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Intraoperative hypertensive crisis due to undiagnosed phaeochromocytoma during spinal surgery – a case report

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Competing interests

The authors declare no competing interests.

Keywords

Intraoperative Hypertension – Phaeochromocytoma – Metastasis – Endocrine Activity – Catecholamines

Summary

Phaeochromocytomas and paragangliomas are catecholamine-producing neuroendocrine tumours arising from chromaffin cells of the adrenal medulla or extraadrenal paraganglia. The phaeochromocytoma belongs to the rare tumours and as such occurs in less than 0.1 % of the general population. Atypical presentation or lack of clinical signs can lead to some pheochromocytomas being misdiagnosed as other abdominal tumours or being accidentally discovered. Due to the potential for life-threatening surgical and anaesthesiological complications in patients with phaeochromocytoma not treated preoperatively with alpha-blockers, this tumour type should be included in the differential diagnosis of abdominal tumours of unknown origin.

The authors present a rare case of intraoperative hypertension in a 37-year-old male patient during emergency spine stabilisation surgery. Spine stabilisation had to be done because of a sudden onset of paraplegia due to a pathological spine fracture caused by spinal metastases of an unknown tumour. After excluding more common causes of hypertension such as pain, inadequate depth of anaesthesia, a dislocation of the IV lines and even malignant hyperthermia, we came to conclusion that, considering the preoperative CT and MRT-scans, the presumed liver tumour was in fact a gigantic phaeochromocytoma and that the metastases are active. The diagnosis of phaeochromocytoma was confirmed with urinary catecholamine panel and MRI on the first postoperative day.

Due to unspecific clinical presentation and large amount of "silent" phaeochromocytomas, the main problem is to anticipate it in the first place. Once the phaeochromocytoma has been anticipated, intraoperative management should then follow the same principles that apply to elective cases. A step-by-step approach and eliminating more common conditions, may leave us with a "zebra" – a common presentation of an uncommon disease.

Introduction

Phaeochromocytomas and paragangliomas are catecholamine-producing neuroendocrine tumours arising from chromaffin cells of the adrenal medulla or extraadrenal paraganglia [1]. The phaeochromocytoma belongs to the rare tumours and occurs in less than 0.1 % of the general population. Its annual European incidence rate amounts to 0.2 cases per 100,000 people [2,3]. About 10 % of all phaeochromocytomas and 34 % of the paragangliomas have already metastasised at initial presentation [4]. The traditional "rule of 10s" states that 10 % of phaeochromocytomas are extraadrenal, 10 % are malignant, 10 % are bilateral, 10 % are found in normotensive patients, and 10 % are familial, appears to be outdated, as there are much more malignant (29 %), extraadrenal (24 %) and/or familial (32 %) cases reported [3,5].

Typical symptoms of phaeochromocytoma include hypertension and hypertensive crisis, headache, palpitations and anxiety. They are caused by the release of catecholamine and are triggered by stress and therefore often occur episodically. Surgery can also trigger life-threatening complications, such as hypertensive crisis and haemodynamic instability [6]. Atypical presentation or lack of clinical signs can lead to some phaeochromocytomas being misdiagnosed as other abdominal tumours [7,8,9] or accidentally being discovered using imaging methods which had been performed for other reasons [10]. Due to potential life-threatening surgical and anaesthesiological complications in patients with phaeochromocytoma who had not been treated with alpha-blockers preoperatively, this tumour type should be included in the differential diagnosis of abdominal tumours of unknown origin [7].

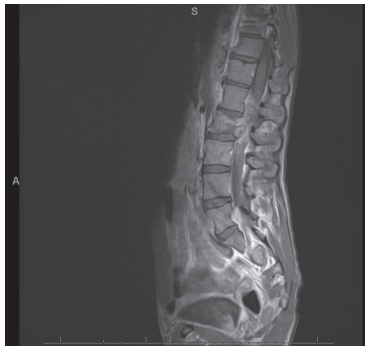
We report the case of a patient with a hypertensive crisis during emergency spine stabilisation which ultimately led to a diagnosis of phaeochromocytoma.

