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PSMA expression in Schwannoma: A potential clinical mimicker of metastatic prostate carcinoma☆

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Abstract

Objectives: Radioimmunoscintigraphy using a radiolabeled antibody against prostate-specific membrane antigen (PSMA) is frequently used to detect prostate carcinoma (PCa) recurrence and metastasis to lymph nodes, soft tissues, and bone. PSMA expression has been shown in occasional nonprostatic neoplasms (e.g., urothelial adenocarcinoma) and in the vasculatures of other malignancies. PSMA expression has not been described in benign neoplasms. Recently, during evaluation of a prostatic carcinoma patient, we encountered a false positive PSMA radioimmunoscintigraphy scan in a pathologically confirmed Schwannoma (SCH) lesion. The current study further evaluates PSMA expression in Schwannomas.

Methods: Eleven SCH were retrieved from our surgical pathology archives. Representative sections were immunostained with monoclonal antibody for PSMA. PSMA expression was evaluated in tumor cells and lesional vessels. Extent of staining was calculated as percent of positive cells in highest areas of expression. Positive staining was considered focal, multifocal, or diffuse based on the percent of positive cells: <5%, 5% to 75%, and >75%, respectively.

Results: All 11 SCH showed tumoral and or vascular staining; 7 (7/11) displayed both vascular and tumoral cell staining; the remaining 4 had only vascular staining (2/11) or tumor cell staining (2/11). The extent of tumoral cell and vascular staining varied widely among lesions (tumor cells: focal in 8 and diffuse in 1; vascular: focal in 7, multifocal in 1, and diffuse in 1 lesion).

Conclusion: This is the first report of PSMA expression in a benign neoplasm. Given our finding of frequent expression of PSMA in Schwannomas, they should be clinically considered in the differential diagnosis of a lesion that is positive on PSMA radioimmunoscintigraphy study performed during a metastatic work-up of PCa patient.

Keywords: Prostate; Prostate specific membrane antigen; Schwannoma

1. Introduction

Prostatic specific membrane antigen (PSMA) is one of multiple prostate tissue specific markers that has been applied by pathologists to help establish prostatic cell lineage. PSMA is a transmembrane glycoprotein with a glutamate carboxypeptidase activity that has also been associated with tumor angiogenesis [1–6]. PSMA has been exploited as a target for diagnosis and imaging in PCa patients as well as a potential therapy target. Radioimmunoscintigraphy using a radiolabeled prostate-specific membrane antigen antibody is frequently used to detect prostatic carcinoma recurrence or metastasis to lymph nodes, soft tissues, or bone [7–13].

Schwannoma (SCH), also known as neurolemmoma, is a benign peripheral nerve sheath neoplasm. Recently, during evaluation of a prostatic carcinoma patient, we encountered a positive PSMA radioimmunoscintigraphy scan in a pathologically confirmed Schwannoma lesion leading to an initial clinical false impression of metastatic PCa. The current study further evaluates PSMA expression in SCH lesions.

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2. Materials and methods

In addition to the initial case with false positive PMSA scan, 10 archival schwannoma lesions diagnosed at different anatomical sites were retrieved from our surgical pathology files. Immunohistochemistry for PSMA was performed using Ventana automated immunostainer and i-view immunolabeling kit (Ventana Medical Systems, Tucson, AZ). Antigen retrieval with Standard CC1 (EDTA buffer) followed by incubation with primary antibody (PSMA clone 3E6,1:100; DAKO Cytomation, Carpentaria, CA). PSMA expression in tumor cells and lesional vessels was evaluated by two pathologists. Extent of staining was calculated as percent of positive cells in highest areas of expression. Positive staining was considered focal, multifocal, or diffuse based on percent of positive cells: <5%, 5% to 75%, and >75%, respectively.

3. Results

3.1. Clinical and anatomical features

Patients age ranged in age from 31 to 78 years (mean 54.4 years). SCH anatomical locations included: soft tissue [4], auditory canal [3], mediastinum [1], spinal cord [2], cerebropontine angle [1]. The tumors ranged in size from 1.5 to 12.5 cm (mean 3.8 cm). All studied tumors were sporadic. Clinicopathological data are summarized in Table 1. A photomicrograph of a representative H and E section is demonstrated in Fig. 1.

