CASE REPORT

Incidental paraganglioma of the urinary bladder in a 66-year-old woman

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SUMMARY

A 66-year-old female patient was referred to urology department when a bladder mass was incidentally found on a transvaginal ultrasound scan. Cystoscopy revealed a small, smooth mass just above the trigone which appeared to be covered with normal urothelium. The histology from this growth after transurethral resection revealed a paraganglioma of the bladder. We will discuss the management of this case and literature review of this finding in this study.

BACKGROUND

Paragangliomas are rare tumours and are even more rarely found in the urinary bladder. We present a case of an incidental paraganglioma in the bladder.

CASE PRESENTATION

A 66-year-old woman was referred to our urology department in July 2011 for urgent investigation of an incidental bladder growth. This was imaged on a transvaginal ultrasound scan (USS) that was arranged by the patients' general practitioner to review her left ovary after she had presented with discomfort in her left iliac fossa. The USS did not reveal any abnormality in the left adnexa.

She had a medical history of hypertension which was well controlled with a diuretic, gastro-oesophageal reflux which was managed with omeprazole and irritable bowel syndrome for which she took mebeverine when required. She previously had a hysterectomy and right salpingo-oophorectomy for fibroids and a laparoscopic cholecystectomy for gallstone disease. She had hormone replacement therapy which she stopped 10 years previously. She was otherwise fit and healthy.

INVESTIGATIONS

The USS had reported a 7 mm round echo-bright area arising from the bladder base which appeared to be representing a soft tissue mass (figure 1). The patient denied any urinary symptoms or haematuria. She was normotensive with her medical treatment and her routine urine test was normal. Flexible cystoscopy confirmed a small, smooth lesion over the trigone. This appeared to be covered with normal mucosa.

Shortly after the cystoscopy a transurethral resection (TUR) was performed which measured the growth to be around 8 mm; the growth was resected deep to detrusor muscle with no clinical evidence of residual tumour (figures 2–4).

DIFFERENTIAL DIAGNOSIS

Pathology examination of the specimen showed a fairly well circumscribed but non-encapsulated tumour contained within the submucosa (figure 5). The tumour was composed of fairly large, polygonal chief cells with reddish brown cytoplasm, arranged in a nested (zellballen) pattern separated by numerous small blood vessels (figures 6 and 7). The overlying urothelium was normal but the tumour appeared to be involving at least one resection margin although there was no obvious vascular invasion.

On immunohistochemistry, the cells were strongly positive for neuroendocrine markers such as chromogranin A (figure 8), CD56 and synaptophysin, but labelling of sustentacular cells with S100 protein was inconclusive. Staining for cytokeratins AE1/AE3, CK7 and CK20 was negative, thereby excluding a carcinoid tumour. Staining was also negative for MART1/Melan A (melanoma marker cocktail), vimentin and renal cell carcinoma marker. The tumour was therefore confirmed by immunohistochemistry as a paraganglioma.

After discussion at our local Urology Multi-Disciplinary Team (MDT) meeting the patient underwent a CT scan of the chest, abdomen and pelvis to exclude further extra-adrenal paragangliomas and she was referred to the Regional Neuro-Endocrine Specialist MDT.

Her urine was tested repeatedly for catecholamines which was clear. 5-Hydroxyindoleacetic acid urine testing for carcinoid tumour was also negative. Metaiodo-benzylguanidine scan (MIBG) did not show any adrenal or extra-adrenal paragangliomas and there was no abnormal uptake in the

Figure 1 Transvaginal ultrasound scan, sagittal view of the bladder showing an echo-bright area arising from the base of the bladder wall.

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Figure 2 Cystoscopic image of bladder growth above the bladder trigone.

bladder. She also underwent an MRI of the pelvis which did not reveal any bladder wall abnormality.

It was confirmed that this patient had an isolated, non-secreting paraganglioma of the urinary bladder.

TREATMENT

She was referred back to our urology department for a second inspection of her bladder to ensure there is no residual tumour. Repeat cystoscopy revealed a normal-looking bladder with scar formation at the site of the previous resection. The scar tissue was resected and also a deep muscle biopsy was taken. The histology from this specimen was normal with no residual or recurrent tumour.

