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PRIKAZ PRVE LAPAROSKOPSKE ADRENALEKTOMIJE ZBOG FEOHROMOCITOMA U PEDIJATRIJSKOJ POPULACIJI U REPUBLICI SRBIJI

Apstrakt: Feohromocitom je tumor porekla medule nadbubrežne žlezde koji se karakteriše povišenim lučenjem kateholamina. Incidenca javljanja feohromocitoma je od 3 do 8 slučajeva na milion stanovnika, od čega se oko 10 do 20% dijagnostikovanih feohromocitoma javlja u pedijatrijskoj populaciji, sa većom učestalošću kod dečaka u odnosu na devojčice. Kod 1,7% pedijatrijske populacije sa hipertenzijom uzrok hipertenzije je feohromocitom. Zbog glavobolja i verifikovane hipertenzije na dvadesetčetvoročasovnom holter monitoringu krvnog pritiska, pacijentkinji starosti 13 godina učinjen je ultrazvuk, a potom scintigrafija i magnetna rezonanca abdomena na kojima je opisana ovalna promena iznad desnog bubrega promera oko 4,5 cm suspektna na feohromocitom. Funkcionalnim ispitivanjem u uzorku dvadesetčetvoročasovnog urina dokazane su povišene vrednosti noradrenalina čak 45 puta veće od referentnih, kao i povišene vrednosti dopamina. Nakon adekvatne pripreme fenoksibenzaminom i bisoprololom u trajanju od dve nedelje, učinjena je desna laparoskopska adrenalektomija u Univerzitetskoj dečijoj klinici u Tiršovoj, što ujedno predstavlja i prvu operaciju ovog tipa u pedijatrijskoj populaciji. Intraoperativno, maksimalna vrednost tenzije bila je 180/120 mmHg. Patohistološkim nalazom potvrđen je feohromocitom. Iako je redak uzrok hipertenzije u pedijatrijskoj populaciji, mlade pacijente sa de novo otkrivenom hipertenzijom treba ispitati u pravcu mogućeg feohromocitoma. Laparoskopska adrenalektomija, kako kroz lateralni

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transabdominalni tako i kroz posteriorni retroperitoneoskopski pristup, predstavlja zlatni standard za lečenje feohromocitoma i u adultnoj i u pedijatrijskoj populaciji.

Abstract: Pheochromocytoma is a tumor that arises from adrenal medulla and it is characterized by increased secretion of catecholamines. The incidence of pheochromocytoma is 3 to 8 cases per million inhabitants, of which about 10 to 20% of diagnosed pheochromocytomas occurs in the pediatric population, with a higher frequency in boys. In 1.7% of the pediatric population with hypertension, the cause of hypertension is pheochromocytoma. Due to headaches and verified hypertension on twenty-four-hour holter blood pressure monitoring, the 13-year-old female patient underwent ultrasound, followed by scintigraphy and magnetic resonance imaging of the abdomen, which described an oval change above the right kidney about 4.5 cm in diameter suspected of pheochromocytoma. Twenty-four-hour urine cateholamines showed elevated noradrenaline values as much as 45 times higher than the reference range, as well as elevated dopamine values. After adequate preparation with phenoxybenzamine and bisoprolol for two weeks, a right laparoscopic adrenalectomy was performed at the University Children's Clinic in Tirsova, which is also the first operation of this type in the pediatric population. Intraoperatively, the maximum value of tension was 180/120 mmHg. Pathohistological findings confirmed pheochromocytoma. Although a rare cause of hypertension in the pediatric population, young patients with newly diagnosed hypertension should be examined for possible pheochromocytoma. Laparoscopic adrenalectomy through both the lateral transabdominal and posterior retroperitoneoscopic approach is the gold standard for the treatment of pheochromocytomas in both the adult and pediatric populations.

Uvod

Feohromocitom je redak neuroendokrini tumor porekla medule nadbubrežne žlezde koji se manifestuje povišenim lučenjem kateholamina (adrenalina, noradrenalina i/ili dopamina) (1, 2). Godišnja incidencija javljanja je 2–9 na 1.000.000 stanovnika (2). Klinički znaci i simptomi feohromocitoma obuhvataju stanja do kojih dovodi kateholaminski eksces, prvenstveno hipertenzija (80,7%), glavobolja (60,4%), palpitacije (59,3%), dijaforeza (52,4%), a u manjoj meri i umor, gubitak u kilaži, crvenilo kože, abdominalni bol i povišene vrednosti glikemije. Zbog nespecifičnosti simptomatologije, klinička dijagnoza je otežana s obzirom na širok spektar diferencijalne dijagnoze (ekstraadrenalni paragangliomi, anksiozna stanja, esencijalna hipertenzija, hipertireoza, karcinoidni sindrom i drugih), zbog čega se o feohromocitomu govori kao o „Velikom imitatoru".

