**A Rare Case of Bilateral Pheochromocytoma Presenting with Unilateral Lumbar Pain: A Case Report**

**Title Page**

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**Key Clinical Message**

Bilateral pheochromocytomas can present with unilateral lumbar pain and without typical symptoms. This case demonstrates the consideration of pheochromocytomas in differential diagnosis, even in normotensive patients, to ensure timely intervention and avoid misdiagnosis.

**Introduction**

Pheochromocytoma is a neoplastic growth of the adrenal medulla that classically presents with recurrent paroxysmal episodes of headaches, palpitations, diaphoresis, pallor, and secondary hypertension. Less common clinical manifestations could include abdominal masses, while flank pain is only rarely found to be associated with the tumor [(1)](https://www.zotero.org/google-docs/?dz0Wkh). The majority of the tumors are unilateral, while the occurrence of bilateral tumors usually indicates an associated familial condition, e.g., multiple endocrine neoplasia (MEN type II) or Von-Hippel Lindau (VHL) syndrome [(2)](https://www.zotero.org/google-docs/?ZRWUxG). Still, sporadic cases of bilateral pheochromocytoma have also been reported in the literature. This case report is per CARE guidelines [(3)](https://www.zotero.org/google-docs/?PR5Vtb). Written informed consent was obtained from patient to publish this report in accordance with the journal’s patient consent policy. In this case report, we describe an incidental identification of bilateral pheochromocytoma within a young female who initially presented with unilateral flank pain.

**Case history/examination:**

This report describes the case of a woman in her early thirties who presented to the Urology department of Pakistan Kidney and Liver Institute, Lahore, with right lumbar pain. Her pain had been intermittently present for 10 months and was appreciated to be moderate-to-severe in intensity, dull in character, non-colicky, non-radiating, and self-resolving. She denied hematuria, while no concomitant symptoms indicate a urinary tract infection. Pain was not associated with any gastrointestinal symptoms. The lady also denied experiencing any episodic sweating, palpitations, or tremors, and there was no medical background of hypertension.

**Methods:**

The patient’s abdomen was scanned using contrast CT, which demonstrates the possibility of bilateral adrenal tumors with central necrosis **(Figure 1)**. The right and left tumors were found to be displacing the inferior vena cava (IVC) on the right and the splenic artery on the left. A subsequent adrenal Doppler scan was performed, which revealed an ill-defined, hypoechoic solid mass measuring 3.9 x 3.3 x 4.1 cm in dimensions within the right flank. Left adrenal Doppler demonstrated a similar mass measuring 5.1 x 3.3 x 4.8 cm in dimensions. Bilateral masses showed poor vascularity. CT angiogram did not showcase any evidence of focal hemorrhage, necrosis, or calcification. Afterward, the endocrinology team assessed the possibility of bilateral pheochromocytomas. Adrenal hormonal profiling was carried out, and it showed significantly elevated plasma metanephrine levels. The following results were reported: plasma metanephrine (>600 pmol/L), plasma normetanephrine (>800 pmol/L), post-dexamethasone suppression serum cortisol (5 µg/dL), serum aldosterone (15 pmol/L), and aldosterone/renin ratio (1.35). Urinary vanillylmandelic acid (VMA) levels were normal. The serum calcium profile was also reported to be normal.

To rule out the possibility of extra-adrenal neuroendocrine tumors, a DOTA scan was performed, which ruled out any lymph nodal, visceral, or osseous involvement. A multidisciplinary team meeting suggested bilateral adrenalectomy. The patient was subsequently started on oral doxazosin as a prophylactic measure for intraoperative hypertensive crisis. The lady was then admitted by the Urology team and underwent bilateral total robotic/open adrenalectomy. Due to some involvement of IVC, the right robotic surgery was subsequently transformed into open adrenalectomy. No hypertensive episodes were noted intraoperatively.

Post-surgical immunohistochemical analysis showed positive results for synaptophysin and S100, two major neuroendocrine markers of pheochromocytoma. No lymphovascular or capsular invasion or peri-adrenal soft tissue involvement was confirmed on histopathological analysis. In the postoperative period, the patient was commenced on oral steroid replacement therapy with hydrocortisone.

