

## CASE REPORT

# Bladder pheochromocytoma: Case presentation and the use of OctreoScan<sup>®</sup> for localization of extra-adrenal tumor sites in a pediatric patient

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**An eleven year old boy presented with headaches and dizziness associated to micturition. On radiologic imaging, he was found with a bladder mass. The biochemical work up was suggestive of pheochromocytoma. An OctreoScan (111 In-pentreoctide) was used to rule out metastatic extension or other extra-adrenal**

**locations of the pheochromocytoma. OctreoScan data correlated well with other radiologic studies, operative findings and with the final diagnosis, validating its use on pediatric patients.**

*Keywords: ooBladder, oOctreoScan, oPheochromocytoma, Paraganglioma.*

**B**ladder pheochromocytomas represent less than 0.1% of all bladder tumors (1-3). They have been reported in patients between 11 and 78 years of age with a peak incidence between the third and fifth decade of life, with males and females equally affected. The most common manifestation of bladder pheochromocytoma is painless hematuria in 55-65% of cases (3,4). The micturition symptoms have been reported in 47-67% of patients and include headaches, fainting, palpitations, blurred vision, sweating and hypertension. In this study, we present an 11-year-old boy with classic micturition symptoms secondary to a bladder pheochromocytoma, and validated the use of the octreoscan in detecting extraadrenal locations for this tumor.

### Case Report

An 11-year-old Hispanic boy with a medical history of bronchial asthma and severe headaches for the past sixteen months was evaluated in our clinic. The headaches worsened two weeks prior to admission and were associated to dizziness and paleness. The patient indicated that the headache episodes occurred or were elicited during or shortly after voiding.

Because of the symptoms, he had required two hospitalizations. A full neurologic work up, including brain magnetic resonance imaging (MRI) and electroencephalogram (EEG), was performed on this patient. He was diagnosed with absence seizures and migraine headaches and was started on Depakote and Inderal.

An evaluation conducted by his primary physician during a post-micturition episode of headache revealed that his heart rate and blood pressure were 110 bpm and 180/110 mmHg, respectively.

The plasma levels of total catecholamines, norepinephrine and free normetanephrine, (Table 1) and the urine catecholamines, particularly norepinephrine (Table 2) were elevated. Abdominal and pelvic ultrasound showed a hypoechoic oval mass at the anterior-inferior wall of the urinary bladder. A spiral abdominal and pelvic computerized tomography (CT) scan with contrast

**Table 1.** Plasma catecholamines

Test	Normal range	Observed
Total Plasma Catecholamines	0-642 pg/ml	<b>3621</b>
Plasma Norepinephrine	0-399 pg/ml	<b>3588</b>
Plasma Epinephrine	0-99 pg/ml	23
Plasma Dopamine	0-142 pg/ml	32
Plasma Metanephrine	< 0.50 nmol/L	<0.20
Free Plasma Normetanephrine	< 0.50/nmol/L	<b>4.18</b>
Free Calcitonin	0-11.5 pg/ml	8.5
Intact PTH	250-630 pg/ml	37

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**Table 2.** Urine catecholamines

Test	Normal Range	Sample 1	Sample 2
	(24 hr).		
Total Urine Catecholamine Free	1-115 mcg/24 hr	<b>503</b>	<b>773</b>
Urine Epinephrine	0-20 mcg/24 hr	6	<10
Urine Norepinephrine	15-80 mcg/24 hr	<b>497</b>	<b>783</b>
Urine Dopamine	65-400 mcg/24 hr	271	363
Urine Vanillylmandelic Acid	2-10 pg/ml	2	
Urinary Homovanillic Acid	0-9.2 mg/24hr	4.7	