Ukoliko se posumnja na feohromocitom dijagnoza se potvrđuje kombinacijom laboratorijskih analiza (određivanje kateholamina i metanefrina u 24h urinu) i vizuelizacione dijagnostike (ehosonografija, multislajsna kompjuterska tomografija (MSCT), magnetna rezonanca (MRI)), među kojom značajnu ulogu ima i scintigrafija sa I^{123}-MIBG kao radiofarmakom izbora, gde se kod feohromocitoma očekuje njegova pojačana akumulacija u regiji nadbubrega (2). 10–20% feohromocitoma se dijagnostikuje u dečijem uzrastu, a smatra se da se kod 1,7% dece sa hipertenzijom radi o feohromocitomu kao uzroku. Prosečan uzrast pacijenata sa dijagnozom feohromocitoma je 11–13 godina, uz predominaciju muškog pola, prema nekim autorima čak i u odnosu 2:1 (1, 2). Klinička slika i dijagnostički metod se ne razlikuju značajno od adultne populacije, sa posebnim osvrtom na genetski skrining i isključivanje sindromskih stanja u sklopu kojih se feohromocitom javlja (Von Hippel-Lindau (VHL) sindrom, Multipla endokrina neoplazija (MEN) 2A i 2B sindrom i neurofibromatoza tip 1 (NF1)) (1).

U ovom radu predstavljamo prvi slučaj elektivne laparoskopske operacije kod pacijenta sa klinički manifestnim feohromocitomom u dečijem uzrastu u Univerzitetskoj dečijoj klinici Tiršova.

Prikaz slučaja

Pacijentkinja uzrasta 12 + 10/12 godina, TV – 166 cm, TM – 55,8 kg hospitalizovana je radi ispitivanja eritematoznog raša na obrazima i povremenih glavobolja. Unazad 2 godine je na terapiji Sioforom zbog povišenih vrednosti glikemije našte. U toku hospitalizacije uočeno je da je glavobolja praćena skokom tenzije, zbog čega je indikovan holter monitoring krvnog pritiska. Na dvadesetčetvoročasovnom holter monitoringu 96% izmerenih tenzija u budnom stanju više od 135/85 mmHg. Potom je učinjen ultrazvuk abdomena, na kome je uočena ovalna promena promera 4,5x4,8 cm na gornjem polu desnog bubrega, zbog čega je učinjena i magnetna rezonanca (MRI). Na MRI (Slika 1) opisana je hiperintezna promena promera 4,5 cm na gornjem polu desnog bubrega. Zbog kliničkih znakova, kao i vizuelizovane promene na nadbubregu učinjena je scintigrafija celog tela, a zatim je određen i hormonski status nadbubrežnih žlezda. Na scintigrafiji je prikazano pojačano nakupljanje radiofarmaka u predelu desnog nadbubrega (Slika 2). Kortizol i ACTH su bili u referentnim vrednostima. U 24-časovnom urinu uočene su povišene vrednosti noradrenalina u 2 merenja i dopamina u jednom uzorku (Tabela 1). Na osnovu navedenih analiza postavljena je dijagnoza feohromocitoma, zbog čega je indikovano operativno lečenje uz adekvatnu preoperativnu pripremu fenoksibenzaminom i bisoprololom. Nakon dvonedeljne pripreme fenoksibenzaminom sprovedeno je operativno lečenje u Univerzitetskoj dečijoj klinici u Tiršovoj. Sprovedena je desna laparoskopska adrenalektomija lateralnim transperitonealnim pristupom. Intraoperativno, maksimalna vrednost tenzije bila je

180/120 mmHg. Za intraoperativnu kontrolu tenzije korišćen je natrijum-nitroprusid. Postoperativni tok je prošao uredno, četvrtog postoperativnog dana pacijentkinja je otpuštena iz bolnice. Patohistološkim nalazom potvrđen je feohromocitom. Tenzija na kontroli mesec dana nakon operativnog lečenja iznosila je 105/60 mmHg. Uzete su analize za genetsko ispitivanje – u radu.