**Discussion:**

Our report highlights the significance of safely recognizing the rare clinical manifestations that could be indicative of an underlying sinister condition. It is quite uncommon to consider pheochromocytoma as a differential diagnosis in the absence of the classical signs induced by a surge in plasma catecholamine levels. However, abdominal flank pain can be remotely indicative of an underlying adrenal lesion [(4,5)](https://www.zotero.org/google-docs/?LzFXbC). In one small case series of nine histopathologically-proven pheochromocytoma cases, all individuals were normotensive at the time of diagnosis and primarily presented with abdominal pain. Furthermore, one patient was also found to have a normal urinary metanephrine profile [(6)](https://www.zotero.org/google-docs/?ae91le).

Classically, up to one-tenth of pheochromocytomas can be bilateral [(2)](https://www.zotero.org/google-docs/?1vI2Sx). Furthermore, pheochromocytomas can constitute up to 5% of bilateral adrenal incidentalomas [(7)](https://www.zotero.org/google-docs/?CF04i1). Although quite rare, pheochromocytomas can arise bilaterally without any association with germline mutations. Our case report excluded any biochemical or radiological evidence of non-adrenal endocrine lesions, but a genetic analysis of the patient could not be performed. In one broad study incorporating a total of 112 patients, either synchronous or metachronous tumors were isolated in up to fourteen (12.5%) individuals, out of whom 11 cases had an underlying mutation for VHL or MEN type II [(8)](https://www.zotero.org/google-docs/?zE1VLB). In a broad study that included 625 participants, the overall incidence of RET mutation was reported to be up to 54%, whereas VHL gene mutation was found in approximately 35% of cases [(9)](https://www.zotero.org/google-docs/?sovKQk). It is also noteworthy that type 1 neurofibromatosis and Sturge-Weber syndrome may also predispose patients to a significantly higher risk of bilateral adrenal medullary tumors [(2)](https://www.zotero.org/google-docs/?Q13tZ8). Hence, where genetic studies are not feasible, it may be advisable to arrange long-term follow-up to allow surveillance for second primary neoplasms.

In addition to lacking a prior background of paroxysmal hypertension, our patient did not suffer from any intraoperative or postoperative hypertensive crises. Regardless, the patient was commenced on alpha-1 antagonists preoperatively. Normally, perioperative hypertensive crises can be encountered among up to 20% of patients undergoing pheochromocytoma resection; this may potentiate the overall incidence of intraoperative bleeding as well as postsurgical hemodynamic instability [(10)](https://www.zotero.org/google-docs/?8U1LIQ). Hence, perioperative administration of antihypertensives is a recommended action, even for normotensive pheochromocytomas [(6)](https://www.zotero.org/google-docs/?oZ5KnE).

Our patient did not undergo cortical-sparing surgery (CSS) and had to be commenced on life-long steroid replacement therapy. Bilateral total adrenalectomy often predisposes to a subsequent risk of Addisonian crisis or iatrogenic Cushing’s syndrome [(9)](https://www.zotero.org/google-docs/?8rPS9O). Although variable reports exist, CSS can avert long-term adrenal insufficiency in approximately 23-55% of the cases [(8,9,11)](https://www.zotero.org/google-docs/?vfT1ga). This helps lower the odds of an Addisonian crisis by approximately three times [(12)](https://www.zotero.org/google-docs/?f72W9N). Interestingly, CSS also carries a risk of tumor recurrence in the adrenal remnant, albeit low (7-13%) [(9,13)](https://www.zotero.org/google-docs/?kYGLNr). This is significantly higher in contrast to total adrenalectomy, where the latter merely carries a minimal risk (~ 3%) of localized tumor recurrence in the adrenal bed [(12,13)](https://www.zotero.org/google-docs/?Pmpq7m). Preoperatively, it is essential to carefully balance the risk of tumor recurrence against the potential complications arising from adrenal insufficiency [(14)](https://www.zotero.org/google-docs/?Sr3EsC). Current recommendations favor cortical-sparing surgery (CSS) as the optimal surgical approach, accompanied by vigilant postoperative surveillance for tumor recurrence [(11)](https://www.zotero.org/google-docs/?GMQXvx).

