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TRANSRECTAL ULTRASONOGRAPHY FOR THE EARLY DIAGNOSIS OF ADENOCARCINOMA OF THE PROSTATE: A NEW MANEUVER DESIGNED TO IMPROVE THE DIFFERENTIATION OF MALIGNANT AND BENIGN LESIONS

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ABSTRACT

Purpose: Transrectal ultrasound can reveal potentially malignant prostate lesions while they are still small. However, based on ultrasound alone they are often difficult to distinguish from benign focal lesions. We tested the reliability of a new technique for the sonographic evaluation of typical prostate lesions in differentiating adenocarcinoma from benign lesions.

Materials and Methods: During 18 months 398 consecutive male patients 45 to 76 years old underwent transrectal ultrasound for the early detection of prostate cancer. When suspicious hypoechoic lesions were noted in the peripheral regions of the prostate, moderate pressure was applied on the lesion using the ultrasound probe to evaluate consistency. Based on the response lesions were classified as deformable (the shape changed from approximately spherical to oval) or nondeformable (the original shape was retained). All lesions were then diagnosed based on fine needle biopsy.

Results: Peripheral hypoechoic prostate lesions were sonographically identified in 146 of 398 patients (36.7%). In 68 cases nondeformable lesions proved to be adenocarcinoma in 63 (92.6%), and chronic prostatitis and/or adenomatous hyperplasia in 5. In contrast, 62 of the 78 deformable nodules (79.5%) showed histological features of hyperplasia and/or chronic inflammation. The remaining 16 nodules, which showed more limited changes in shape during compression, were characterized by hyperplasia with acute inflammatory changes. In 5 cases there was also evidence of adenocarcinoma.

Conclusions: Ultrasound guided compression of suspicious prostate lesions detected on transrectal sonography is a simple, rapid and reliable maneuver that may increase the diagnostic potential of this examination.

KEY WORDS: prostate, ultrasonography, prostatic neoplasms, diagnosis

Prostate carcinoma is one of the most common tumors in middle-aged and elderly men throughout the world and the third most frequent cause of death from cancer after carcinoma of the lung and intestine. In 1954 the autopsy study of Franks demonstrated that approximately 30% of all men in the sixth decade of life and 67% of those between 80 and 90 years had carcinoma of the prostate, although the tumor was not always the cause of death.[1] Given increased life expectancy the frequency of prostate cancer is certainly on the increase and can be expected to reach new heights in the near future.

Early diagnosis is not easy, mainly because of the absence of symptoms in early stages of the disease. The neoplastic focus is usually located in the peripheral posterior regions of the prostate, which are relatively removed from important structures such as the prostatic urethra and, thus, are unlikely to give rise to symptoms.[2] Carcinomas that arise in the internal portion of the prostate are rarer and generally less aggressive.[3,4] Treatment possibilities and prognosis depend largely on early diagnosis while the tumor is still asymptomatic (stages T1–T2). For this reason all men older than 45 years are generally advised to undergo digital rectal examination at least once yearly regardless of whether they are symptomatic.[5]

Recently prostate cancer screening has relied increasingly on ultrasonography with laboratory tests, such as prostate specific antigen (PSA) determination.[6–8] Transrectal ultrasound with high definition probes can in fact reveal potentially malignant prostate lesions while they are still small and circumscribed. However, based on ultrasound features alone it is often quite difficult to distinguish these small tumors from benign focal lesions such as localized inflammatory changes and nodular hyperplasia, which are quite common in older men. Biopsy is the only means of making a definitive diagnosis.[9,10]

There are currently no reliable standardized criteria for ultrasound identification of small prostate cancer. To avoid subjecting the patient to an invasive procedure when a suspicious lesion is detected on transrectal ultrasound the decision to perform biopsy is usually based on a number of factors, including PSA, associated symptoms, lesion size and patient preference. Unless the suspicion of malignancy is supported by other factors we generally defer biopsy and advise the patient to repeat the screening examination within 12 months. If the evolution of clinical and ultrasound findings supports the suspicion of prostate carcinoma, ultrasound guided fine needle biopsy of the lesion is performed to establish a definitive diagnosis. In an attempt to improve this selection process we developed a new technique for sonographic evaluation of typical prostate lesions that are considered to be potentially neoplastic, that is hypoechoic subcap-

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sular lesions located in the periphery of the prostate. We tested the reliability of this approach for differentiating adenocarcinomatous lesions from benign processes in a large group of males who underwent ultrasound screening for prostate cancer.[11]

MATERIALS AND METHODS

During the 18-month period of February 2000 through June 2001, 398 consecutive male patients between ages 45 and 76 years underwent screening studies for the early detection of prostate cancer. The screening protocol included transrectal ultrasonographic examination of the prostate, urinalysis, acid phosphatase and PSA (normal range 0 to 3 ng./ml.). Ultrasound was performed with a (SSA 270 Toshiba Medical Systems, Tokyo, Japan) scanner equipped with a high frequency (7.5 MHz.) biplanar (linear array and convex) probe. The dimensions and contours of the prostate were recorded as well as any calcifications or adenomatous lesions. Special attention was focused on hypoechoic lesions in the periphery of the prostate, the contours of the overlying capsule (such as indentation, interruption and blurring) and any changes involving the seminal vesicles (such as enlargement, which may reflect tumor infiltration of the ejaculatory ducts).