Diskusija

Prve uspešne operacije kod pacijenata sa feohromocitomom izveli su Ru (Cesar Roux, 1857–1934), u Švajcarskoj, i Čarls Mejo (Charles Horace Mayo, 1865–1939), u SAD, 1926. godine (3). Laparoskopska adrenalektomija (LA) je godinama unazad zlatni standard u operativnom lečenju feohromocitoma još od 1992. godine, kada je objavljen rad Mišela Ganjea (Michael Gagner), u kome su prezentovane prve tri uspešne laparoskopske adrenalektomije, korišćenjem laparoskopskog lateralnog transperitonealnog pristupa (LTA – lateral transperitoneal approach) (4). Pored navedenog, laparoskopska adrenalektomija može se izvesti i kroz prednji transperitonealni i retroperitonealni pristup (5).

U Centru za endokrinu hirurgiju Kliničkog centra Srbije LTA se koristi kao rutinska procedura od 2012. godine. Laparoskopska adrenalektomija je posebno indikovana za funkcionalne tumore manjih dimenzija, kao i afunkcionalne tumore, za koje je sa velikim stepenom sigurnosti isključena maligna alteracija (5, 6). LTA nije bez nedostataka. Apsolutne kontraindikacije predstavljaju tumor dimenzija iznad 15 cm, lokalna invazija tumora, suspektni adrenokortikalni karcinom (ACC) i metastatski feohromocitom, dok među relativne kontraindikacije spadaju povišen kardiopulmonalni rizik i perzistentna koagulopatija (7–9). Intraoperativno održavanje hemodinamske stabilnosti u toku operativnog lečenja feohromocitoma predstavlja poseban izazov, te je poređenje hemodinamske stabilnosti tokom laparoskopske i otvorene hirurgije predmet brojnih istraživanja, sa rezultatima koji ukazuju na nepostojanje statistički značajne razlike u incidenciji i stepenu hemodinamske nestabilnosti, dužine operacije i gubitka krvi za ova dva pristupa (9–14). Kim i saradnici (15) su došli do zaključka da je procenat pacijenata sa intraoperativnom hipertenzivnom krizom manji kod LTA u odnosu na otvoreni pristup (0,6 ± 0,5% tokom LTA i 1,67 ± 1,1% tokom otvorenog pristupa, p = 0,0146). Ova studija je takođe pokazala da je postoperativno započinjanje oralnog unosa brže kod pacijenata koji su operisani laparoskopski (1,1 ± 0,3 dana) u odnosu na otvoren pristup (2,6 ± 1,3 dana, p = 0,0037). Takođe, postoji statistički značajna razlika u dužini postoperativnog boravka (LTA 5,6 ± 2 dana, u odnosu na otvoreni pristup 12,4 ± 3,5 dana, p=0,0001). Uz to, manja je upotreba analgetika nakon laparoskopske u odnosu na otvorenu operaciju. Mikoli i sar. ukazuju na značajno smanjenje dužine postoperativne hospitalizacije kod laparoskopski operisanih pacijenata (4,1 ± 2,3 dana) u odnosu na otvoreni pristup (7,2 ± 2,6 dana, p < 0,02) (16).

Slične podatke objavljuju i Zeh i saradnici, koji ističu visoko statistički značajno skraćenje dužine hospitalizacije kod laparoskopski operisanih pacijenata (6 dana) u odnosu na otvoren pristup (15 dana) – u radu navedeno sa 5 na 1 dan? (17) Mikoli i sar. ukazuju na nešto duže trajanje laparoskopskih intervencija (182 ± 115 minuta) nego otvorenog pristupa (142 ± 29 minuta, $p < 0,02$) (16). Čeh i sar. navode da dužina trajanja laparoskopske operacije ne zavisi od toga da li je pacijent prethodno imao simptome – 182 minuta (90–305 min), ili je tumor otkriven slučajno – 193 minuta (130–340 min) (18). Prosečan gubitak krvi tokom laparoskopskih operacija varira od 342mL – Mikoli i sar. (16), do 130mL – Jeneček i sar. (19). Slične rezultate su našle i ostale studije koje su se bavile upoređivanjem laparoskopske i otvorene hirurgije.

Rezultati dobijeni iz našeg prezentovanog slučaja odgovaraju rezultatima istraživanja drugih autora u pogledu da je kod pacijenta oralni unos hrane i tečnosti započet drugog postoperativnog dana, a da je adekvatna kontrola bola postignuta uz minimalnu dozu analgetika, i da je pacijent otpušten trećeg postoperativnog dana. Međutim, kada se posmatra volumen izgubljene krvi, procenat prevođenja u otvoreni pristup, postoperativni boravak i postoperativni nivo hemoglobina, kao i javljanje perioperativnih komplikacija, veličine tumora i ASA skor, ne postoje značajne razlike između feohromocitoma i drugih adrenalnih tumora koji su operisani laparoskopskim pristupom (20–22).

