

Prostatic Carcinoma: Histologic Grading and Metastasis

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THE purpose of this study is to evaluate the possibility that certain histologic features of human prostatic adenocarcinoma correlate with the ability of the tumor to metastasize to other organs.

MATERIALS AND METHODS

This study was based on 41 individuals with biopsy and autopsy evidence of adenocarcinoma of the prostate gland. The patients were among a group of 1450 consecutive patients who came to autopsy at the Veterans Administration Hospital in West Haven, Connecticut. They had been treated with chlorotrianisene, an estrogenic compound, after the clinical and biopsy diagnoses had been established. The clinical charts, autopsy records, and the biopsy and autopsy histologic sections were reviewed in each case for this study.

Tumors were graded using histologic features. Three grades were used. The best differentiated tumors mimicked the pattern of prostatic glandular structures most closely and formed small atypical ducts; these were called grade 1 tumors (Fig. 1). Grade 2 tumors were those with a cribriform (sieve-like) pattern (Fig. 2). Grade 3 tumors consisted of solid sheets of tumor cells with no ductal or glandular patterns (Fig. 3). In all grades of tumor, nucleoli were prominent in the nuclei, and at least one focus of perineural invasion was found in each primary tumor.

Grading was performed twice on all autopsy specimens of the primary tumors and metastases. It was done four times on each biopsy specimen. Grading was done after random sorting of all of the slides, without knowledge of the case identification number or of the grade assigned to other portions of the tumor of the same patient.

RESULTS

Grading of the tumors was remarkably constant. In no instance was a tumor that had been called a grade 1 tumor called a grade 2