When 1 or more suspicious hypoechoic lesions were noted in the peripheral regions of the prostate, ultrasound guided compression was performed in an attempt to clarify the hardness of the lesions. This maneuver, which we recently developed, consists of the application of moderate pressure on the lesion in an anteroposterior direction using the rectal ultrasound probe. Based on the response to this maneuver lesions were divided into 2 broad categories, namely deformable lesions—those with a shape that changed from approximately spherical to oval with the long axis perpendicular to the compression vector, which in our experience are unlikely to be prostate carcinomas, and nondeformable lesions—those that retained the original shape during compression, which we consider more likely to be neoplastic (figs. 1 and 2). The presence or absence of pain at compression of the lesion was also noted.

In all patients with suspicious lesions regardless of the results of the compression test ultrasound guided fine needle lesional biopsies were performed with the informed consent of the patient. Members of the urology department at our hospital obtained the biopsies via a transperineal approach. Colt (Sterylab, Rho, Milan, Italy) 18 gauge cutting needles were used with a freehand technique and at least 3 passes were made at the level of each hypoechoic lesion. Coagulation parameters were assessed in all patients before biopsy. Antibiotic coverage was provided for 6 days after the procedure.

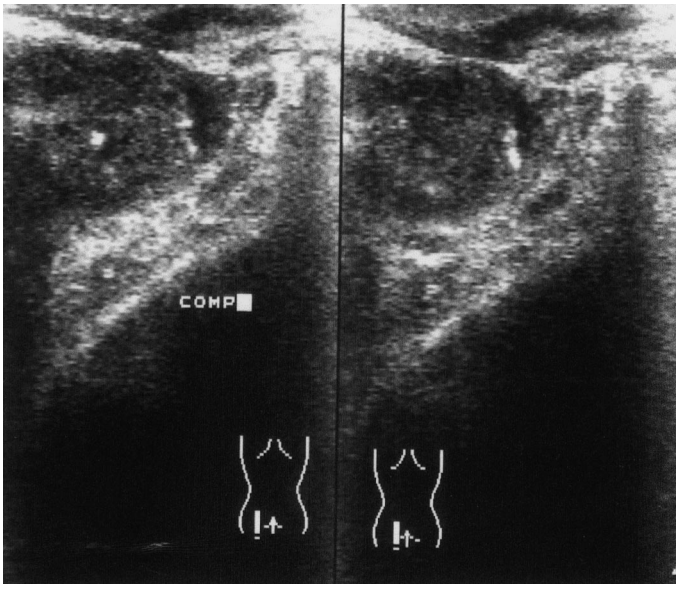

FIG. 1. Transrectal ultrasound with linear array probe shows small hypoechoic subcapsular prostate lesion in periphery of prostate (left). When pressure was applied with probe, lesion shape changed from spherical to oval. This deformability was considered indicative of nonmalignant lesion.

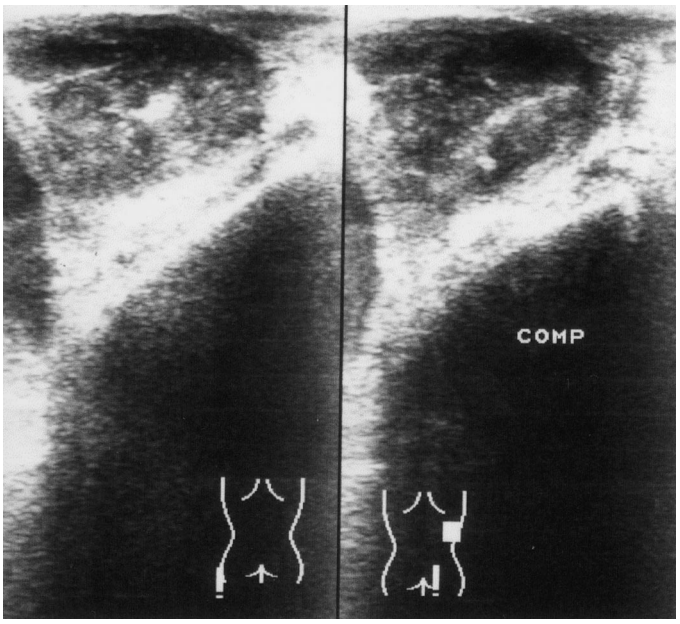

FIG. 2. Transrectal ultrasound with linear array probe reveals small hypoechoic subcapsular prostate lesion in periphery of prostate (left). Lesion retained original shape when pressure was applied with probe (right). This nondeformability was considered indicative of probable malignancy.

