

The metastatic potential of prostate carcinomas composed entirely of single malignant glands

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Summary. Consecutive staging lymphadenectomies on 1046 patients with prostate carcinoma identified 275 patients with metastases in a total of 1115 regional lymph nodes. No prostate carcinomas composed entirely of single malignant glands metastasized and no patient had metastases composed entirely of single malignant glands. All prostate carcinomas that metastasized had cribriform and/or undifferentiated histological patterns in the prostate and in the metastases. These findings suggest that identification of cribriform and/or undifferentiated histological patterns, through rebiopsy or further examination of the surgical specimen, should be considered prior to subjecting patients with prostate carcinomas composed entirely of single malignant glands to therapy or procedures directed against the possibility of metastatic disease.

Key words: Prostate carcinoma – Staging lymphadenectomies – Metastatic prostate carcinoma – Well-differentiated prostate carcinoma

Introduction

The histology of prostate carcinoma has often been shown to affect the likelihood of metastases with 'poorly differentiated' prostate carcinoma metastasizing more frequently than 'well-differentiated' cases (Barzell et al. 1977; Prout et al. 1980; Zincke et al. 1982; Smith et al. 1983). In an attempt to identify histological patterns of prostate carcinoma which metastasize rarely the current study examined 1046 consecutive staging lymphadenectomies to determine whether prostate carcinomas composed entirely of single malignant glands metastasize

size to regional lymph nodes and whether the metastases in regional lymph nodes are composed entirely of single malignant glands.

Materials and methods

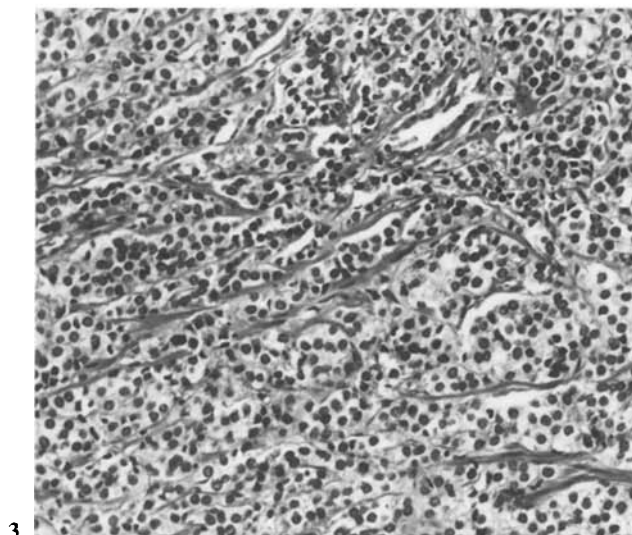
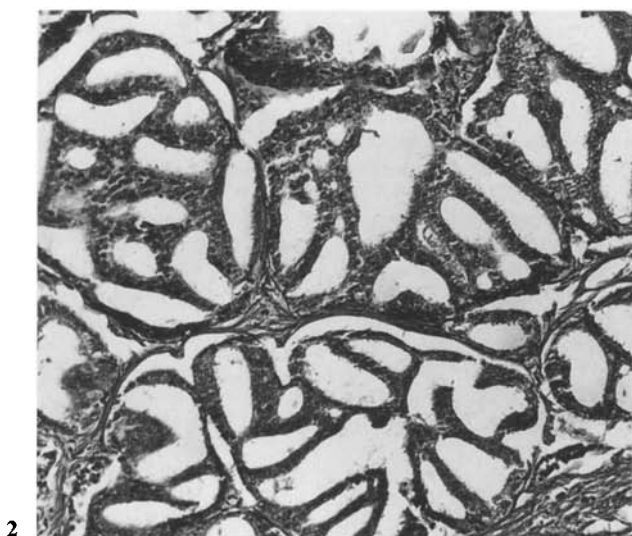
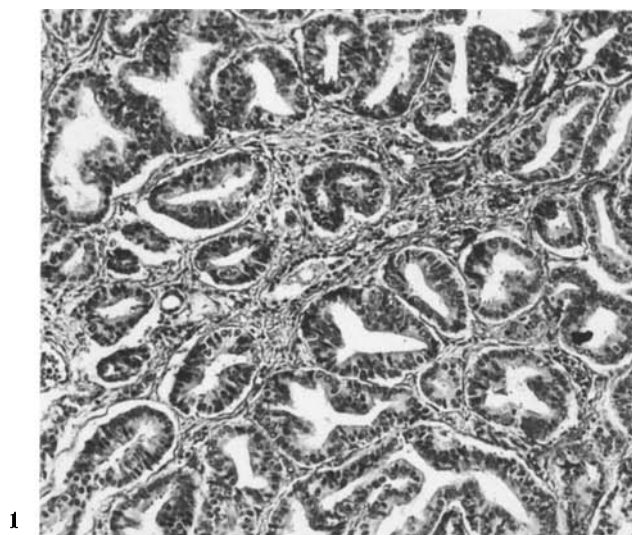
One thousand and forty-six consecutive staging lymphadenectomies performed following a needle biopsy or TURP (transurethral resection of the prostate) showing prostate carcinoma were identified. The criteria for staging lymphadenectomies were 1) confirmed histologic diagnosis of prostate carcinoma in needle biopsy or TURP specimen, 2) prostate carcinoma clinically confined to the prostate, or 6 cm or less in size if extending beyond the capsule of the prostate, 3) no evidence of metastases. Depending on the operative findings and the judgement of the surgeon, the staging lymphadenectomies removed all or part of the obturator, hypogastric, external iliac, internal iliac and common iliac lymph nodes bilaterally. These lymph nodes are referred to as regional lymph nodes in the current study.