3.2. PSMA expression

PSMA immunostain results are detailed in Tables 2 and 3. All 11 cases demonstrated at least focal positive immunostaining for PSMA with various distribution patterns. Staining was restricted to Schwann cells alone in 2/11 (Fig. 2A and B) and lesional vessels alone in 2/11 (Figure 2C) lesions. In the remaining 7 cases, a combined vascular and Schwann cell staining pattern was present. Among 9 cases with only positive vascular positivity, the percentage of positive tumor cells was <5% in 7, 5% to 75% in 1, and 75% in the remaining cases. Among 9 cases with positive lesional Schwann cell staining, 8 demonstrated focal (<5% positive cells) staining and 1 case had a diffuse >75% staining distribution. Lesional cell staining was of cytoplasmic pattern.

Table 1
Clinical and demographical characteristic of Schwannoma cases

Case	Age	Size (cm)	Sex	Site
1	31	5.5	F	Mediastinum
2	48	1.5	M	L4-5 root
3	79	4.2	F	Chest wall
4	48	1.2	F	Auditory canal (Acoustic Neuroma)
5	41	12.5	M	Chest wall
6	58	5.5	M	Cerebropontine Angle (Acoustic Neuroma)
7	51	1.5	F	Auditory canal (Acoustic Neuroma)
8	70	2.8	M	Spinal cord
9	68	2.0	M	Auditory canal (Acoustic Neuroma)
10	35	3.8	F	Arm
11	70	1.5	F	Neck

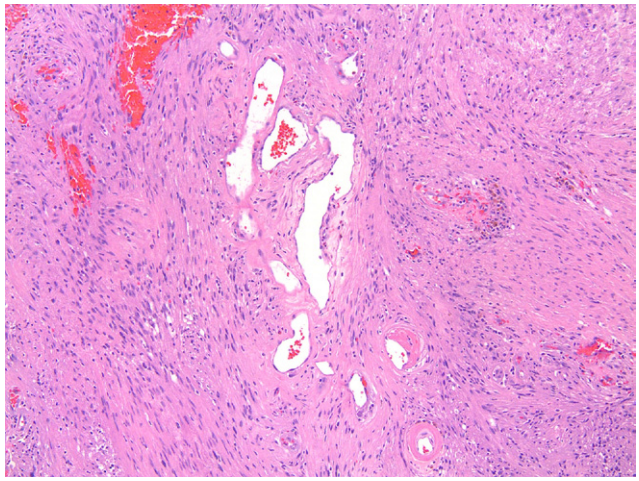

Fig. 1. Histologic section of a Schwannoma showing typical palisaded spindle cell morphology within cellular regions containing thickened wall hyalinized vessels. (H and E stain, 100× magnification). (Color version of figure is available online.)

4. Comment

PSMA is expressed in normal and hyperplastic prostate epithelial cells as well as in prostate adenocarcinoma cells with a positivity rate ranging from 55% to 100% in both tissue microarray and routine tissue section studies [13–16]. It is expressed at low levels in benign prostatic epithelium and is highly up-regulated in prostatic adenocarcinoma of various grades. PSMA immunohistochemical expression patterns include cytoplasmic, apical, and cytoplasmic staining with membranous accentuation [13,17,18]. Several prior studies have documented PSMA expression in nonprostatic normal and malignant neoplastic tissues [13–15], although its positivity seems to be less intense than that in the prostatic epithelium, PSMA staining in nonprostatic cells is usually of cytoplasmic pattern. PSMA has also been demonstrated to be expressed by tumor-associated neovasculature at different sites [4–6]. To our knowledge, despite the wide array of previously studied lesions, PSMA expression has not been previously shown in benign neoplasms prior to the current study [15].

Radiolabeled antibodies against PSMA have been developed and applied for *in vivo* localization of metastatic prostatic cancer and to enhance delivery of treatment to targeted prostatic cancer cells [11,12]. Evidently, the utility of mark-