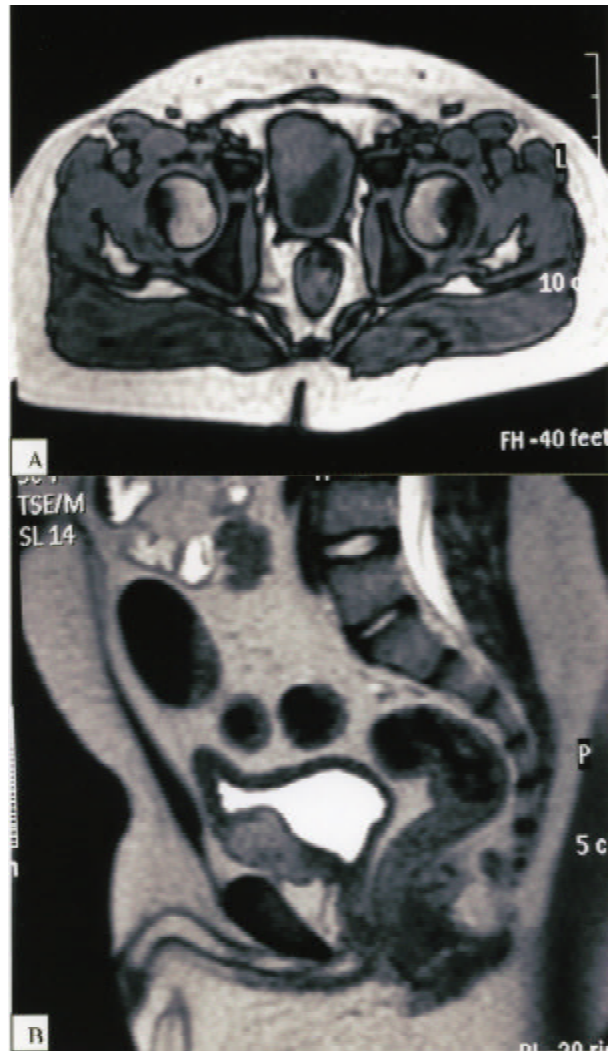
demonstrated a well circumscribed 3.5 x 2.5 x 2.5 cm oval shaped mass at the right anterior-inferior wall of the urinary bladder (Figure 1). Gadolinium enhanced MRI of abdomen and pelvis showed an isointense anterior bladder wall



**Figure 1.** Abdomino-pelvic CT scan with IV contrast. Note well circumscribed oval mass involving the right anteroinferior wall of the bladder.

lesion on T1 weighted images, that was slightly hyperintense on T2 weighted images (Figures 2 A and B). There was no evidence of metastatic lesions or extra-adrenal tumoral sites on either CAT scan or MRI. To evaluate for synchronous or metastatic lesions, a 111-In-pentetreotide scan (OctreoScan) was performed instead of a 131-metaiodobenzylguanadine (MIBG) scan, since the patient was allergic to iodine. The OctreoScan showed persistent focal activity at the urinary bladder after voiding with no evidence of metastatic disease (Figure 3).

The patient was hospitalized for pre-operative preparation and optimization. He received aggressive infusion of crystalloids, and blockade was done using doxazosin and diltiazem. After a week of preparation, the patient was taken to the operative room, where a diagnostic cystourethroscopy was performed, followed by a partial cystectomy. Tumor was removed completely with wide tumor-free margins of resection confirmed by frozen



**Figure 2.** A. MRI T1. Isointense mass at the right anteroinferior wall of the bladder. B. MRI T2. Hyperintense mass at the bladder

section. The bladder was closed in two layers without any compromise in bladder capacity. There was no need for inotropics at the operating room, but a low dose labetalol drip was infused as a preventive measure.

On microscopy, the tumor showed a Zellballen pattern with prominent vascular networks. The cells had abundant eosinophilic cytoplasm and indistinct cell membranes (Figure 4). Well formed membrane bound neurosecretory granules were evidenced on electron microscopy.

The patient was discharged home off antihypertensive medications. He was normotense and the post micturitional headache episodes disappeared. Follow up plasma and urine catecholamines were normal on follow up visits more than eighteen months after surgery.

