinoma of the large bowel entered the study. None of the patients underwent any form of tumour-specific therapy prior to operation. After careful examination and preparation of the resected specimens, the tumour stage was determined (Table 1). The tumour-draining lymph nodes were cut through a median section to obtain representative areas of cortex, paracortex, and MC. The tissue was embedded in paraffin. 4 μm thick sections were stained with H&E, PAS, and GIEMSA. Immunoglobulin light chains (lambda and kappa) in all and heavy chains (gamma, alpha, mμ) in some lymph nodes were visualized by the PAP-method described by Sternberger et al. (1970). The number of mature PC (eccentric cart-wheel nucleus, abundant basophilic cytoplasm, and pale paranuclear area) in the MC of each lymph node was calculated in GIEMSA stains according to the standardized system proposed by Cottier et al. (1973). The following semiquantitative scale was used: Group 1 (0/+): very low or low numbers of PC, either loosely scattered throughout the pulp, or occasionally forming small clusters of cells (Fig. 1).
Group 2 (++): moderate numbers of PC which form disseminated, medium-sized foci (Fig. 2).
Group 3 (+++): marked – reactive – plasmacytosis; PC build up extensive sheets of cells often broadening the MC (Fig. 3).

The PC content of lymph node metastases was evaluated according to a four-grade-scale as previously described (Horny and Horst 1986). For statistical evaluation the chi-square-test was used.

Results

Lymph nodes were excluded from the analysis either if they contained no or only hypoplastic MC, in particular, axillary nodes with severe lipomatous atrophy. Nodes with extensive metastatic deposits

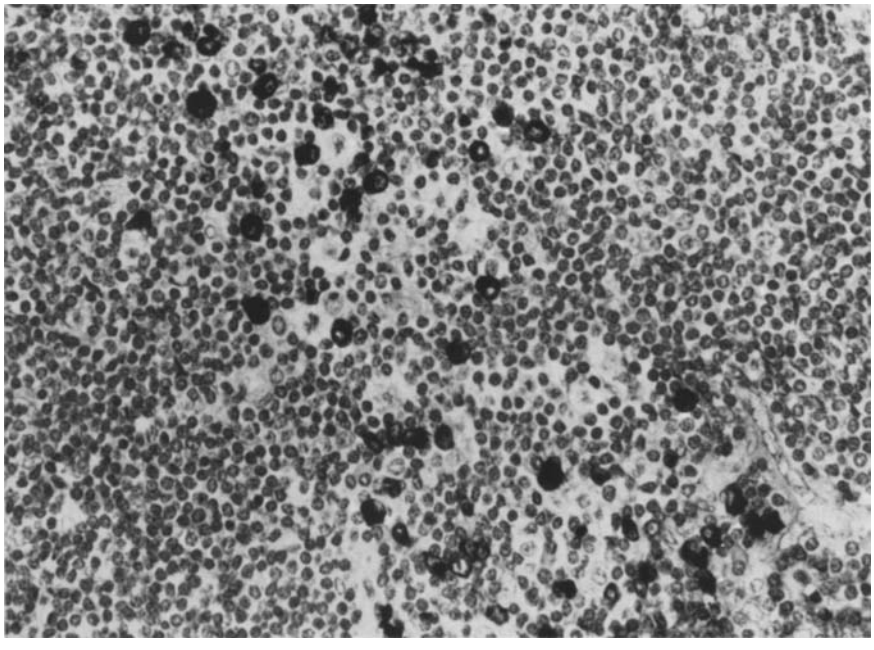

Fig. 1. Tumour-draining paracolic lymph node showing low numbers of plasma cells which are loosely scattered throughout the pulp. PAP, kappa light chain, ×140

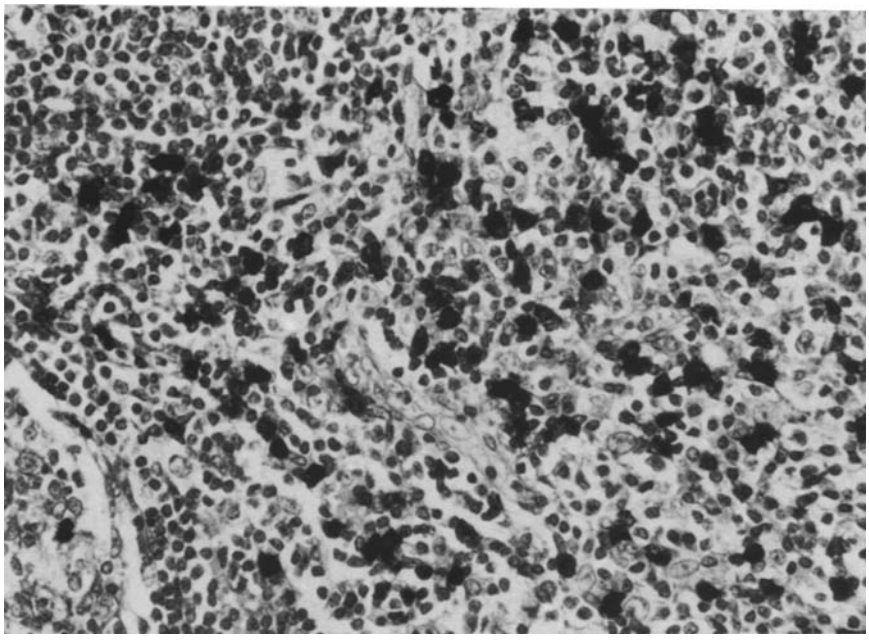

Fig. 2. Medullary cord of a tumour-draining paracolic lymph node with a moderate increase of plasma cells. PAP, kappa light chain, ×140