Glavni intraoperativni izazov u toku operacije feohromocitoma je, nezavisno od hirurškog pristupa (LTA ili otvoreni), identifikovanje adrenalne vene. Kod otvorenog pristupa presecanje vene je izvodljivo nakon intraoperativne mobilizacije tumora, što se u ranijim istraživanjima pokazalo zaslužnim za nastanak hipertenzivne krize (23). Upravo sa tom idejom su Fernandez-Kruz i saradnici (24) pre 20 godina ukazali da laparoskopski pristup feohromocitomu smanjuje intraoperativno oslobađanje kateholamina u statistički značajno manjoj meri u odnosu na otvoreni pristup, što, sledstveno, umanjuje rizik za razvoj hipertenzivne krize, time što se tokom operacije minimalno manipuliše tumorom, što su istakla i druga istraživanja koja su se ovom tematikom bavila (10, 25). Iako, po pravilu, laparoskopski pristup poboljšava vizualizaciju adrenalne vene, iz našeg iskustva ovo zna biti veoma otežano zbog okolnog masnog tkiva. Laparoskopsku adrenalektomiju klinički verifikovanog feohromocitoma trebalo bi da izvode iskusni endokrini hirurzi, s obzirom na to da se, prema literaturi, konverzija u otvorenu hirurgiju javlja u približno 2% slučaja, a konverziju može uraditi samo hirurg koji je iskusan i u otvorenoj adrenalektomiji (7). Glavni razlozi za konverziju su, najpre, nekontrolisano krvarenje, adhezije, gojaznost, ali i povreda okolnih organa, hernije, uvećana jetra ili nedostatak iskustva hirurga (7–9, 26, 27). Šen i saradnici su pokazali da gojaznost (BMI preko 24 kg/m2) i veličina tumora (≥5 cm) kod feohromocitoma predstavljaju prediktivni faktor za konverziju (26).

Slučaj koji prezentujemo prema nalazima ove studije bio je u visokom riziku za konverziju, a jedan od razloga što do toga nije došlo jeste što je u Centru za endokrinu

hirurgiju pre prezentovanog slučaja izvedeno preko 100 LTA, kako za feohromocitom tako i za druge funkcionalne i afunkcionalne adrenalne tumore. Iz našeg iskustva, baš kao i iz podataka iz navedene literature, LTA je povezana sa ređim komplikacijama u odnosu na otvoreni pristup (npr. respiratorne i infekcije rane, manja incidencija povrede organa) (26–28). Iz svega priloženog se može sa sigurnošću istaći da je laparoskopska adrenalektomija kod operacije feohromocitoma sigurna i efikasna hirurška procedura, za čiji su dobar ishod neophodne tačna i precizna vizuelizaciona dijagnostika, kao i preoperativno i intraoperativno postupanje iskusnog hirurga, a uz dobru koordinaciju sa anesteziološkim timom.

Zaključak

U prethodnim decenijama korišćenje minimalno invazivnih tehnika radikalno je promenilo hirurški pristup nadbubrežnoj žlezdi. Objavljivani radovi i naučna literatura ukazuju na prednosti laparoskopskih zahvata, u odnosu na otvoreni hirurški pristup u pogledu bezbednosti, efikasnosti i komplikacija, te predstavlja zlatni standard u lečenju svih tumora nadbubrežne žlezde. Uz preoperativnu pripremu fenoksibenzaminom i bisoprololom u trajanju od dve nedelje, praćene adekvatnom hidracijom, laparoskopska operacija feohromocitoma je sigurna i efikasna u lečenju feohromocitoma kako u adultnom tako i u pedijatrijskom uzrastu.