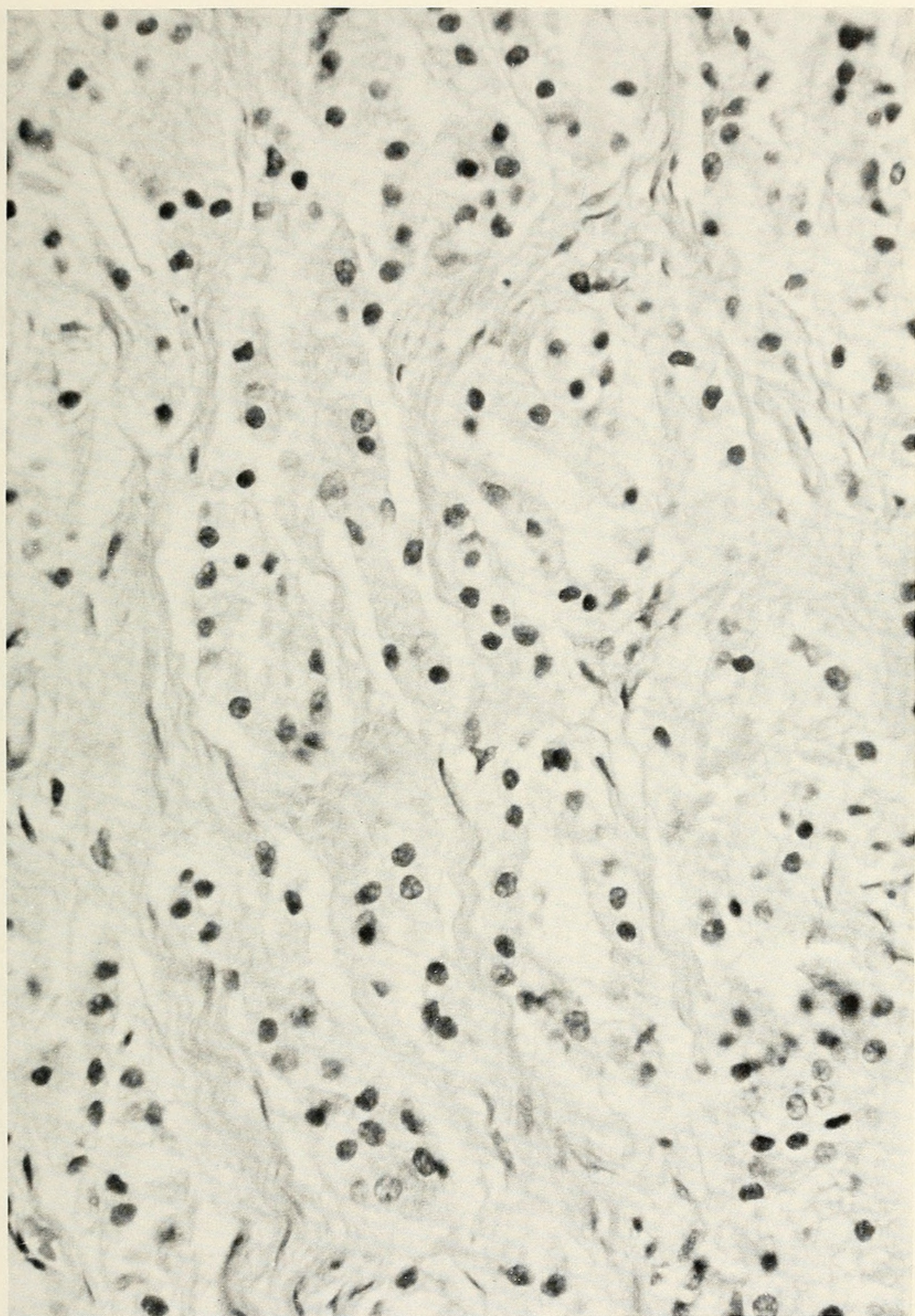


Fig. 1. Grade 1 adenocarcinoma of prostate. Single layer of atypical cells forms the duct-like structures. Hematoxylin and eosin stain, $\times 400$.

