

# Clinical Manifestations of SDH Associated Bladder Paragangliomas

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## Introduction

Succinate dehydrogenase B (*SDHB*) germline mutations are associated with predominantly extra-adrenal paragangliomas (PGLs) and high rates of metastatic disease. Bladder PGLs are a rare form of chromaffin cell tumours arising from the bladder wall.

## Objectives

We present a retrospective case series of five of eight subjects (62.5%) subjects with bladder PGLs found to have *SDHB* mutations identified between 1989-2013.

Figure 1. *SDHB*-related bladder PGLs – disease characteristics

Subject	Family History	Gender	Mutation			Amino acid	Age	Signs/Symptoms
			Mutations	Exon	Type			
1	Nil	M	c.292 T>C	4	Missense	p.Cys98Arg	47	Hypertension Palpitations Micturition attacks
2	Mother died (32 years) Carotid body tumour	M	c.590C>G	6	Missense	p.Pro197Arg	24	Headache Palpitations Diaphoresis Micturition attacks
3	Mother died (39 years) Metastatic PGL	M	c.406delA	4	Nonsense	p.Ile136X	29	Asymptomatic
4	Nil	M	c.590C>G	6	Missense	p.Pro197Arg	18	Hypertension Headaches Blurred vision Micturition attacks
5	Nil	F	c.118A>G	2	Missense	p.Lys40Glu	68	Hypertension Palpitation Diaphoresis

- Tumour extension through the lamina propria in 4/5 (80%) subjects.
- Distant metastatic disease developed in 2/5 (40%) subjects.
- A non-invasive 5.4 mm bladder PGL was identified and excised via the *SDHB* surveillance program (Table 1 and Figure 2).
- One subject died from metastatic disease 6 years after the initial diagnosis

Figure 2. MRI pelvis-diffusion-weighted image of a 5.4mm bladder PGL

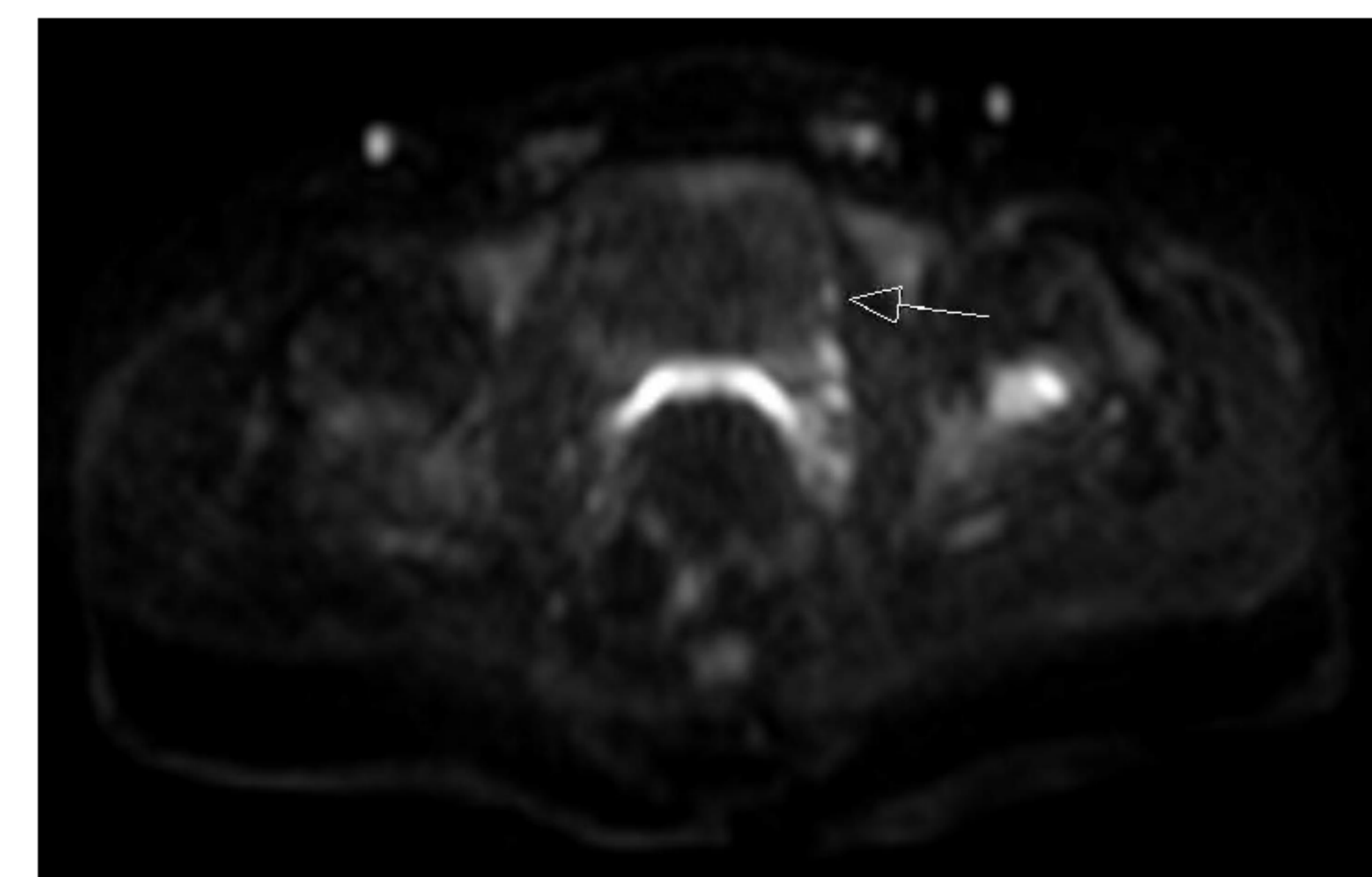


Table 1. Disease surveillance regimen for *SDHB* related chromaffin tumours at our institution

Genetic mutation	Catecholamines/ metanephrines	Imaging (preferably MRI)	
		Region	Frequency
<i>SDHB</i>	Annually	Abdomen Neck/thorax/pelvis	Annually 2 yearly

## Conclusion

Currently, disease surveillance regimens for detecting occult PGLs in asymptomatic carriers of *SDHB* mutations are in place but there remains debate about modality and frequency of surveillance.

This case series highlights:

- The bladder as a 'hot-spot' for *SDHB* associated paragangliomas
- The high rate of metastasis associated with *SDHB* associated bladder paragangliomas
- Micturition-related symptoms are common but may be associated with disease which is already locally invasive.
- Intensive surveillance regimens, with a focus on the bladder can allow early identification and treatment of potentially aggressive disease.

