Perineural Spread of Pelvic Malignancies

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Introduction

Perineural spread is an alternate mean of spread in various malignancies. It is most commonly described in connection with head and neck cancers and histologically with squamous cell carcinoma or melanoma. Perineural spread in visceral organ malignancies frequently occurs in pancreatic cancer, but has been demonstrated in prostate cancer, rectal cancer, bladder cancer or cervical cancer on small case series or in individual case reports.

The purpose of this study was to review our institutional series of patients with perineural spread of pelvic malignancy in search of clinical and imaging patterns.

Material & Methods

We retrospectively reviewed cases of perineural tumor spread. We excluded the cases without histological confirmation of perineural spread and the cases with widespread pelvic disease. We recorded in detail all demographic data (age, sex), history (original cancer, initial symptoms, duration, character and laterality of symptoms), physical examination (pain, weakness, sensory loss), electrodiagnostic results, imaging studies including magnetic resonance imaging (MRI) and 18Fluoro-deoxy-glucose Positron emission tomography/Computed tomography (FDG PETC/CT) or 11C-Choline Positron emission tomography/ Computed tomography (Choline PET/ CT), evidence of other metastatic disease and follow-up status and interval.

Results

History and Evaluation: Ten patients (8 men, 2 women) were included in the study (prostate cancer n=5; rectal cancer n=2, bladder cancer n=2, cervical cancer n=1). Clinical data for each patient are in Table 1. Mean age was 69 years (range 48-85 years). Pain was the initial symptom in 6 patients; pain and weakness in 1 patient; weakness in 1 patient; and 2 patients were asymptomatic. In 1 patient the symptoms of the lumbosacral plexopathy preceded the tumor diagnosis by 3 months; in other patients the mean time from the original tumor diagnosis to the initial symptom was 67 months (range 1 month – 18 years). On presentation, 8 symptomatic patients had combination of pain, sensory loss and weakness predominantly expressed in L5-S1 dermatomes. Of 8 symptomatic patients, 7 had unilateral symptoms, 1 had bilateral symptoms. EMG (n=9) demonstrated lumbosacral plexopathy in 8 patients; in 1 patient it was normal. Six patients had no signs of distant metastatic disease at the time of the lumbosacral plexopathy diagnosis; 2 patients had metastases in lungs, one patient had metastases in pelvis and one had solitary metastasis in liver.

Imaging: On MRI (n=10) the affected nerves were enlarged on T1-weighted sequences, hyperintense on T2-weighted sequences and demonstrated thick (perifascicular) enhancement after gadolinium application. Details of the imaging characteristics are in Table 2. Occasionally the nerves demonstrated a nodular appearance suggestive of localized tumor proliferation or perineural spread with “skip lesions”. The most frequently affected spinal nerves were L5 to S2; 3 patients had intradural extension of the tumor. MRI findings correlated with increased uptake on FDG PET/CT (n=4) and ^{11}C-Choline PET/CT (n=3) scans. Additional details are listed in Table 2.

Outcome: Seven patients were alive at the time of the last follow-up. Mean time from the initial symptom to the last follow-up was 51 months.

Figure 1

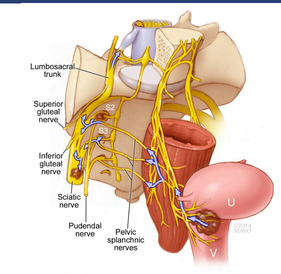

Figure 1: Artistic rendering of the proposed pathway of spread from the cancer bed (uterine cervix in this instance) to the lumbosacral plexus along the splanchnic nerves and then proximally to the spinal nerves or distally to the sciatic nerve. (By permission ©Mayo Foundation for Medical Education and Research. All rights reserved.)