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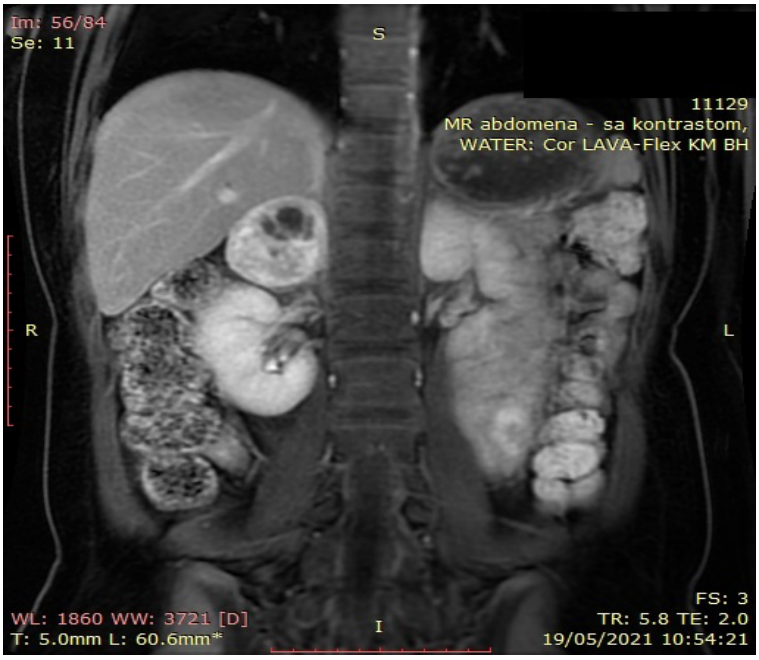
Slika 1. MRI prikaz hiperintenzne promene na gornjem polu desnog bubrega



Slika 2. Scintigrafski prikaz pojačanog nakupljanja radiofarmaka u desnom nadbubregu

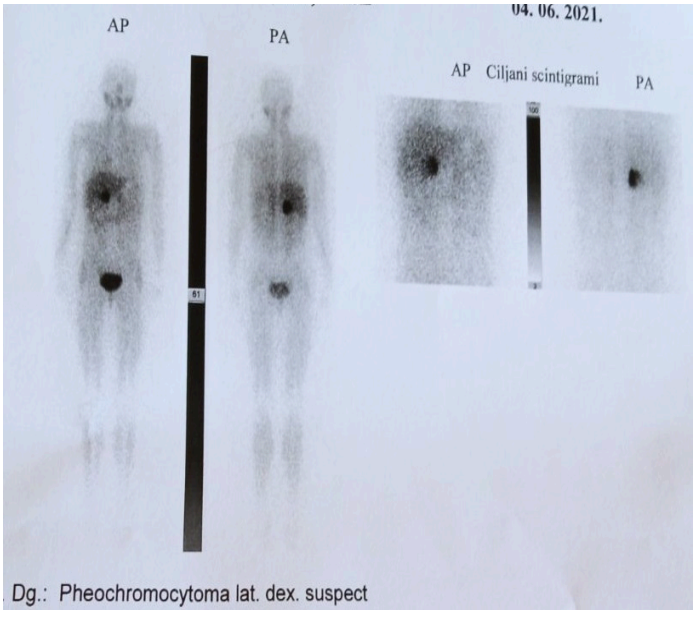


Tabela 1. Vrednosti kateholamina u 24-časovnom uzorku urina

	I uzorak	II uzorak	Referentna vrednost
Adrenalin	58,2	9,5	180
Noradrenalin	**26632,1**	**4943,4**	570
Dopamin	**6891,9**	1430,5	3240
Normetanefrin	3,1	3,26	3,6

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CASE REPORT OF THE FIRST LAPAROSCOPIC ADRENALECTOMY TREATMENT OF PHEOCHROMOCYTOMA IN PEDIATRIC POPULATION IN REPUBLIC OF SERBIA

Abstract: Pheochromocytoma is a tumor that arises from adrenal medulla and it is characterized by increased secretion of catecholamines. The incidence of pheochromocytoma is 3 to 8 cases per million inhabitants, of which about 10 to 20% of diagnosed pheochromocytomas occurs in the pediatric population, with a higher frequency in boys. In 1.7% of the pediatric population with hypertension, the cause of hypertension is pheochromocytoma. Due to headaches and verified hypertension on twenty-four-hour holter blood pressure monitoring, the 13-year-old female patient underwent ultrasound, followed by scintigraphy and magnetic resonance imaging of the abdomen, which described an oval change above the right kidney about 4.5 cm in diameter suspected of pheochromocytoma. Twenty-four-hour urine cateholamines showed elevated noradrenaline values as much as 45 times higher than the reference range, as well as elevated dopamine values. After adequate preparation with phenoxybenzamine and bisoprolol for two weeks, a right laparoscopic adrenalectomy was performed at the University Children's Clinic in Tirsova, which is also the first operation of this type in the pediatric population. Intraoperatively, the maximum value of tension was 180/120 mmHg. Pathohistological findings confirmed pheochromocytoma. Although a rare cause of hypertension in the pediatric population, young

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patients with newly diagnosed hypertension should be examined for possible pheochromocytoma. Laparoscopic adrenalectomy through both the lateral transabdominal and posterior retroperitoneoscopic approach is the gold standard for the treatment of pheochromocytomas in both the adult and pediatric populations.