Case Presentation

A 37-year-old male patient was admitted due to a sudden onset of an incomplete paraplegia. The paraplegia was preceded by several weeks of back pain treated with diclofenac and tramadol, the latter having been prescribed by a general physician. Other than that, the patient reported of an unintentional weight loss over the previous year. The initial CT scan revealed a pathological fracture of the second lumbar vertrebra (L2), multiple osteolytic spinal metastases of a previously unknown tumour and a large, presumably tumorous, inhomogeneous retroperitoneal mass directly below the liver, measuring 14 x 14 x 17cm. A subsequent MRI scan revealed the osteolytic metastasis of the second lumbar vertebra (L2) that reached into the spine, into the paravertebral soft tissue, and cranial und caudal from the first to third lumbar vertebra (L3), causing compression of the myelon (Fig. 1). The retroperitoneal tumour was also better visualised in the MRI scan (Fig. 2) An emergency decompression surgery with dorsal stabilisation was indicated and the patient was brought into the operating theatre.

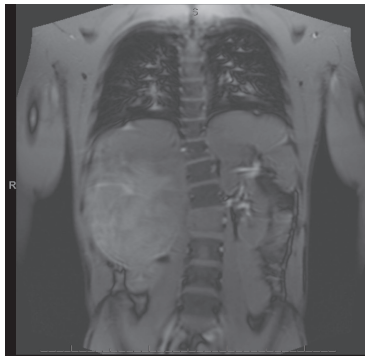
A physical exam prior to surgery revealed a BMI of 20.38 kg/m^2, a blood pressure of 131/77 mmHg, a heart rate of 70 bpm and SpO_2 of 98 %. After the induction of anaesthesia (using a previously inserted 18 gauge intravenous cannula), performed as RSI (using 20 µg sufentanil, 150 mg propofol and 50 mg rocuronium), the patient remained haemodynamically stable, and after the insertion of two 14 gauge intravenous cannulas, arterial line and nasogastric tube, could be brought in the prone position for the surgery, according to SOP. Positioning of the patient proceeded without any problems and the surgery began. For the maintenance of anaesthesia we used sevoflurane at 1.6–2.0 end-expiratory vol% and repetitive boli of sufentanil.

Fig. 1



Osteolytic metastasis of the second lumbar vertebra (L2).

Fig. 2



Retroperitoneal tumour.

105 minutes into the surgery, the patient became hypertensive, with an increase in systolic blood pressure up to 160 mmHg. Since there was no reaction to the administration of sufentanil (up to this point a total dose of 65 µg), a bolus of 150 µg clonidine was administered. After an initial decrease, the blood pressure started to increase again, despite a remifentanil infusion at a rate of 0.3 µg/kg/min, a sevoflurane rate of 2.0–2.2 end-expiratory vol% and an adequate relaxation of the patient. Despite administration of a total of 600 µg clonidine, fractioned over the next 30 minutes, the blood pressure remained increased up to 180 mmHg and a sinus tachycardia of up to 110 bpm occurred. The IV lines were checked for dislocation and functionality, there were no respiratory problems, the patient's temperature was within normal range, so was the level of end-expiratory CO_2. Arterial blood gas analysis (ABG) elicited no abnormalities except for a rise in lactate and subsequent acidosis with a pH of 7.29. An administration of 5 mg metoprolol failed to induce a decrease in both blood pressure and heart rate, and it was only after two 10 mg boli of urapidil that the blood pressure started to decrease. However, this effect was short-lived, the patient's blood pressure increased to 210/90 mmHg within the next 10 minutes. At that point, we started a continuous infusion of sodium nitroprusside at a rate of 0.5 µg/kg/min and titrated it up to 4 µg/kg/min.

We noticed that the patient's blood pressure increased every time the surgeons were operating into the metastasis and decreased in the subsequent minutes. Although it is a rare finding, we suspected that the metastasis could have originated from a neuroendocrine tumour and that the initially assumed liver tumour seen in CT- and MRI-scans could in fact be a gigantic phaeochromocytoma with active metastases.

Blood pressure began to stabilise after the administration of a total of 3 mg phentolamine (fractioned in 1 mg boli over the period of 15 minutes), but still increased whenever the surgeons started operating directly on metastatic tissue. The operation lasted 310 minutes and the sodium nitroprusside infusion was stopped after the operative manipulations on metastatic tissue had been terminated. The patient was extubated 30 minutes after the completion of the operation. Upon awakening, he had no pain, was able to move all of his limbs and was brought to an intensive care unit for further observation. On the way to the intensive care unit, the patient developed a tachycardia of up to 120 bpm and his blood pressure was at 170/82 mmHg. Orientational transthoracic echocardiography showed no abnormalities in heart contractions and a regular right and left ventricle. Intraoperative and postoperative ECG findings revealed that there were no abnormalities apart from a sinus tachycardia.

