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Original contribution

Histologic findings on prostate needle core biopsies following cryotherapy as monotherapy for prostatic adenocarcinoma

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Summary The histologic features seen in the prostate following cryotherapy can be highly variable. However, most previous studies were performed on specimens following salvage cryotherapy, which introduces additional confounding variables of the histologic changes after the other primary treatment modalities. We examined prostate needle core biopsies from a cohort of patients following cryotherapy as monotherapy for prostatic adenocarcinoma, to evaluate the true spectrum of morphologic changes in the prostate. Cases that had prior radiation therapy or androgen-deprivation therapy were excluded from the study. Thirty cases were identified. The average patient age was 69 years (range, 51-81 years), and the average time interval between cryotherapy and repeat biopsy was 19.2 months (range, 2-60 months). The original Gleason scores were as follows: 3 + 3 = 6 in 14 (46%) of 30 cases, 3 + 4 = 7 in 8 (27%) of 30 cases, 4 + 3 = 7 in 2 (7%) of 30 cases, 4 + 4 = 8 in 3 (10%) of 30 cases, 4 + 5 = 9 in 2 (7%) of 30 cases, and 5 + 4 = 9 in 1 (3%) of 30 cases. Postcryotherapy, 11 of 30 cases (37%) had recurrent/residual prostatic adenocarcinoma, which showed no therapy-related changes, similar to the residual benign glands. Gleason scores were higher in 5 (46%) of 11 cases, same in 4 (36%) of 11 cases, and lower in 2 (18%) of 11 cases. Multiple additional histologic findings were documented. Unlike other nonsurgical therapeutic modalities, cases with recurrent/residual prostatic adenocarcinoma and benign glands showed therapy-related changes predominantly involving the stroma. It is therefore conceivable that benign or malignant prostatic glands are either completely destroyed during cryotherapy or left unaltered if not in the direct field of cryoablation.
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1. Introduction

The treatment for prostate cancer has traditionally relied both on surgical and nonsurgical therapies. Although radical prostatectomy is still a very popular treatment modality, patients and clinicians are increasingly looking for nonsurgical

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Table 1 Overall histologic findings in all cases postcryotherapy

Histologic features postcryotherapy	Frequency (%)
Recurrent/residual prostatic adenocarcinoma	11/30 (37%)
Gleason scores	
Higher than previous	5/11 (46%)
Same as previous	4/11 (36%)
Lower than previous	2/11 (18%)
Chronic inflammation	24/30 (80%)
Myxoid stromal change	24/30 (80%)
Stromal hemosiderin	21/30 (70%)
Stromal fibrosis	9/30 (30%)
Necrosis	8/30 (27%)
Calcifications	6/30 (20%)
Acute inflammation	5/30 (17%)
Granulomas	4/30 (13%)
Hemorrhage	4/30 (13%)
Vessel wall thickening/prominent endothelial cells	3/30 (10%)
Squamous metaplasia	3/30 (10%)

treatments, which might reduce the unwanted side effects of prostatectomy (eg, urinary incontinence and erectile dysfunction). The traditional nonsurgical options have been androgen-deprivation therapy and radiation therapy. Both of these treatments introduce well-documented posttherapy changes in the prostate, which need to be recognized by the surgical pathologist when dealing with a prostatic core biopsy or a radical prostatectomy specimen following these treatments.

Another nonsurgical treatment technique is cryosurgical ablation of the prostate or cryotherapy. First introduced in the 1960s, cryotherapy was shown to have comparable 10-year survival as surgery and radiation [1]. However, cryotherapy also had significant morbidity. Freezing of the urethra caused urethral sloughing, rectal freezing resulted in rectourethral fistulas, and cutaneous fistulas were also a possibility [2]. As a result, cryotherapy was all but abandoned until the 1990s when new techniques including the use of transrectal ultrasound and a urethral warming device significantly decreased these adverse effects [3]. New advances such as the use of smaller gauge probes, argon-based probes (as opposed to traditional nitrogen-based), and improved imaging techniques have all lead to increased efficacy with a decrease in severe side effects [4]. Another critical advantage of cryotherapy is the fact that it can be safely used as an alternative therapeutic approach in patients who are not good surgical candidates for radical prostatectomy.

Multiple studies have shown the treatment-related effects of both radiation therapy and androgen-deprivation therapy on the histology of both prostatic adenocarcinoma and the benign gland [5-7]. There have been only a few studies published on the specific changes introduced by cryotherapy. Borkowski et al [8] published a study of 17 patients with primary cryotherapy with a single follow-up biopsy at 3 months. In this series, necrosis was the most common finding [8]. One reason for this is that cryotherapy has often been used as a "salvage" technique when another nonsurgical treatment has failed [9]. Because of these confounding factors, it can be difficult to separate out which histologic changes were caused by which prior treatments.

In this study, we describe the histopathologic features seen in a cohort of prostate needle core biopsies after cryotherapy as monotherapy for prostatic adenocarcinoma. In this way, we are evaluating the true spectrum of morphologic changes seen in benign and malignant prostatic glands and stroma induced by cryotherapy.

2. Materials and methods

2.1. Case selection and histologic examination

A search was made through the urologic pathology files at our institution for patients with prostate needle core biopsies

Table 2 Histologic findings (precryotherapy and postcryotherapy) and cryotherapy protocol in all cases with residual/recurrent prostatic adenocarcinoma postcryotherapy

	Precryotherapy findings		Cryotherapy procedure		Postcryotherapy findings		
	Gleason score (highest)	Tumor location	Cryotherapy date	Cryotherapy location	Gleason score	Tumor location	Biopsy date
Patient 1	3 + 3 = 6	Right	March 2005	Bilateral	3 + 4 = 7	Left	October 2006
Patient 2	4 + 4 = 8	Left	January 2005	Bilateral	3 + 4 = 7	Right	May 2007
Patient 3	3 + 3 = 6, 3 + 4 = 7	Right and left	July 2006	Bilateral	4 + 3 = 7	Right	August 2008
Patient 4	3 + 4 = 7	Right	August 2006	Bilateral	3 + 4 = 7	Right	June 2008
Patient 5	4 + 4 = 8, 4 + 5 = 9	Right and left	July 2006	Bilateral	4 + 4 = 8, 4 + 4 = 8	Right and left	July 2008
Patient 6	3 + 3 = 6	Left	May 2006	Left	3 + 3 = 6	Right	August 2008
Patient 7	4 + 3 = 7, 4 + 3 = 7	Right and left	January 2007	Bilateral	4 + 4 = 8	Left	September 2008
Patient 8	3 + 3 = 6	Right	February 2007	Bilateral	4 + 4 = 8, 4 + 4 = 8	Right and left	September 2008
Patient 9	4 + 3 = 7, 4 + 4 = 8	Right and left	August 2005	Bilateral	4 + 3 = 7, 4 + 4 = 8	Right and left	August 2010
Patient 10	3 + 3 = 6, 3 + 4 = 7	Right and left	November 2008	Bilateral	4 + 3 = 7, 4 + 4 = 8	Right and left	February 2011
Patient 11	3 + 3 = 6	Left	March 2009	Left	3 + 3 = 6, 4 + 3 = 7	Right and left	February 2011