Introduction

Pheochromocytoma (PHEO) is a rare, neuroendocrine tumor that arises from the adrenal medulla, and is manifested by oversecretion of catecholamines (adrenaline, noradrenaline, and/or dopamine) (1, 2). The annual global incidence rate is around 2-9 per 1 000 000 inhabitants in general population (2). Clinical signs and symptoms of PHEO include conditions that catecholamine excess leads to, primarily – hypertension (80.7%), headache (60.4%), palpitations (59.3%), diaphoresis (52.4%), and, in lesser extent, fatigue, weight loss, flushing, abdominal pain and hyperglycemia. Because of highly unspecific symptomatology of PHEO, clinical diagnosis can be made extremely difficult considering the broad spectrum of differential diagnoses (extra adrenal paragangliomas, anxiety disorders, essential hypertension, hyperthyroidism, carcinoid syndromes, and many others), which is why PHEO is often referred to as the "Great Mimic" (2).

If there is a clinical suspicion of PHEO, the diagnosis is confirmed by a combination of laboratory analyses (catecholamines and metanephrines in 24-hour urine assessment) and anatomical imaging (echosonography, multislice computed tomography (MSCT), magnetic resonance imaging (MRI)), as well as much important functional imaging, such as scintigraphy with I^{123}-MIBG as radiopharmaceutical of choice, where in PHEO the expected finding is intense accumulation of radiopharmaceutical in adrenal region (2).

10–20% of PHEO is diagnosed in pediatric age, and is showed that 1.7% of children with hypertension has a PHEO as an underlying cause. In pediatric population, median age for diagnosing PHEO is 11–13 years, with predominance in boys, by some authors even as much as 2:1 (1, 2). Methodology of diagnostic is for the most part unchanged compared to adult population, but genetic screening and elaborate diagnostics should be taken with goal of ruling out PHEO-associated syndromes (Von Hippel-Lindau (VHL) syndrome, Multiple endocrine neoplasia (MEN) 2A and 2B syndromes and neurofibromatosis type 1 (NF1)) (1).

In this paper we present first case of elective laparoscopic adrenalectomy in patient with clinically manifested pheochromocytoma in pediatric age in University Children's Hospital – Tiršova.

Case presentation

Female patient aged 12 + 10/12, with body height of 166 cm and body weight of 55.8 kg is admitted to hospital for evaluation of flushing of the cheeks and frequent headaches. 2 years prior to the hospitalization the patient had metformin introduced because of elevated fasting glycemia. During the hospitalization it was noted that headaches were always followed by blood pressure (BP) elevation, which is why holter monitoring of BP was indicated. On 24-hour BP holter monitor, 96% of all registered BP values were over 135/85 mmHg. Afterwards, an abdominal ultrasound was conducted which revealed a solid oval nodule 4.5x4.8 cm in diameter on top of the upper pole of the right kidney. Later on, MRI confirmed a hyperintense nodular mass 4.5 cm in diameter in region of right adrenal gland (Image 1). Due to clinical signs, as well as visualized adrenal mass, a whole body scintigraphy was performed, cateholamine and metanephrine assessment in 24-hour urine sample. Scintigraphy showed intense accumulation of radiopharmaceutical in right adrenal region (Image 2). Elevated values of noradrenaline were detected in two 24-hour urine samples, as well as elevated dopamine values in one of the samples (Table 1). Cortisol and ACTH were in reference range. Considering the results of the whole diagnostic procedure mentioned above, the diagnosis of PHEO was confirmed, indicating surgical treatment after adequate preoperative pharmacological preparation with phenoxybenzamine and bisoprolol in duration of 2 weeks. Surgical treatment was then undertaken in University Children's Hospital - Tiršova and right laparoscopic adrenalectomy was performed by lateral transperitoneal approach (LTA). Intraoperatively, the highest BP value was 180/120 mmHg. For intraoperative BP control sodium-nitroprusside was used. Postoperative course went well, and patient was discharged from the hospital by the fourth postoperative day. Pathohistological finding confirmed PHEO. BP on the first follow-up, a month after surgical treatment was 105/65 mmHg. Gene testing bloodwork was conducted - currently pending.