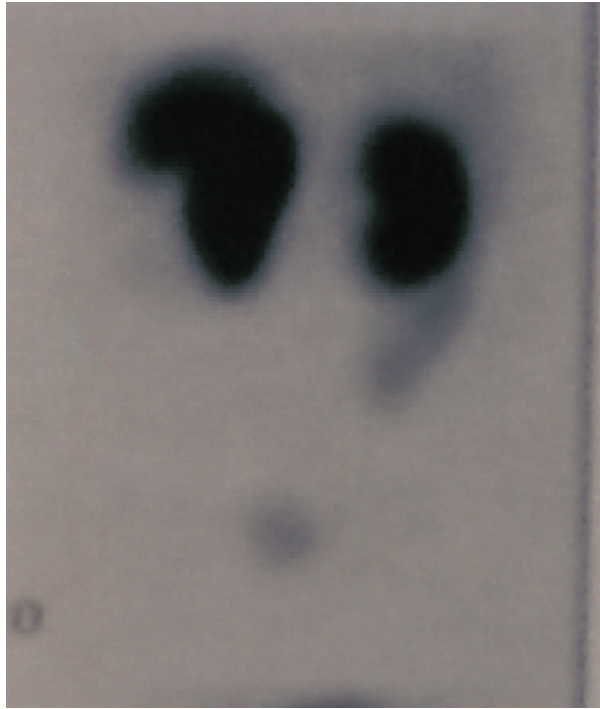
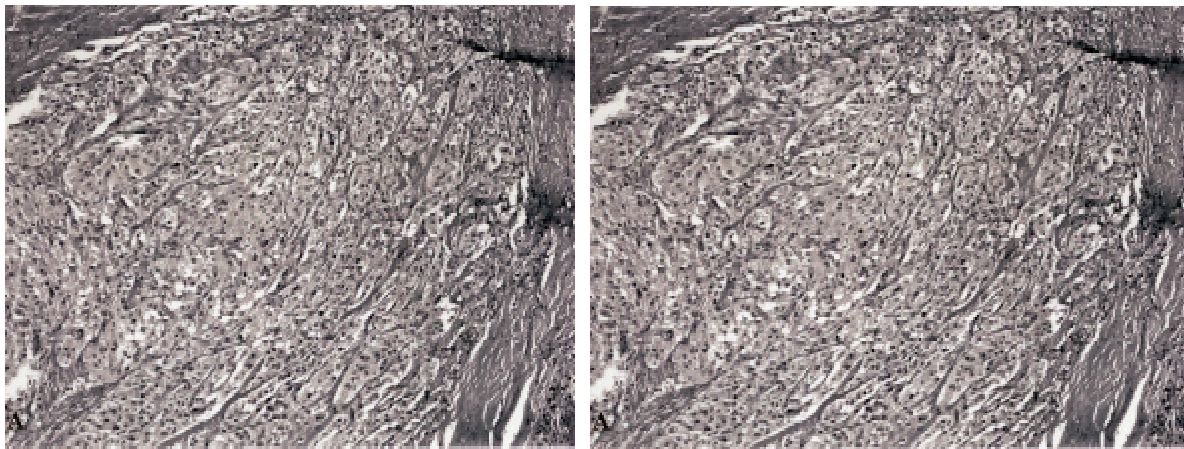


Figure 3. Octreoscan with SPECT. Persistent focal activity on the urinary bladder after voiding consistent with known urinary bladder pheochromocytoma. No evidence of metastatic disease.

adults. A slight female preponderance has been found (2). It has been estimated that 29-31% of these tumors occur at extra-adrenal sites. The malignancy rate for extrarenal pheochromocytomas is 29-40% compared to 10% for pheochromocytomas of adrenal gland origin. The most common location of extra-adrenal pheochromocytomas is the superior para-aortic area, followed by the organ of Zuckerkandl, and then the bladder in ten percent of the cases (2).

Bladder pheochromocytoma represents less than 0.1% of all bladder tumors (3). It has been reported on patients between 11 and 78 years of age, with a peak incidence between the third and fifth decade of life. Males and females are equally affected. On previous studies, the rate of malignancy of these tumors was 15%. Approximately 17% of bladder pheochromocytomas are non functional tumors (4,5).

The most common manifestation of bladder pheochromocytoma is painless hematuria in 55-65% of cases (3,4). Micturition symptoms have been reported in 47-67% of patients and include: headaches, fainting, palpitations, blurred vision, sweating and hypertension. It is important to point out that these symptoms can be elicited by bladder distention, abdominal palpation, defecation and sexual intercourse (1,6).