Six hours after ICU admission, the patient showed no neurological deficits and was haemodynamically stable under a continuous infusion of urapidil given at a rate of 20 mg/h. The consultant endocrinologist ordered the urinary catecholamines panel and it confirmed the diagnosis of a neuroendocrine tumour (Tab. 1).

After a fourteen-day course of phenoxybenzamine and propranolol, resection of the tumour was scheduled. The surgery team removed the right adrenal gland bearing a gigantic tumour measuring 23 x 16 x 9 cm in total and weighting 1675 g (Fig. 3). Anaesthesia for tumour removal surgery was uneventful and the patient could be transferred to a normal ward after 24 h observation on ICU. Subsequently, pathohistological diagnostics revealed a malignant phaeochromocytoma and the postoperative PET scan disclosed the existence of multiple active osteolytic metastases (Fig. 4).

Tab. 1
Catecholamine panel urine.

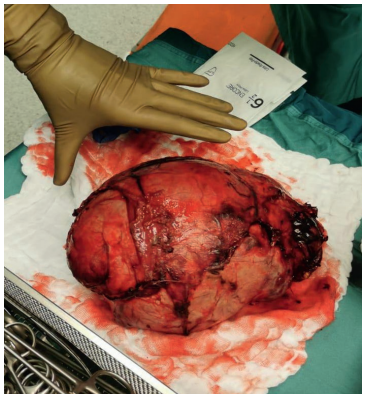
	Result	Reference
pH urine	5.0	<4.5
Adrenaline (U)	220.1 µg/l	
Adrenaline/d	990.5 µg/24 h	<20
Noradrenaline (U)	>1,000 µg/l	
Noradrenaline/d	>4,500 µg/24 h	<70
Dopamine (U)	>1,000 µg/l	
Dopamine/d	>4,500 µg/ml	200–600
Metanephrine (U)	14,094 µg/24 h	<350
Normetanephrine	>11,250 µg/24 h	<450

Discussion and conclusion

The differential diagnosis of a hypertensive crisis is broad. Since profound hypertension of any cause may result in acute cardiac, renal, and neurological injury, identifying the primary event is important and may be challenging. In our case, we started with excluding the common causes of intraoperative hypertension – inadequate analgesia or depth of anaesthesia, dislocation of IV. lines, then continued with further investigations to exclude malignant hyperthermia and, finally, considering the preoperative CT and MRI scans, came to the diagnosis that proved correct.

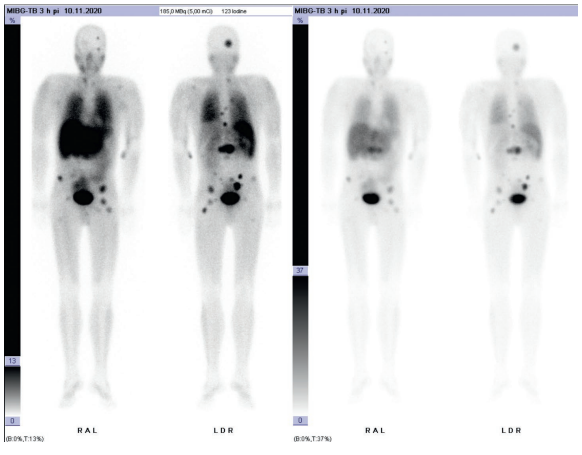
The guidelines for the perioperative management of patients with phaeochromocytoma are both well-established and evidence-based [3,11,12]. However,

Fig. 3



Right adrenal gland with a gigantic tumour (23 cm x 16 cm x 9 cm), weighing 1,675 g.

Fig. 4



PET scan: Multiple active osteolytic metastases.

due to unspecific clinical presentation and large amount of "silent" phaeochromocytomas, the main problem remains to suspect its existence in the first place. Once a phaeochromocytoma is suspected, intraoperative management should follow the same principles as in the elective cases.

Even though it is rare, phaeochromocytoma remains a frequently overlooked diagnosis. A series of autopsies showed that its fatal complications had preceded the diagnosis in about 50 % of cases [13]. Another series of autopsies of patients diagnosed postmortem with phaeochromocytoma showed that about 25 % died during or immediately after surgeries unrelated to phaeochromocytoma [14].

A review of 62 cases of phaeochromocytoma presenting during the initial surgery showed a perioperative mortality of 8 %, even though the other authors described it to be as high as 40 % [15]. Interestingly enough, phaeochromocytoma was suspected intraoperatively in just 26 % of those cases.

