Unusual Hyperechoic Appearance of Prostate Cancer on Transrectal Ultrasonography

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Summary—A series of 157 patients with prostate cancer underwent transrectal ultrasonography prior to radical prostatectomy. In 112 patients (71.3%) the tumours appeared hypoechoic relative to the echo pattern of the normal peripheral zone; in 43 (27.4%) they appeared isoechoic, and in only 2 (1.3%) did they appear purely or predominantly hyperechoic. These 2 hyperechoic tumours were unusual ductal adenocarcinomas with central necrosis and dystrophic calcification within solid tumour nests, a pattern similar to that of comedo-carcinoma of the breast. Calcification within prostate cancer was found in 4 of the 157 radical prostatectomy specimens, including 2 other hypoechoic cancers which contained intraluminal or psammomatous calcification. Although the most common sonographic appearance of localised prostate cancer is hypoechoic, a predominantly hyperechoic pattern is seen occasionally and suggests the presence of a high grade ductal adenocarcinoma.

Lesions within the prostate can be divided into 3 major groups on the basis of echogenicity: hypoechoic or echopenic lesions which are less echogenic than the normal peripheral zone; isoechoic lesions with sonographic characteristics similar to those of the normal peripheral zone tissue; and hyperechoic or echodense lesions which are more echogenic than the normal peripheral zone. A mixed echogenic pattern results when a lesion has both hypoechoic and hyperechoic areas (Rifkin et al., 1989). Although a number of earlier studies reported that prostate cancer typically appeared hyperechoic (Resnick et al., 1978; Rifkin et al., 1983), Lee et al. (1985) presented the first convincing evidence that a hypoechoic area in the peripheral zone was a reliable criterion for the diagnosis of prostate cancer. Several subsequent studies have shown that prostate cancer does not always appear hypoechoic and that many lesions are, in fact, isoechoic (Dähnert et al., 1986a,b; Griffiths et al., 1987; Jones et al., 1989; Shinohara et al., 1989). The 2 unusual hyperechoic prostate cancers reported here comprised only 1 to 2% of the early stage prostate cancers we examined (Egawa et al., 1989; Shinohara et al., 1989). Both of these tumours demonstrated an unusual pathological pattern, a ductal adenocarcinoma with central necrosis and dystrophic calcification.

Case Reports

Case 1. A 64-year-old man received external beam radiotherapy (6800 cGy) beginning in June 1979 for a moderately differentiated (Gleason score 6) prostate cancer palpably confined to 1 lobe (clinical stage B1). In April 1987 he underwent a transurethral resection of the prostate (TURP) for lower tract obstructive symptoms. At that time he was found to have adenocarcinoma (moderately differentiated, Gleason score 7) in 75% of the chips. Rectal examination revealed a flat fibrotic prostate without nodularity. Metastatic evaluation included chest X-ray, computed tomography and magnetic resonance imaging of the abdomen and pelvis, radioisotopic bone scan, and evaluation of serum markers (acid phosphatase and alkaline phosphatase), which were within normal limits. Transrectal ultrasonography with the Aloka SSD 520 chair-type radial scanner equipped...
with 7.0 MHz radial transrectal probe revealed a large hyperechoic area in the left peripheral and transition zones with acoustic shadowing (Fig. 1). In addition, there was a hypoechoic lesion in the right peripheral zone posteriorly, near the base, which bulged into the surrounding tissue. The hypoechoic lesion was interpreted as prostate cancer with extracapsular extension (Fig. 1A, arrowhead). The patient underwent salvage radical retropubic prostatectomy with bilateral pelvic lymph node dissection (Neerhut et al., 1988). Pathologically the operative specimen showed a poorly differentiated adenocarcinoma (Gleason score 8) with microscopic extracapsular extension. The surgical margins were negative. The histological sections showed a ductal adenocarcinoma of the prostate with central necrosis and dystrophic calcification within solid tumour nests, a pattern similar to that of comedo-carcinoma of the breast (Haagensen and Asch, 1981) (Fig. 2). The total tumour volume was 3.4 ml. When the sonographic images were compared with corresponding pathological sections, the hyperchoic areas corresponded to the areas of calcification (Fig. 1). The hypoechoic area on the right side proved to be an edge artifact. The patient died in February 1988 from a second primary small cell cancer of the lung.