Prostate carcinoma, in the current study, refers to prostate adenocarcinoma composed of varying proportions of three histological patterns similar to those described by Mostofi (1976) and Dohm (1985): glandular (single malignant glands) (Fig. 1), cribriform (Fig. 2), and undifferentiated (non gland forming) (Fig. 3). Dysplasia of the prostate, as defined by Kastendieck et al. (1976a) was strictly separated from prostate carcinoma and not evaluated in the current study.

Single malignant glands refer to malignant glands which may be large, small, or intermediate in size and corresponds to the World Health Organization classification of 'adenocarcinoma of acinar pattern' (WHO 1980). The single malignant glands may be crowded, but not fused, with minimal or abundant intervening stroma. Cribriform prostate carcinoma refers to prostate carcinoma perforated with multiple glandular spaces without intervening stroma. Undifferentiated prostate carcinoma refers to non-gland forming prostate carcinoma which may occur in sheets, cords, or as individual cells.

Results

Consecutive staging lymphadenectomies on 1046 patients with prostate carcinoma identified 275 patients with metastases in a total of 1115 regional lymph nodes. The 1046 patients had an



overall average age of 63 years with an age range from 49 to 74 years. The 275 patients with metastases had an average age of 62.6 years and the 771 patients without metastases had an average age of 63.1 years.

The H&E slides from the diagnostic needle biopsy or TURP specimens were available for review on 933 of the 1046 patients undergoing lymphadenectomies and on 254 of the 275 patients with metastases in the lymphadenectomy specimens. Sixty-seven of the diagnostic needle biopsies or TURP specimens contained prostate carcinoma composed entirely of single malignant glands. All of the remaining needle biopsies or TURP specimens contained areas of cribriform and/or undifferentiated prostate carcinoma and the majority of these needle biopsies or TURP specimens contained single malignant glands in addition to cribriform and/or undifferentiated prostate carcinoma.

None of the 67 needle biopsies or TURP specimens composed entirely of single malignant glands had metastases in the staging lymphadenectomies. All of the prostate carcinomas with metastases in the staging lymphadenectomies contained cribriform and/or undifferentiated prostate carcinoma in the needle biopsy or TURP specimens. In addition to cribriform and/or undifferentiated prostate carcinoma 176 of the prostate carcinomas which metastasized also contained single malignant glands in the needle biopsies or TURP specimens.

Every patient with metastatic prostate carcinoma had cribriform and/or undifferentiated (non gland forming) metastases in the lymph nodes. In addition, metastatic single malignant glands were identified in 537 of the 1115 lymph nodes and an additional 35 lymph nodes contained primarily single malignant glands. No patient had metastases composed entirely of single malignant glands.