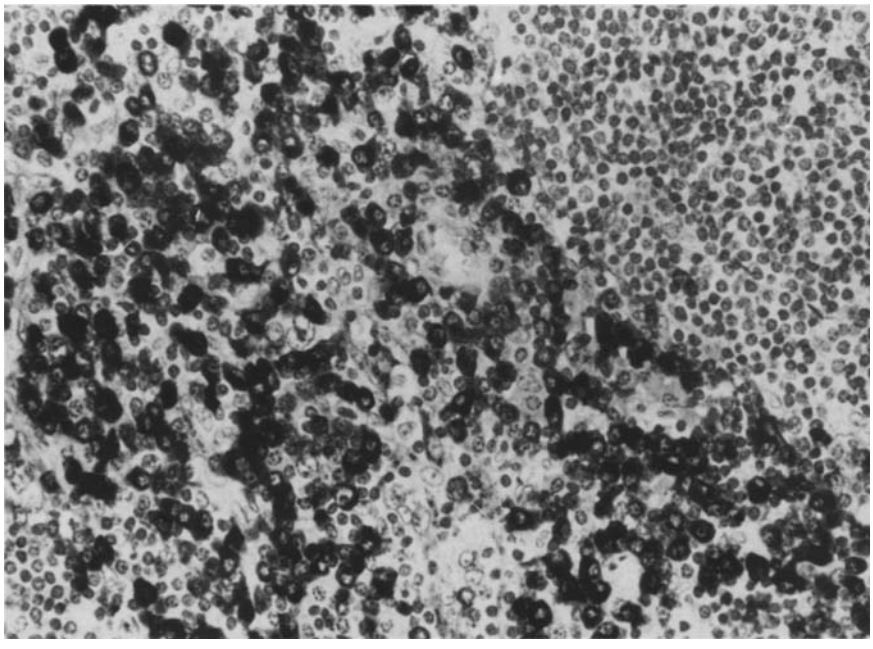

Fig. 3. A marked reactive plasmacytosis in the medullary cord of a tumour-draining paracolic lymph node. A lymphatic follicle is also shown (top right). PAP, kappa light chain, ×140

with destruction of MC were also excluded. Thus, 597 of 808 axillary, and 94 of 162 paracolic lymph nodes were considered. Demonstration of intracytoplasmic lambda and kappa light chains excluded monoclonality even in severe plasmacytoses with considerable extension of the MC. The lymph nodes which had also been stained for the immunoglobulin heavy chains showed a reaction pattern similar to the findings in normal or reactive lymph nodes previously described by Curran et al. (1982). So, mμ containing cells dominated in germinal centers while gamma positive plasma cells were mainly found in the pulp of MC.

The degree of plasmacytic infiltration in tumour-draining axillary and paracolic lymph nodes is shown in Table 2. While only 1.5% of the axillary lymph nodes exhibited a marked plasmacytosis (+++), this was true for 28.7% of the paracolic lymph nodes ($p<0.0001$). Conversely, 83.9% of the axillary, but only 51.1% of the paracolic lymph nodes contained low numbers of PC (0/+). A moderate degree of infiltration (++) was ob-

Table 2. Degree of plasmacytic infiltration (0/+: low, ++: moderate, +++: marked) in the medullary cords of lymph nodes (LN) draining invasive ductal breast cancer and invasive adenocarcinoma of the large bowel

Degree of plasmacytic infiltration	Tumour-draining axillary LN	Tumour-draining paracolic LN
0/+	501 (83.9)	48 (51.1)
++	87 (14.6)	19 (20.2)
+++	9 (1.5)	27 (28.7)
	$n=597$ (100%)	$n=94$ (100%)

Table 3. Degree of plasmacytic infiltration (0/+: low, ++: moderate, +++: marked) in the medullary cords of lymph nodes (LN) draining invasive ductal breast cancer and invasive adenocarcinoma of the large bowel. The cases were separated according to the absence or presence of metastatic deposits in regional LN (0=nodal-negative cases; +=nodal-positive cases)

Degree of plasmacytic infiltration	Axillary LN		Paracolic LN	
	0	+	0	+
0/+	281 (83.6)	220 (84.3)	13 (27.7)	35 (74.5)
++	48 (14.3)	39 (14.9)	14 (29.7)	5 (10.6)
+++	7 (2.1)	2 (0.8)	20 (42.6)	7 (14.9)
	$n=336$ (100%)	$n=261$ (100%)	$n=47$ (100%)	$n=47$ (100%)

served in 14.6% of the axillary and in 20.2% of the paracolic lymph nodes.