**Figure 4.** A. Note cells arranged in nests surrounded by a delicate vascular network. H & E 20X. B. The cells contain abundant eosinophilic cytoplasm and indistinct cell membranes. There is mild nuclear atypia. H & E 40X.

## Discussion

About ten percent of all pheochromocytomas arise at extra-adrenal sites (1). They tend to occur in the second or third decade of life. Children demonstrate higher incidence of extrarenal pheochromocytomas when compared to

The biochemical diagnosis of bladder pheochromocytoma depends on elevation of urinary or plasma catecholamines or its metabolites. On a recent review, the most sensitive test for the biochemical diagnosis of pheochromocytoma was plasma metanephrine level with a sensitivity of 99% and specificity

of 89% (7,8). One third of the cases that present isolated elevation of plasma or urine norepinephrine will end up being diagnosed as extra-adrenal pheochromocytoma. In contrast, when urine or plasma epinephrine levels represent more than 20% of the total catecholamine level, it is likely that the pheochromocytoma is of adrenal origin (2).

The radiologic study of choice for the localization of pheochromocytoma is the contrast enhanced CAT scan with a reported sensitivity of 90-100% for adrenal lesions and 90% sensitivity for extra-adrenal pheochromocytoma (2,7). MRI has also been recognized as an useful imaging modality for the diagnosis of pheochromocytoma, especially because of the hyperintense appearance of pheochromocytoma on T2 weighted images (1,9).

The 131-metaiodobenzylguanadine (MIBG) scan has been used to localize pheochromocytoma with a sensitivity that ranges from 77 to 90% and a specificity that fluctuates between 95 and 100% (7). Recently, 111-In pentreotide scan (OctreoScan) has been used to localize these lesions and has been described as being more sensitive for the detection of metastatic lesions (9-12). In this patient, OctreoScan was used due to the patient's history of allergy to iodine.

The treatment of choice for bladder pheochromocytoma is partial cystectomy. It is recommended that patients are prepared (7-14 days) for surgery with an alpha-blocker like phenoxybenzamine and a beta-blocker if tachycardia is present. Aggressive intravenous hydration with crystalloids is needed due to the severe peripheral vasoconstriction in these patients. Alpha-methyl-tyrosine has also been used as an additional therapeutic agent, since it blocks the catecholamine synthesis pathway (13). Several articles have reported the use of calcium channel blockers as the only antihypertensive medication for the preoperative preparation of patients with pheochromocytoma (14-15). Our patient was preoperatively prepared with doxazosin, a selective alpha-blocker, and diltiazem, a calcium channel blocker. Following tumor removal, a nuclear scan must be performed and the patient must be followed with periodic urinary and serum levels catecholamines.

## Conclusion

We presented the case of an 11-year-old boy with classic micturition symptoms secondary to a bladder pheochromocytoma. Laboratory work up showed elevated plasma and urine catecholamine levels and imaging studies demonstrated a bladder mass. An OctreoScan was performed instead of a MIBG scan to evaluate for metastatic or synchronous lesions, since the patient was

allergic to iodide. The boy was treated pre-operatively with alpha blockers, aggressive IV fluids, and calcium channel blockers. A partial cystectomy was performed as treatment for the bladder pheochromocytoma. The correlation of the OctreoScan results with other radiologic studies and final pathology validated its use. This offers a viable diagnostic option in the evaluation of extra-adrenal pheochromocytomas. At present, the patient is free of recurrent disease.

## Resumen

En este estudio se evaluó a un niño de 11 años que se presentó con síntomas de dolor de cabeza y mareos asociados con micción. En los estudios radiológicos, se encontró una masa en la vejiga. Los estudios bioquímicos sugirieron un feocromocitoma. Se utilizó el OctreoScan para descartar lesiones metastáticas o alguna localización extra-adrenal de feocromocitoma. El resultado de este estudio correlacionó adecuadamente con los otros estudios radiológicos, hallazgos operatorios y la patología final.

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