Fifty-four of the 1046 patients had radical prostatectomies at the time of lymphadenectomy. The histology of prostate carcinoma in the radical prostatectomy specimen was generally less differentiated than the histology of prostate carcinoma in the biopsy or TURP specimen. Thirteen of these 54 patients had metastases in regional lymph nodes. The histology of prostate carcinoma in the

Fig. 1. Photomicrograph of prostate carcinoma demonstrating single malignant glands separated by intervening stroma (H&E $\times 80$)

Fig. 2. Photomicrograph of prostate carcinoma demonstrating cribriform patterns (H&E $\times 80$)

Fig. 3. Photomicrograph of prostate carcinoma demonstrating undifferentiated (non gland forming) patterns (H&E $\times 80$)

metastases was similar to the histology of prostate carcinoma in the radical prostatectomy specimen.

Discussion

Numerous studies have demonstrated that 'well-differentiated' prostate carcinoma has a limited ability to metastasize. Zincke et al. (1982) found that none of 38 Grade 1 (Mayo Grade 1) prostate carcinomas metastasized to regional lymph nodes. Prout et al. (1980) found that none of 16 well-differentiated prostate carcinomas metastasized to regional lymph nodes. However, Barzell et al. (1977) found that 3 of 19 (16%) well-differentiated prostate carcinomas metastasized to regional lymph nodes and Smith et al. (1983) found that 12 of 125 well-differentiated prostate carcinomas metastasized to regional lymph nodes.

A difficulty in evaluating the metastatic potential of well-differentiated or Grade 1 prostate carcinoma has been its definition. This term may refer to prostate carcinoma composed entirely of single malignant glands or to prostate carcinoma containing varying amounts of cribriform and/or undifferentiated prostate carcinoma in addition to single malignant glands. The current study did not attempt to define 'well-differentiated' prostate carcinoma. However, we found that prostate carcinomas composed entirely of single malignant glands, without foci of cribriform and/or undifferentiated prostate carcinoma, did not metastasize to regional lymph nodes and no patient had metastases composed entirely of single malignant glands (SMG's). Presumably, previous studies that reported metastases from well-differentiated prostate carcinoma were referring to prostate carcinomas with cribriform and/or undifferentiated histological patterns in addition to SMG's.

The staging lymphadenectomies in the current study were performed on patients without clinical evidence of metastases and presumably contained a spectrum of recent to well-established metastases. Further, survival data suggests that regional lymph nodes may be one of the initial sites of metastatic prostate carcinoma since some patients have apparently been cured of metastatic prostate carcinoma after removal of metastases in regional lymph nodes (Scardino and Carlton 1983). Consequently, the current study presumably contained a spectrum of recent to established metastases in one of the initial anatomical locations of metastatic prostate carcinoma.

Caution should be exercised when evaluating the metastatic potential of prostate carcinoma

composed entirely of SMG's since Kastendieck (1976b) has shown that prostate carcinomas dedifferentiate with time and Brawn (1983) has demonstrated that the incidence of metastases increases with dedifferentiation. Consequently, prostate carcinomas composed entirely of SMG's may, with time, dedifferentiate into cribriform and/or undifferentiated histological patterns capable of metastasizing. Further, it is well known that the correlation between the histological patterns of biopsy and prostatectomy is poor (Kastendieck 1980a, b; Dohm 1985). Additionally, Helpap (1980) and Kastendieck (1980a) have demonstrated that cribriform and/or undifferentiated prostate carcinoma are often present adjacent 'atypical hyperplasia'. This suggests that there may be a similar association between cribriform and/or undifferentiated prostate carcinoma and SMG's. Consequently, thorough histological examination of the surgical specimen or rebiopsy of the prostate may be necessary to determine whether cribriform and/or undifferentiated histological patterns are present adjacent prostate carcinoma which appear to be composed entirely of SMG's.

The current study does not suggest that patients with prostate carcinoma composed entirely of SMG's do not require therapy since these tumours may metastasize if they dedifferentiate into cribriform and/or undifferentiated histological patterns. Further, prostate carcinomas which appear to be composed entirely of SMG's may be found on further examination of the surgical specimen or rebiopsy of the prostate to contain cribriform and/or undifferentiated histological patterns. However, keeping these reservations in mind, the current study suggests that prostate carcinomas composed entirely of SMG's rarely metastasize to regional lymph nodes and metastases from prostate carcinoma are rarely composed entirely of SMG's. Consequently, an attempt to identify cribriform and/or undifferentiated histological patterns, through rebiopsy or further examination of the surgical specimen, should be considered prior to subjecting patients with prostate carcinoma composed entirely of single malignant glands to therapy or procedures directed against the possibility of metastatic disease.

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