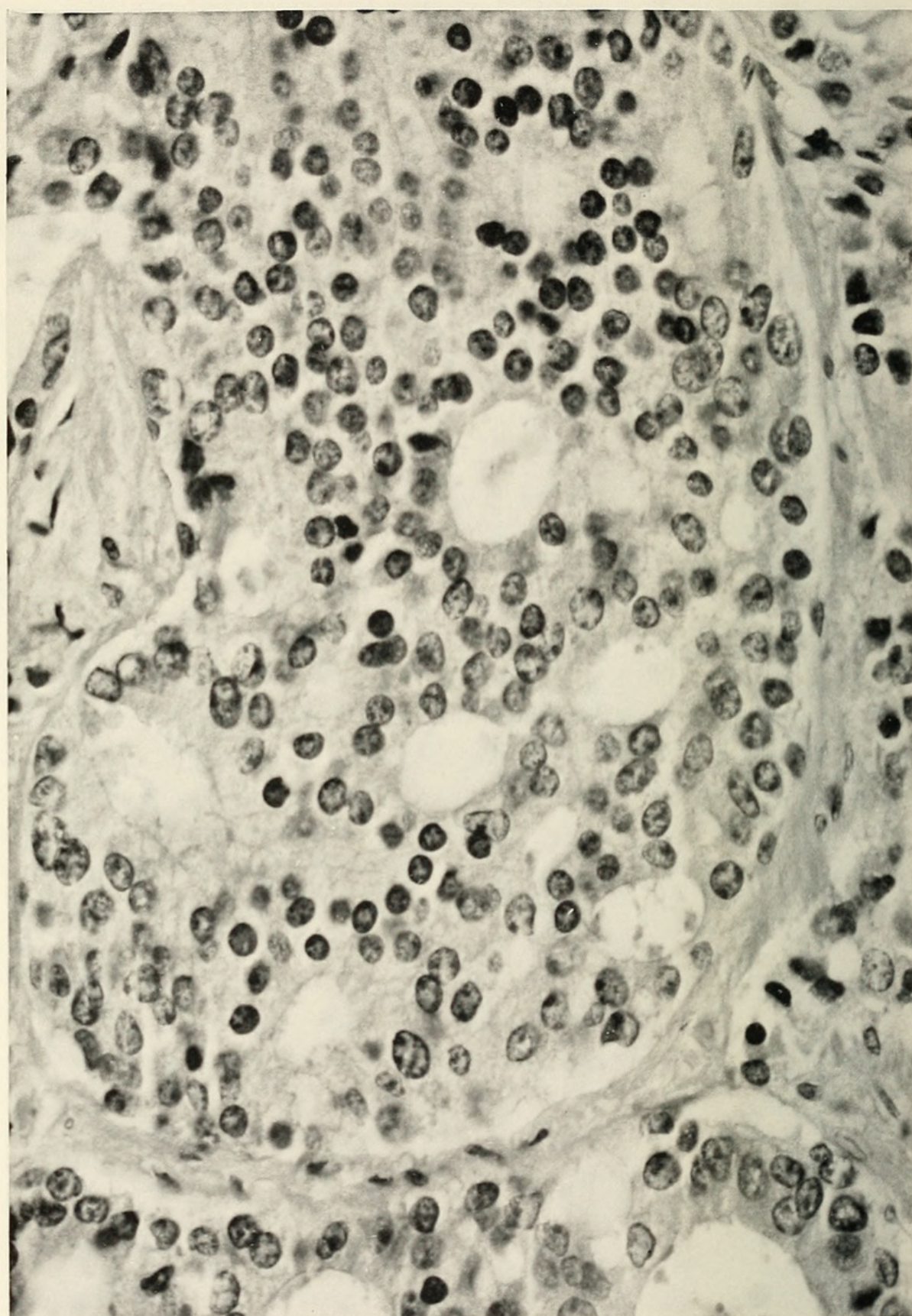


Fig. 2. Grade 2 adenocarcinoma of prostate. Cribriform pattern. Hematoxylin and eosin stain, $\times 400$.