Case 2. A 66-year-old man underwent transurethral resection of the prostate in 1981 for benign prostatic hypertrophy. Subsequent digital rectal examinations revealed a palpable nodularity, although digitally guided transrectal biopsies on 6 separate occasions were negative. Rectal examination revealed a firm and enlarged left lobe which was suspected to be prostate cancer. The right lobe was also granular and firm, and the clinical stage was judged to be B2 (both lobes involved). A digitally-guided needle biopsy revealed adenocarcinoma of the prostate (Gleason score 9). Metastatic evaluation was unremarkable. The pre-operative ultrasound with an Aloka SSD 520 chair-type radial scanner equipped with 7.0 MHz transrectal probe revealed a hyperechoic area in the left lobe and irregularity and convexity of the posterior aspect of the gland, suggesting extracapsular extension (Fig. 3A). Radical retropubic prostatectomy and bilateral lymph node dissection were performed in January 1986. The tumour was a ductal adenocarcinoma (Gleason score 9) with extension outside the prostate and a positive surgical margin. Comedo-like tumour nests exhibited central necrosis and dystrophic calcification (Fig. 4). The total tumour volume was 10.8 ml. Sonographically the tumour appeared hyperechoic, with smaller hypoechoic areas (Fig. 3). Thereafter, the patient under-
Fig. 2 Case 1. (A) Whole-mount step-section (corresponding to level P6 in Fig. 1B) showing tiny black dots, which represent calcifications within the tumour (arrows). (H and E, reduced from × 3.5). (B) Histological section showing unusual ductal adenocarcinoma (Gleason score 8) with comedo-like necrosis and secondary calcification. (H and E × 62.5).

went post-operative radiotherapy (6000 cGy) for local control; 44 months after surgery he remained free of disease.

Discussion

In the early experience with transrectal ultrasonography, prostate cancer was often reported to have a hyperechoic or echodense appearance (Resnick et al., 1978; Rifkin et al., 1983). With modern equipment and wider experience, most investigators have confirmed that the sonographic appearance of prostate cancer is characteristically hypoechoic (Lee et al., 1985; Dähnert et al., 1986a,b; Griffiths et al., 1987; Jones et al., 1989; Shinohara et al., 1989). Several studies have compared prostate sonograms with whole mount histological sections of radical prostatectomy or autopsy specimens, finding that 40 to 76% of prostate cancers appeared echopenic or hypoechoic, while 14 to 39% appeared isoechoic. A hyperechoic pattern (pure or mixed) has been observed with an incidence varying from 0 to 30% (Dähnert et al., 1986a,b; Jones et al., 1989; Shinohara et al., 1989).

In a comparison of 49 radical prostatectomy specimens with sonograms obtained in vivo or in vitro, Dähnert et al. (1986a,b) found that none of the tumours appeared hyperechoic. Rifkin et al. (1989) recently reported that 10% of prostate cancers were subtly hyperechoic and 20% had a mixed echogenic pattern. They also reported that the echogenicity was correlated with stromal fibrotic changes or collagen content, although more than half of their pathological specimens were obtained by biopsy alone. In a previous study, Rifkin et al. (1986) also noted a few instances of acoustic shadowing from within an area of cancer, which they explained as calculi rather than malignancy. Jones et al. (1989), in an attempt to determine the echogenicity of prostate cancer using autopsy specimens, noted that 20% of 29 tumours appeared hyperechoic. The increased echogenicity was attributed to randomly distributed and irregularly shaped calcifications inside the tumours. No other histopathological features were found to be related to the hyperechogenicity of these tumours (Jones et al., 1989). In our earlier study we found a predominantly hyperechoic pattern in only 1.4% of 70 instances in which serial transverse sonograms were compared with whole mount step-sections of radical prostatectomy specimens (Shinohara et al., 1989).

There are a number of reasons for the various echogenic patterns of prostate cancer. These include the size, grade and location of the tumour (Shinohara et al., 1989), desmoplastic reactions to the cancer (Rifkin et al., 1989), the pattern of infiltration of cancer into normal tissue (Lee et al., 1985; Shinohara et al., 1989), and the presence of calcification within the tumours (Griffiths et al., 1987; Jones et al., 1989; Shinohara et al., 1989). However, the apparent variation in the reported incidence of hyperechogenicity of prostate cancer seems to be related chiefly to the use of different (subjective) definitions of "hyperechoic" in the reported studies. Purely or predominantly hyperechoic tumours seem to be uncommon (none of 49 in the series of Dähnert et al., 1986a and 2 of 157 in the present series).
The 2 hyperechoic tumours in our series were rare ductal adenocarcinomas with central necrosis and calcification. Foot et al., (1950) proposed a classification for prostate cancers that recognised ductal type adenocarcinoma. Most adenocarcinomas within the peripheral zone of the prostate are made up of small glands which appear to arise from acini or peripheral ducts (Foot et al., 1950; Dube et al., 1973; Greene et al., 1979; Wheeler, 1989). In a review of 4286 consecutive adenocarcinomas of the prostate, Dube et al. (1973) found that purely ductal adenocarcinomas accounted for only 1.3%, while mixed acinic and ductal adenocarcinomas made up 4.8% of the total cases. Prostatic adenocarcinomas of the ductal type are, therefore, uncommon. Ductal adenocarcinoma arising from the peripheral prostatic ducts has been shown to form comedo-like necrosis with many of the lumina filled with eosinophilic necrotic debris (Dube et al., 1973; Greene et al., 1979). This necrotic debris may undergo dystrophic calcification (Gibbs et al., 1975; Kovi et al., 1979).