Table 2 – Imaging data

Case #	Organ	Age	Sex	Laterality	Spinal Nerves	Peripheral Nerves	Intradural extension	Route of spread*	FDG PET/CT	11C-Choline PET/CT
1	Rectum	48	f	right	L5-S1	sciatic	-	+	n/a	n/a
2	Rectum	50	m	right	S1	sciatic	-	-	n/a	n/a
3	Prostate	60	m	left	L5-S3	intrapelvic sciatic	-	+	n/a	n/a
4	Cervix	61	f	left	L5-S3	sciatic	-	+	S2, sciatic	n/a
5	Prostate	64	m	bilat	S2-3 bilat, L4-S1 R	sciatics	+	-	S1 bilat, sciatics, L L5	S1 bilat, sciatics, L L5
6	Prostate	70	m	left	L4-S4	sciatic	+	+	n/a	n/a
7	Bladder	71	m	right	L5-S2	sciatic	-	+	n/a	n/a
8	Prostate	77	m	right	S1-S3	intrapelvic sciatic	+	-	n/a	S1
9	Bladder	83	m	left	L4-S1	obturator, sciatic	-	+	L4-S1	n/a
10	Prostate	85	m	right	S1-S3	sciatic	-	+	sciatic	sciatic

*Unilaterally thickened and enhancing perirectal fascia suggestive of perineural tumor spread along the splanchnic nerves.

Table 1 – Clinical data

Case	Organ	Age	Sex	Time to initial symptom from T Dg	Initital symptom	Laterality	Physical Examination			EMG	Other metastases at the time of the LSP diagnosis	Follow Up Status
							Pain	Weakness	Sensory loss			
1	Rectal	48	f	x	x	right	no	normal	normal	n/a	lung	alive
2	Rectal	50	m	x	x	right	no	normal	normal	normal	liver	alive
3	Prostate	60	m	-3m	pain	left	S1, perianal	glutei, hamstrings	saddle anesthesia	LSP (L5-S1)	no	alive
4	Cervix	61	f	1m	pain	left	S1	sciatic palsy	L5-S1	sciatic palsy except normal biceps femoris	no	died
5	Prostate	64	m	6y	weakness	bilat	buttock bilat, right S1	left sciatic palsy, left adductors 3/5, right sciatic 3-4/5, right adductors 4/5	L5,S1 bilat, perianal	bilat LSP, more left	pelvis	alive
6	Prostate	70	m	9y	pain, weakness	left	L5, S1	sciatic 4/5	L5, S1	LSP (L5-S2)	no	died
7	Bladder	71	m	7m	pain	right	S1	hamstrings 3/5, otherwise sciatic 1/5	L5, S1	LSP (L5-S2)	no	alive
8	Prostate	77	m	6y	pain	right	S1	sciatic 4/5	S1	LSP (L5-S1)	no	alive
9	Bladder	83	m	3y4m	pain	left	L5, S1	adductors 3/5, foot dorsiflexion 2/5, plantar flexion 4/5	distal LLE	LSP (obturator and mild peroneal neuropathy)	lung	died
10	Prostate	85	m	18y	pain	right	L5, S1	sciatic 3-4/5,	L5, S1	proximal sciatic neuropathy	no	alive

Anatomy & Mechanism

In the pelvis, the autonomous visceral innervation is provided by the parasympathetic pelvic splanchnic nerves derived from the S2-S4 spinal nerves and by the sympathetic sacral splanchnic nerves from the sacral sympathetic chain. These splanchnics merge to form the inferior hypogastric plexus, which innervates the pelvic organs. The inferior hypogastric plexus further receives input from the sympathetic superior hypogastric plexus in the form of the left and right hypogastric nerves. This is true for the rectum, uterus, prostate and partly the bladder. The different parts of the urinary bladder receive different innervation based on its embryological origin. The trigone that constitutes the posterior wall is innervated by lumbar splanchnic nerves via the hypogastric nerves while the rest of the bladder receives predominantly parasympathetic innervation derived from the pelvic splanchnic nerves.

As already demonstrated in prostate[1, 3, 6], cervical[5] and rectal cancer[2], the tumor cells infiltrate the inferior hypogastric plexus and spread to the lumbosacral plexus along the splanchnic nerves. Infiltration of the pelvic sympathetic system can produce “hot and dry foot” syndrome. From the plexus cancer spreads distally to the sciatic nerve or proximally to the spinal nerves or even intradurally (Fig. 1). This applies to the lateral walls and the dome of the bladder as well; the tumors invading the trigone spread predominantly to the lumbar plexus along the lumbar splanchnic nerves and then can again extend beyond the plexus proximally to the spinal nerves or even intradurally,cancer can extend in the opposite direction to the obturator nerve.

The histologic basis for perineural tumor spread is perineural invasion, which is present in nearly all radical prostatectomy specimens[4], in as much as 47.7%[7] of radical cystectomy specimens and in approximately 30% of rectal cancer cases[8].

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