RESULTS

In the 398 men screened urinalysis results and acid phosphatase levels were normal. Only 36 patients (9%) reported symptoms. Peripheral hypoechoic prostate lesions were sonographically identified in 146 of the 398 men (36.7%) examined. Of these 146 men 36 (24.7%) were symptomatic with mildly increased urinary frequency in 14, nocturia in 19, microhematuria in 2 and hemospermia in 1. PSA in these cases was 0.5 to 10 ng./ml.

The results of the ultrasound guided compression test revealed nondeformable lesions in 68 of the 146 patients (46.6%). Only 14 of these 68 individuals had reported symptoms and 10 (14.7%) also experienced pain during the compression maneuver. The remaining 78 men (53.4%), including 22 who had reported symptoms, had lesions that were considered deformable. This group included 62 men with lesions with a shape that clearly changed with pressure and 16 with no deformability (figs. 1 and 2). The maneuver caused pain in 69 of the 78 men (88.5%).

Ultrasound fine needle biopsies of all 146 lesions were obtained. The biopsy procedure was associated with mild self-limited complications in 7 of the 146 cases (4.8%); including microhematuria in 5, hemospermia in 1, local pain in 1 and fever in 1. Histological findings were positive for adenocarcinoma of the prostate in 63 of the 68 patients (92.6%) with nondeformable lesions (fig. 3). In the remaining 5 cases biopsy revealed signs of chronic inflammation and/or adenomatous hyperplasia. In contrast, 62 of the 78 nodules (79.5%) classified as deformable showed histological features compatible with hyperplasia and/or chronic inflammation (fig. 4). The remaining 16 lesions had been classified as deformable,

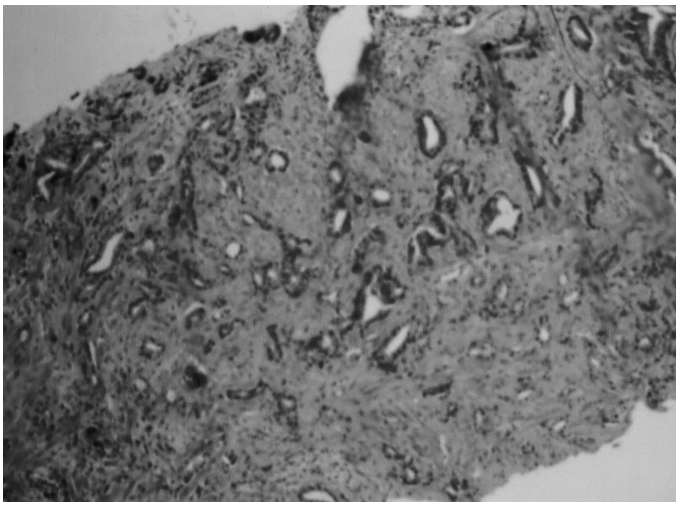

FIG. 3. Histological appearance of nondeformable lesion, which proved to be adenocarcinoma. H & E, reduced from ×10.

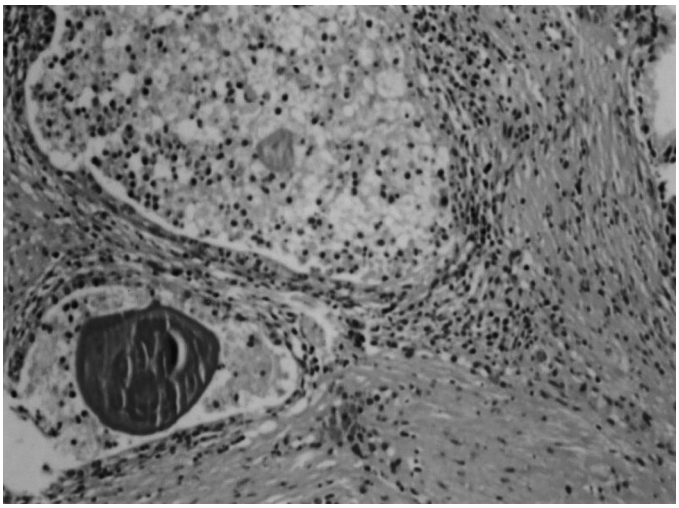

FIG. 4. Histological examination of deformable lesion revealed hyperplasia with inflammatory changes. H & E, reduced from ×10.

although the changes in form provoked by compression were in fact much less evident than in the other 62 deformable lesions. All 16 nodules were histologically characterized by signs of hyperplasia with acute inflammatory changes but 5 (6.4%) also contained evidence of malignancy (adenocarcinoma).