OUTCOME AND FOLLOW-UP

The decision of the Regional Neuro-Endocrine Specialist MDT was to continue her follow-up with further genetic testing and a

Figure 5 Low-power H&E photomicrograph of the tumour (right of picture) with the urothelial surface epithelium visible as a thin line at the left edge of the tissue.

repeat flexible cystoscopy by our department in a year to ensure there is no recurrence.

DISCUSSION

We present a rare case of an incidental, non-secreting paraganglioma in the bladder, measuring at 6×6×4 mm in the resected specimen. Paragangliomas in the urinary bladder are rare tumours and the first ever case was reported by Zimmerman in 1953.^{1–3} It accounts for less than 1% of all phaeochromocytomas, 6–10% of extra-adrenal phaeochromocytomas and less than 0.06% of all bladder tumours.^{1 2 4} Only around 200 cases of urinary bladder paragangliomas have been reported worldwide.^{2 4} They have a tendency towards multicentricity and can be found in unusual locations.⁵

The paraganglia are dispersed collections of specialised neural crest cells associated with autonomic ganglia throughout the body, and comprise of the adrenal medulla, chemoreceptors (the carotid and aortic bodies), the vagal body and cell groups associated with ganglia in the thorax, abdomen and retroperitoneum, as well as other parts of the body including the bladder.⁶

Figure 3 Cystoscopic image of the bladder growth covered with normal-looking urothelium.

Figure 4 Transurethral resection of bladder growth.

Figure 6 Medium-power H&E image of tumour, showing a nested (zellballen) growth pattern of cells with abundant, reddish-brown, granular cytoplasm and fairly regular, vesicular nuclei.

Paragangliomas (or 'extra-adrenal pheochromocytomas') therefore can arise anywhere from the neck to the pelvis.^{1 5 7} They are normally classified as functioning or non-functioning depending on whether they secrete catecholamines.^{2 5} Some paragangliomas behave in a malignant fashion, and in the bladder about 20% do so.³ However, there are no reliable histological indicators of malignancy. No related family history of paragangliomas was found in our patient's case and extensive imaging and investigations ensured a solitary lesion in this patient that was completely excised.

Functioning paragangliomas can present with palpitations, headaches, sweating, dizziness and hypertension.^{1 2 4} When found in the bladder they can present with suprapubic pain, dysuria with or without haematuria and attacks of hypertension during micturition or cystoscopy.^{1 2 4 7} This is thought to happen secondary to detrusor muscle contraction causing release of catecholamines in the circulation.⁴ As mentioned earlier, the patient did not present with any of the above symptoms.

Paragangliomas of the bladder are found to be more common in female patients (3:1 female/male ratio), especially in 20–40 year age group.^{1–3} They are treated either with partial cystectomy or with TUR depending on the extent, size and position

Figure 7 Medium-power H&E image of tumour at right of image, with urothelium at left edge for comparison, separated by vascular stroma.

Figure 8 Equivalent section to figure 5, immunostained with anti-chromogranin A. Similar, strong, brown staining was seen with anti-CD56 and anti-synaptophysin.

of the tumour.^{2 4} For patients with functioning paraganglioma it is important to stabilise hypertension with α -blockers pre-operatively and should be closely monitored for intraoperative hypertensive crisis.¹ In this case, α -blockers were not considered as the patient was not symptomatic and also the growth was initially thought to be a benign fibroma. The tumour was found to be close to the trigone of the bladder which is a very rare location and was easily resected with no intraoperative or post-operative complications. Owing to its position, partial cystectomy would not be possible.

Definitive diagnosis is made by a combination of immunohistochemistry, urine catecholamines and MIBG scintigraphy.² Our patient had a non-functioning paraganglioma that has been completely resected, therefore urine catecholamines and MIBG scintigraphy were negative. The diagnosis was set by histological examination of the specimen and special staining.

Learning points

- Paraganglioma of the urinary bladder is a rare bladder tumour but should be considered in our differential diagnosis prior to resection.
- If a paraganglioma of the bladder is suspected in a symptomatic patient, close monitoring and α -blockers should be considered prior to any instrumentation of the bladder. This is to avoid any intraoperative hypertensive crisis.
- This case highlights the significance and need of a multidisciplinary approach for the diagnosis and management of this case due to its rarity.

Competing interests None.

Patient consent Obtained.

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