**Conclusion:**

This case emphasizes the importance of considering sporadic pheochromocytoma as a differential diagnosis even in the absence of typical symptoms, so as to avoid misdiagnosis and to timely initiate targeted case management.

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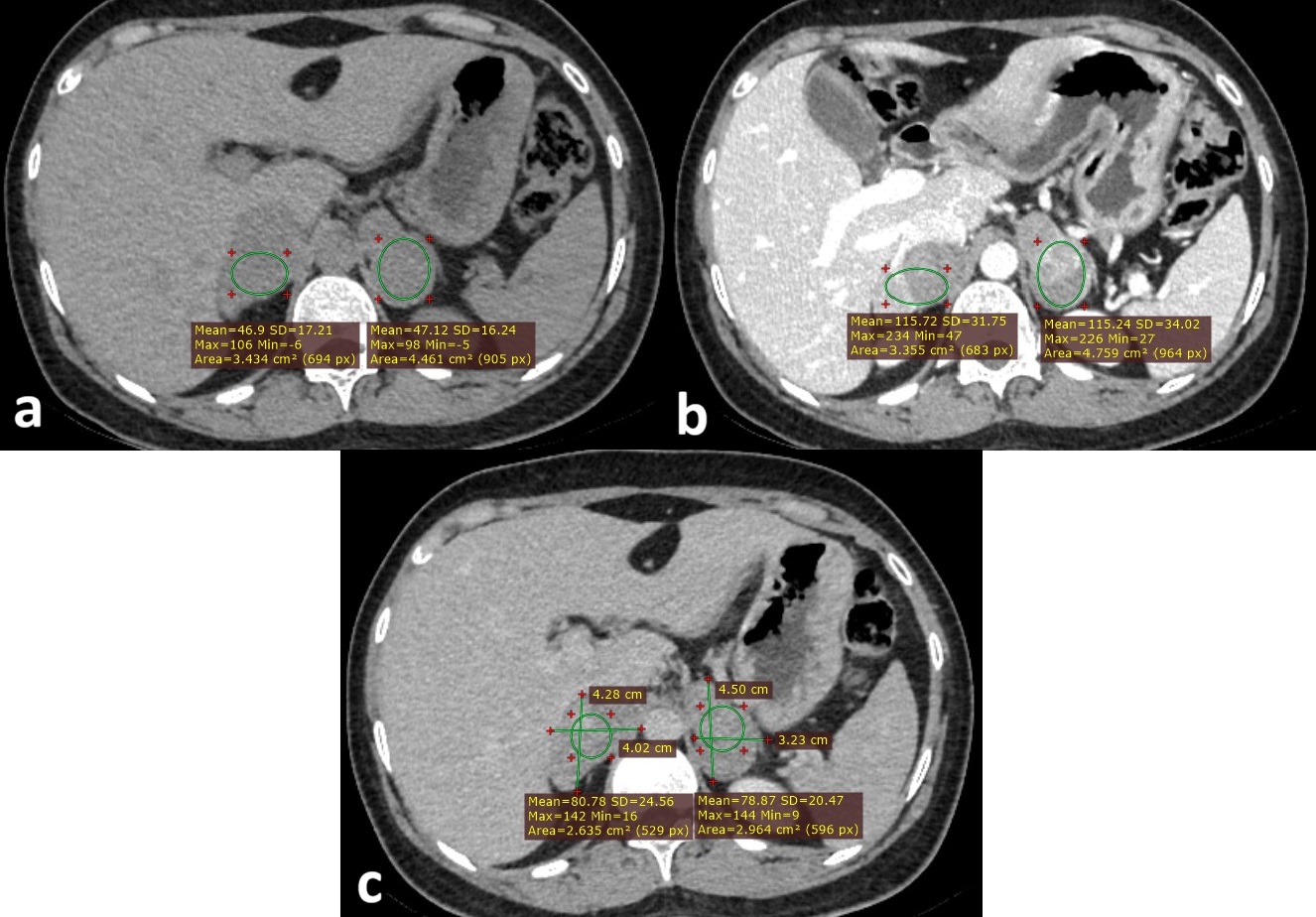


Figure 1: CT demonstrating bilateral pheochromocytomas a) Pre-contrast b) 70 seconds post-contrast c) 15 minutes delayed