A comparison of lymph nodes from nodal-negative with those from nodal-positive cases (i.e. at least one regional lymph node contained metastatic deposits) revealed no significant differences in the axillary lymph nodes. Moreover, both lymph node groups showed nearly equal degrees of plasmacytic infiltration (Table 3). In paracolic lymph nodes, however, a significantly higher incidence ($p<0.001$) of marked plasmacytoses was observed in nodal-negative than in nodal-positive cases (42.6% and 14.9%, respectively). Accordingly, lymph nodes containing few PC predominated in the nodal-positive group (74.5% and 27.7%, respectively).

A comparison of the various tumour stages revealed no significant differences in the PC content of MC in the regional lymph nodes of colorectal carcinomas but also between breast cancers of stages pT1 and pT2. The number of breast cancers of the stages pT3 and pT4 was too small to be included in the statistical analyses.

Finally, in tumour-infiltrated lymph nodes the PC content of the MC was compared with that of the adjacent metastases. It has to be emphasized that the great majority of metastatic lymph nodes were largely destroyed by the tumour (more than 75% of destruction). Thus, 129 of 175 axillary lymph nodes but also 23 of 31 paracolic lymph nodes had to be excluded from the study because the MC was subtotally or totally effaced. The analysis of the remaining lymph nodes (46 axillary and only 8 paracolic) revealed no correlation between the degree of the plasmacytic reaction in the MC and that of the metastases.

Discussion

The present study on the frequency distribution of plasma cells (PC) in the medullary cords (MC) of tumour-draining axillary and paracolic lymph nodes yielded the following results: A marked reactive plasmacytosis occurred significantly more often in paracolic lymph nodes than in axillary lymph nodes, whereas low numbers of PC were observed in most axillary but in only about one half of the paracolic lymph nodes. A comparison of the axillary lymph nodes from nodal-negative cases with lymph nodes from nodal-positive cases revealed no significant differences. The paracolic lymph nodes of nodal-negative patients, however, showed a marked plasmacytosis significantly more often than lymph nodes of nodal-positive patients. No correlations could be found between the PC content of the MC and the tumour stage, and also between the degree of plasmacytic reaction in the lymph node pulp and the adjacent metastasis in tumour-bearing nodes.

In general, paracolic lymph nodes frequently exhibited histological findings indicative of an active humoral immune response. Thus, not only was a moderate or marked plasmacytosis found in nearly half of the 94 paracolic lymph nodes under consideration, but also the degree of germinal center hyperplasia was generally more pronounced in paracolic than in axillary nodes (Horny and Horst 1984). By contrast, axillary nodes are regarded as sites mainly of a cell-mediated immune reaction, histologically realized in prominent paracortical areas (Lennert 1961). The overwhelming majority of axillary lymph nodes contained only small amounts of PC in the MC. These significant histological differences are likely due to the amount of antigenic stimuli reaching axillary and paracolic lymph nodes rather than to effects of the malignant tumour in the draining area. In other words, according to the results of this study anti-

genic material from breast cancers in most cases does not stimulate the plasma cell reaction in the corresponding axillary lymph nodes. Definite conclusions on a possible influence of colorectal adenocarcinomas on the paracolic lymph nodes cannot be drawn from the present morphological data. Since the histomorphology of paracolic lymph nodes also in non-cancerous lesions exhibits a marked follicular lymphatic hyperplasia and plasmacytosis (Lennert 1961), an influence (stimulation?, suppression?) of the primary tumour on the plasma cell content of MC in the draining lymph nodes could not be ascertained. Even suppressive effects of the malignancy on the B-cell system as described by Lewis et al. (1977) in later tumour stages cannot be ruled out.

It is questionable, however, whether or not the influence of a tumour on the immunoreactivity of regional lymph nodes can be clarified with histological methods alone. The major difficulty lies in assessing the "normal" (unstimulated) histological picture of lymph nodes in general and of paracolic lymph nodes in particular. On the one hand, paracolic lymph nodes from patients who undergo surgery for inflammatory diseases of the large bowel obviously do not represent adequate control material. On the other, the nodes gained in autopsies fail to represent a "true" control cohort because of complex and unpredictable alterations of the immune system during death.

Interestingly, the comparison of paracolic lymph nodes from nodal-negative with those from nodal-positive patients revealed significant differences in the degree of plasmacytic infiltration in the MC. Thus, a marked plasmacytosis was much more common in nodal-negative, i.e. prognostically favorable, patients, while low PC-counts occured more often in nodal-positive, i.e. prognostically unfavourable, cases.

In the present study the individual course of the disease of both patients with breast cancer and with adenocarcinoma of the large bowel must be observed for a longer time before the data can be interpreted with regard to prognosis.

Acknowledgements. This study was supported by the Schleswig-Holsteinische Krebsgesellschaft e.V., Kiel and the Tumorzentrum Kiel. The authors are grateful to J. Hedderich for his help in the statistical analysis, to K. Frenken and E. Pflug for their skillful technical assistance, and to J. Heywood for help in preparation of the manuscript.

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Accepted February 10, 1987