DISCUSSION

In recent years the importance of ultrasonography with PSA and free PSA levels for prostate cancer screening has been emphasized by a number of investigators.[6,7] The possibility of a cure depends on the stage of the tumor when it is first detected and the ideal method of screening allows the detection of such lesions while they are still small and localized.[12] For this purpose transrectal ultrasound is clearly more effective than the traditional transpubic study and far superior to transrectal digital examination of the prostate.

Approximately 75% of all prostate carcinomas present sonographically as hypoechoic lesions located in the posterior periphery of the prostate. When the neoplasm is multifocal, there is often an archipelago of lesions, of which the smallest may be isoechoic. Transrectal sonography can reveal larger lesions of this type while they are still too small to be palpated through the wall of the rectum. This advantage can be highly important since autopsy findings indicate that prostate tumors less than 0.5 to 0.8 cm. can generally be considered clinically insignificant.[13–15]

Transrectal ultrasound followed by fine needle lesion biopsy can be considered the gold standard for the early diagnosis of prostate carcinoma.[16–19] However, pathological evaluation of all suspicious lesions is expensive and stressful for the patient. In fact, 55% to 60% of all small hypoechoic subcapsular lesions in the posterior prostate ultimately prove to be benign (acute or chronic inflammatory processes or nodular hyperplasia). Therefore, refinement of the ultrasound criteria for identifying lesions that merit immediate attention is necessary.[20]

While nodular hyperplasia is due to glandular proliferation and dilatation with fibromuscular proliferation of the stroma, the macroscopic appearance of prostatic carcinomas involves compact grayish tissue that strongly resembles normal adjacent tissue. For this reason small tumors are difficult to detect. With time the tumor assumes a yellowish color that reflects an abundance of stromal connective tissue with a scirrhous-like consistency. From the microscopic point of view distinguishing adenocarcinomas and hyperplastic nodules is complicated by the relative scarcity of anaplastic cells in the former. The presence of blood and lymphatic vessels is often decisive. In addition to adenocarcinomas, the prostate sometimes contains squamous cell carcinomas, which may originate from metaplastic cells.

In the current study we evaluated the usefulness of a diagnostic maneuver that we developed for this purpose. Ultrasound guided compression of the lesion using the rectal probe allows the examiner to assess its consistency and this additional information appears to increase the accuracy of ultrasound in terms of its ability to identify lesions with a high risk of malignancy. The maneuver represents a more standardized and objective refinement of the classic method of transrectal digital exploration of the prostate, which has been the mainstay of prostate cancer screening for years.

Of the 68 cases considered positive, that is nondeformable, 63 (92.6%) were histologically confirmed as adenocarcinoma. The same diagnosis emerged for 5 of the 78 nodules (6.4%) classified negative or deformable. Interestingly all 5 false-negative diagnoses were made in the borderline subgroup of 16 men in whom lesions were classified deformable, although changes in shape provoked by the maneuver was quite limited. In contrast, all lesions that responded to the compression maneuver with marked changes in shape proved to be benign. Thus, the method showed 93.2% sensitivity and 78% specificity for identifying prostatic carcinomas. Although 11 of the 16 lesions (68.8%) with limited deformability were ultimately diagnosed as benign (negative), it is possible that the diagnostic significance attributable to this finding may be adjusted (that is classified as a positive rather than a negative response) to increase method specificity without causing an unacceptable decrease in sensitivity. In any case for suspicious hypoechoic lesions that are within this borderline category, even if histology reveals nothing more than an inflammatory process, we still advise our patients to undergo yearly followup transrectal ultrasound with PSA measurement every 6 months.

Combining the pain response with lesion deformability may also increase the accuracy of the method. Pain at compression characterized the 88% of acute inflammatory lesions and was absent in 93% of those that proved to be carcinomas. We are currently investigating the diagnostic value of this combined approach in a larger series of patients.

CONCLUSIONS

Ultrasound guided compression of suspicious prostate lesions detected by the transrectal sonography maneuver is a simple and rapid technique that may increase the diagnostic

potential of this examination. Although its use is effectively limited to subcapsular (peripheral) lesions in the dorsal regions of the prostate, these characteristics apply to approximately 75% of all prostatic carcinomas, including those that are most biologically aggressive. The compression maneuver had high sensitivity and good specificity for distinguishing malignant prostatic lesions. Biopsy remains the only reliable approach for confirming or excluding adenocarcinoma of the prostate. However, the compression maneuver could improve the selection of lesions that require histological analysis and eliminate a number of useless biopsies of benign lesions.

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