There are a number of case reports of previously undiagnosed phaeochromocytomas presenting during surgery [8, 9,16,17,18,19,20] and what they all demonstrate is the importance of staying alert and systematic in emergency situations. A step-by-step approach and the elimination of more common conditions may leave us with a "zebra" – a common presentation of an uncommon disease [21]. This case serves to emphasise the importance of being vigilant and prepared for such unexpected occurrences.

Literature

1. Lenders JW, Eisenhofer G, Mannelli M, et al: Phaeochromocytoma. Lancet 2005;366:665–675
2. Farrugia F, Martikos G, Tzanetis P, Charalampopoulos A, Misiakos E, Zavras N: Pheochromocytoma, diagnosis and treatment: Review of the literature. Endocr Regul 2017;51:168–181
3. Connor D, Boumphrey S: Perioperative care of pheochromocytoma. BJA Education 2016;5:153–158
4. De Filpo G, Maggi M, Mannelli M, et al: Management and outcome of metastatic pheochromocytomas/paragangliomas: an overview. J Endocrinol Invest 2021;44(1):15–25
5. Zelinka T, Musil Z, Dušková J, Burton D, Merino MJ, Milosevic D, et al: Metastatic pheochromocytoma: clinical, genetic, and histopathologic characteristics. Eur J Clin Invest 2011; 41(10):1121–1128
6. Pisarska M, Pedziwiatr M, Budzyński A: Perioperative hemodynamic instability in patients undergoing laparoscopic adrenalectomy for pheochromocytoma. Gland Surg 2016;5:506–511
7. Legocka ME, Toutounchi S, Pogorzelski R, Krajewska E, Celejewski K, Galazka Y: Undiagnosed pheochromocytoma presenting as a pancreatic tumor: A case report. Open Med 2020;15:103–106
8. Wu JS, Ahya SN, Reploeg MD, Singer GG, Brennan DC, Howard TK, Lowell JA: Pheochromocytoma presenting as a giant cystic tumor of the liver. Surgery 2000;128:482–484
9. Wang HL, Sun BZ, Xu ZJ, Lei WF, Wang XS: Undiagnosed giant cystic pheochromocytoma: A case report. Oncol Lett 2015;10(3):1444–1446
10. Baguet JP, Hammer L, Mazzuco TL, Chabre O, Mallion JM, Sturm N, Chaffanjon P: Circumstances of discovery of phaeochromocytoma: a retrospective study of 41 consecutive patients. Eur J Endocrinol 2004;150(5):681–686
11. Naranjo J, Dodd S, Martin YN: Perioperative management of pheochromocytoma. J Cardiothorac Vasc Anaesth 2017; 31(4):1427–1439
12. Ramakrishna H: Pheochromocytoma resection: Current concepts in anesthetic management. J Anaesthesiol Clin Pharmacol 2015;31(3):317–323
13. Lo CY, Lam KY, Wat MS, Lam KS: Adrenal pheochromocytoma remains a frequently overlooked diagnosis. American Journal of Surgery 2000;179(3):212–215
14. Sutton MG, Sheps SG, Lie JT: Prevalence of clinically unsuspected pheochromocytoma: Review of a 50-year autopsy series. Mayo Clin Proc 1981;56:354–360
15. Hariskov S, Schumann R: Intraoperative management of patients with incidental catecholamine producing tumors: A literature review and analysis. J Anaesthesiol Clin Pharmacol 2013;29:41–46
16. Wooster DL, Mitchell RI: Unsuspected phaeochromocytoma presenting during surgery," Can Anaesth Soc J 1981;5:471–474
17. Johnston PC, Silversides JA, Wallace H, Farling PA, Hutchinson A, Hunter SJ, Eatock F, Mullan KR: Phaeochromocytoma crisis: two cases of undiagnosed phaeochromocytoma presenting after elective nonrelated surgical procedures. Case Reports in Anesthesiology 2013; Article ID 514714
18. Myklejord DJ: Undiagnosed pheochromocytoma: the anesthesiologist nightmare. Clin Med Res 2004;2:59–62
19. Bensghir M, Elwali A, Lalaoui SJ, et al: Management of undiagnosed pheochromocytoma with acute appendicitis. World J Emerg Surg 2009;4:35
20. Dabbous A, Siddik-Sayyid S, Baraka A: Catastrophic hemodynamic changes in A patient with undiagnosed pheochromocytoma undergoing abdominal hysterectomy. Anesth Analg 2007;104:223–4
21. Smith CS, Paauw DS: When you hear hoof beats: four principles for separating zebras from horses. J Am Board Fam Pract 2000;13(6):424–429.

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