Kovi et al. (1979) reported that calcification could be identified radiographically in 36% of 874 prostates sectioned at 4 mm and examined in vitro. Only 8% of these prostates contained invasive carcinoma. Distinct calcification was seen occasionally in invasive prostatic carcinoma. When calcification was seen within the carcinoma itself—which was rare—it was found within the necrotic material in the centre of composite glandular structures. They presented a figure illustrating calcification within the necrotic centre of a carcinomatous duct. In prostate glands with carcinoma and calcification, over 90% of calcifications were associated with benign acini or ducts and usually represented calcified corpora amylacea (Kovi et al., 1979). Gibbs et al. (1975) found calcification in 5 of 23 prostate cancers (21.7%). Two of these were ductal carcinoma with fine basophilic granular calcification in the central portion of degenerated masses of malignant cells. The other 3 calcified cancers were microfollicular carcinoma which contained dense acellular eosinophilic secretion with a weak positive staining for calcium. In our series of 157 prostate cancers 2 other microglandular cancers exhibited calcification; 1 contained irregular intraluminal calcification and the other had
psammoma bodies. Both of these tumours appeared hypoechoic sonographically. Microcalcifications are usually undetectable by ultrasonography unless many are packed closely together (Dähnert et al., 1986b).

The most common cause of hyperchoicinity within the prostate is prostatic calculi, which are present in nearly 100% of men over 30 years of age (Horio, 1967). Prostatic calculi increase in number and tend to calcify with ageing. The strong echo reflections from prostatic calculi can be seen in about 80% of men during transrectal ultrasonography of the prostate (Harada et al., 1980). Prostatic calculi characteristically appear in a chain along the “surgical capsule” or the border between the transition zone and the peripheral zone (Harada et al., 1980) (Fig. 5). Although calculi appear hyperechoic, their predictable anatomical location and regular appearance help to distinguish them from dystrophic calcification within prostate cancer (Jones et al., 1989). Calcification within cancers has a more irregular pattern and sometimes extends across zonal boundaries, as in our cases, from the peripheral zone into the transition zone (Figs 1 and

Fig. 4 Case 2. (A) Whole-mount step-section shows an extensive tumour. (H and E × 3.5). The tiny black dots represent calcifications within the tumour (arrows). (B) Representative histological section of ductal adenocarcinoma (Gleason score 9) with comedo-like necrosis and secondary calcification (H and E × 62.5).

Fig. 5 Representative sonogram of the prostate showing multiple prostatic calculi. The calculi are densely echogenic and arranged in a chain along the border between the transition zone and the peripheral zone bilaterally. (A) Transverse image. (B) Longitudinal image.
3). Calcification seems to be associated with large tumours; in our 2 patients the total tumour volumes were 3, 4 and 10.8 ml.

The typical appearance of prostate cancer on transrectal ultrasonography is hypoechoic; hyperechoic cancers are rare. If a hypoechoic area surrounds or is adjacent to a hyperechoic focus, cancer should also be suspected. Other indirect signs of cancer, such as asymmetry of the peripheral zone (Watanabe et al., 1975), irregularity or bulging of the overlying boundary echo, or gross distortion of the internal anatomy of the prostate (Scardino et al., 1989) also suggest the presence of cancer. Such signs should be considered in the context of the other clinical findings, including the results of digital rectal examination and the level of serum PSA.

Signs of cancer, such as asymmetry of the peripheral zone (Watanabe et al., 1975), irregularity or bulging of the overlying boundary echo, or gross distortion of the internal anatomy of the prostate (Scardino et al., 1989) also suggest the presence of cancer. Such signs should be considered in the context of the other clinical findings, including the results of digital rectal examination and the level of serum markers (acid phosphatase and prostate specific antigen). Although most hyperechoic areas within the prostate are benign, the experienced sonographer should be alert to the occasional cancer which appears predominantly hyperechoic on ultrasonography.

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References


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