Discussion

First successful surgical treatment in patients with PHEO was undertaken by Cesar Roux (1857–1934) in Switzerland, as well as Charles Horace Mayo (1865–1939) in the USA in 1926. (3). Laparoscopic adrenalectomy (LA) has been a golden standard in PHEO treatment ever since 1992. when a paper by Michael Gagner was published, in which the first three successful laparoscopic adrenalectomies were presented by using laparoscopic lateral transperitoneal approach (LTA) (4). Other than the mentioned approach, the LA can be done by using frontal transperitoneal, as well as retroperitoneal approach.

In Center for Endocrine Surgery, University Clinical Center of Serbia LTA is being used as routine procedure since 2012. LA is especially indicated for fuctional tumors which are smaller in size, as well as afunctional tumors, for which the chance for malign alteration has been identified as minimal (5, 6). As per every method, LTA is not without flaws. Absolute contraindications include tumors with over 15 cm in diameter, local tumor invasion, suspected adrenocortical carcinoma (ACC) and metastatic PHEO, while the relative containdications include increased cardiopulmonary risk as well as persistent coagulopathy (7–9). Maintaining intraoperative haemodynamic stability during the operation presents a challenge, which is why comparing haemodynamic stability during laparoscopic versus open approach (OA) surgery provides a constant cause for research on this topic, with results that don't show statistically significant difference in incidence and degree of haemodynamic instability, length of operation and loss of blood between these two apporaches (9–14). Kim et al. (15) came to conclusion that the percentage of patients with intraoperative hypertensive crisis is lower in patients operated with LTA compared to OA (0.6 ± 0.5% during LTA and 1.67 ± 1.1% during OA, $p = 0.0146$). This study also showed faster postoperative oral intake in patients in LTA group (1.1 ± 0.3 days) compared to the OA group (2.6 ± 1.3 days, $p = 0.0037$). Also, there was a statistically significant difference in the length of poostoperative hospital stay (LTA 5.6 ± 2 days, OA 12.4 ± 3.5 days, $p = 0.0001$), which was also confirmed by Miccoli et al. (16) (4.1 ± 2.3 days in LTA, 7.2 ± 2.6 in OA, $p < 0.02$). Miccoli's team also compared the length of the very intervention, showing longer length of the intervention for LTA (182 ± 115 minutes) compared to the OA (142 ± 29 minutes, $p < 0.02$). In addition, the need for analgesics usage was shown to be lower after LTA. Comparing the length of LA between hormone producing tumors and incidentalomas Cheah et al. showed that procedures were slightly longer in patients without symptoms of hormone overproduction (193 (130–340) minutes) compared to 182 (90–305) minutes in patients with confirmed syndromes associated with adrenal tumors (17). The average blood loss during the laparoscopic operation varies greatly among different papers with Miccoli et al. (16) showing a loss of average 342 mL and Janetschek et al. (18) showing a loss of average 130 mL of blood. The difference of volume of blood lost, the percentage of conversion of LA into OA mid-procedure, length of postoperative hospital stay, tumor size and ASA score was shown to be not too different between PHEO and other adrenal tumors operated with laparoscopic approach (19–21).

The results of the case we presented match results of other authors that tackled this topic, especially in terms of postoperative oral intake which was started by the second postoperative day, as well as adequate pain control which was achieved with minimal doses of analgesics. The patient was discharged from the hospital on the third postoperative day, which also matches the data gained from earlier research.

Main intraoperative challenge during the PHEO operation, independent of the approach (LTA or OA), is identifying the adrenal vein. With OA, ligating the vein is doable after intraoperative tumor mobilization, which was shown in earlier research to be responsible for the occurrence of hypertensive crisis (22). It is with that idea that Fernandez-Cruz et al. (23) pointed out the advantages of laparoscopic approach for PHEO treatment 20 years ago, showing that LTA lowers intraoperative release of catecholamines with a high statistical significance, lowering in turn the risk for hypertensive crisis occurrence, something that was not unique to just this research (10, 24). Even if LTA makes adrenal vein visualization easier, in our experience, this can be made difficult because of the adjacent adipose tissue. LA of the clinically verified PHEO should be done by experienced endocrine surgery specialists, since the conversion from laparoscopic to OA occurs in about 2% of all cases, which is something that can only be done by surgeons also experienced in the open adrenalectomy (7). Main reasons for conversion could be, primarily uncontrolled bleeding, adhesions, patient obesity, adjacent organ injury, hepatomegaly or lack of surgeon's experience. (7–9, 25, 26). Shen et al. showed BMI values of over 24 kg/m^2 and tumor size of over 5 cm to be good predictive factors for conversion to OA (25).