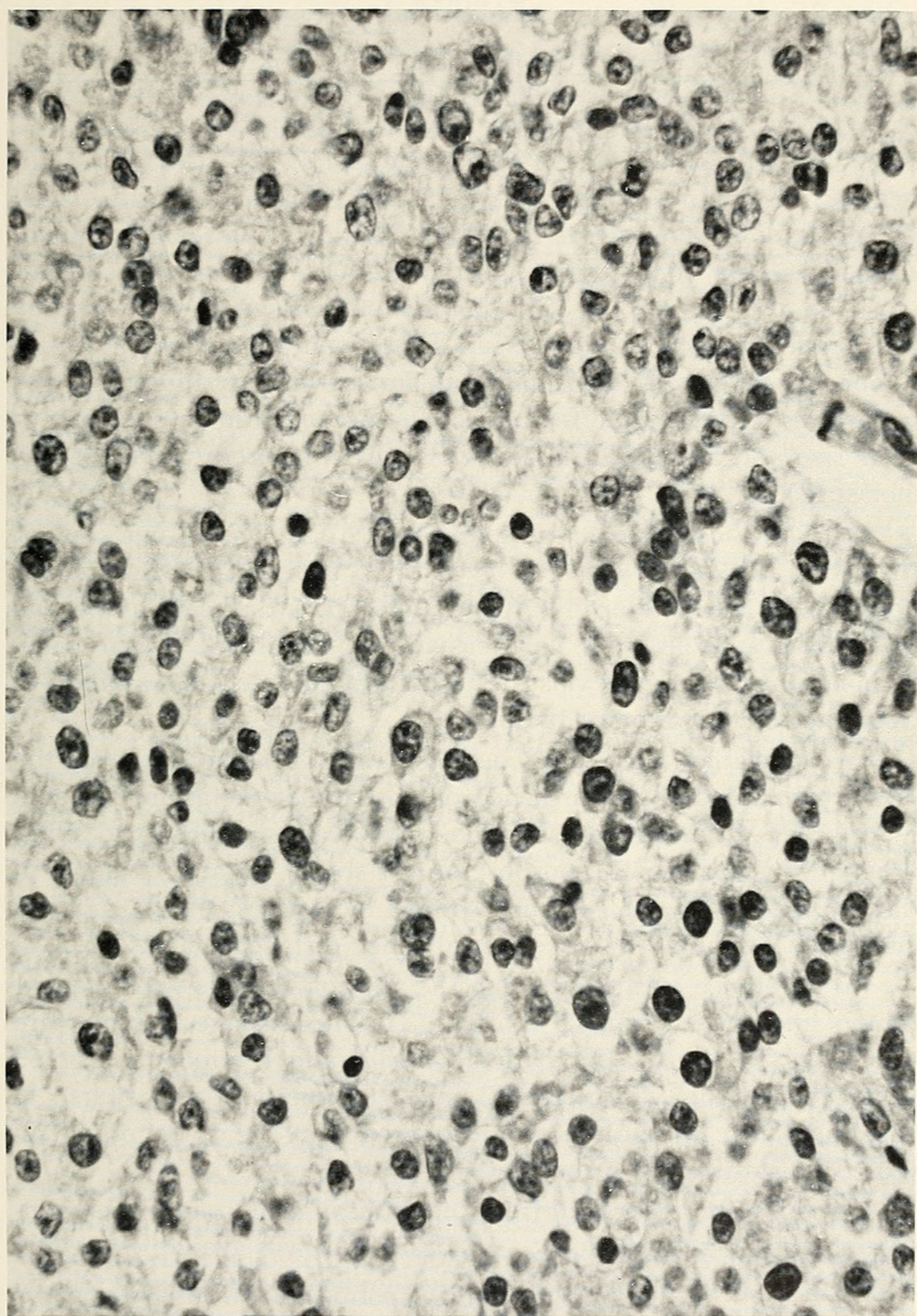


Fig. 3. Grade 3 adenocarcinoma of prostate. Solid pattern. Hematoxylin and eosin stain, $\times 400$.

TABLE 1

Metastasis and histologic grade of tumor

Grade of tumor	Number of patients without metastasis	Number of patients with metastasis	Total
1	18	0	18
2 & 3	5	18	23
Total	23	18	41

Chi-square, 25; p, less than 0.001.

or a grade 3 tumor, or vice versa. In a given patient, the grade of tumor was remarkably constant, both for the primary tumor and the metastases. Even subtle features of the primary tumor, such as nuclear size and amount of necrosis of cells, were reproduced in the metastases.

Metastatic carcinoma was found in 18 patients, 44 per cent of the total. The lungs were involved in 13 patients, the liver in 11, bones in 10, the bladder in 9, lymph nodes in 9, the rectum in 3, the spleen in 2, and the brain, pancreas and thyroid in one patient each. In none of these organs was the pattern of the metastases different from that of the primary tumor.

An association was found between the histologic grade of the primary tumor and the presence or absence of metastases (Table 1). Grade 2 and grade 3 tumors behaved similarly and were grouped together for the purpose of this study. Grade 1 tumors in these patients did not establish distant metastases; of the grade 2 and grade 3 tumors, 78 per cent established distant metastases.

No difference existed between the ages of patients with grade 1 tumors and grades 2 and 3 tumors. The median age of the entire group was 68 years. For patients with grade 1 tumors it was 69 years; for patients with grades 2 and 3 tumors it was 66 years. A chi-square test on the distribution of ages in the two groups revealed no statistically significant difference.

The duration of survival from the onset of symptoms varied considerably among the patients. Accurate data was available for only half of the group, and no statistically significant difference could be shown with respect to grade of tumor. For the 20 patients on whom data is available, the median survival period was 24 months. For patients with grade 1 tumors it was 31 months, and for those with grade 2 and grade 3 tumors it was 9 months. These data sug-

gest decreased longevity for the patients with grades 2 and 3 tumors, but the ranges were so wide that no statistically significant difference could be shown. Survival data is complicated by the fact that the majority of patients died as a result of causes other than their prostatic carcinoma. Only 13 (32 per cent) of the entire group died as a result of this tumor. The remaining 68 per cent died from causes such as myocardial infarction, cerebral hemorrhage, pulmonary thromboembolism, cirrhosis of the liver, pneumonia, or other malignant tumors.

DISCUSSION

This study shows an association between the histologic grade of adenocarcinoma of the prostate and the ability of the tumor to establish metastases. Tumors of the well differentiated pattern that formed ductal structures, the grade 1 tumors, failed to metastasize, whereas the non-ductal tumors, the grade 2 and grade 3 tumors, frequently metastasized. The morphologic pattern of a prostatic adenocarcinoma is an important index of its ability to produce metastases.

Other studies have shown that there is evidence that the histologic grade of tumor correlates with the length of survival of the patients. Muir noted this in 1934, and more recently Bauer et al. and Mellinger et al. have added supporting data. However, the majority of patients with this disease die from other causes, as shown in this study and in a study by the Veterans Administration Cooperative Research Group. Survival data alone give a less direct measure of the behavior of the tumor than do data on the ability to metastasize.

The histologic grade of a given prostatic adenocarcinoma gives an index of its ability to metastasize during therapy with estrogen. Thus, histologic grading has a prognostic significance. Tumors that form simple ductal structures tend not to metastasize; those with non-ductal, cribriform or solid patterns tend to metastasize. A difference in the biological behavior of these tumors is associated with a difference in their histologic morphology.

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