The case we present was, in fact, in high risk for conversion, and one of the bigger reasons it hasn't come to it is because by the time the presented case was treated, over 100 adrenalectomies were performed in Center for Endocrine Surgery, University Clinical Center of Serbia by the use of LTA, both for PHEO, as well as other functional and non-functional adrenal tumors. Our experience also shows that LTA is linked with less frequent complications compared to the OA (wound infection, respiratory infections, lower intraoperative organ trauma incidence), which matches the referenced research (25–27).

Conclusion*:*

For decades, the development of minimally invasive techniques has radically changed the surgical approach to the routine treatment of the adrenal gland diseases, with intensive research continually proving the safety, efficacy and convenience of laparoscopic compared to the open approach, making the laparoscopic adrenalectomy the golden standard for adrenal tumor treatment. Provided the adequate preoperative pharmacological preparation is carried out, along with great intraoperative coordination of experienced surgical and anesthesiological teams, it can be deduced that laparoscopic adrenalectomy stands as the method of choice for the treatment of pheochromocytoma, in both adult and pediatric populations.

Literature

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Image 1. MRI showing hyperintense nodular mass in region of adrenal gland

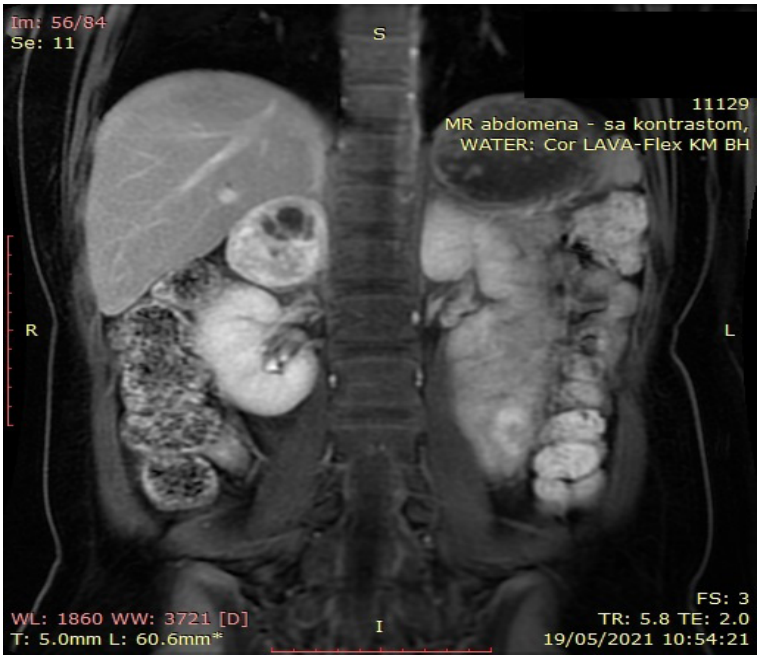

Image 2. Scintigraphic finding of intense accumulation of radiopharmaceutical in adrenal region

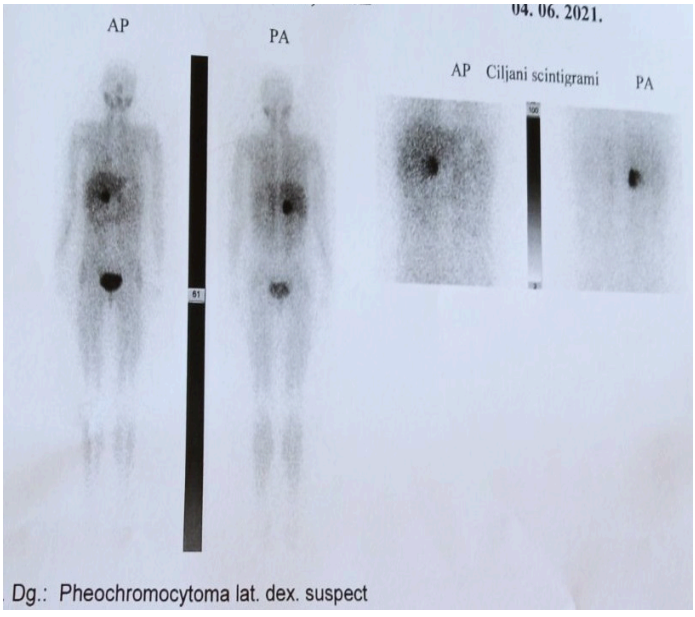

Table 1. Catecholamine values in 2 consecutive 24-hour urine samples

	I sample	II sample	Reference range
Adrenaline	58,2	9,5	180
Noradrenaline	**26632,1**	**4943,4**	570
Dopamine	**6891,9**	1430,5	3240
Normetanephrine	3,1	3,26	3,6