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BRZORASTUĆI TUMOR NADBUBREŽNE ŽLEZDE KOD PACIJENTKINJE SA OPERATIVNO LEČENIM KARCINOMOM DEBELOG CREVA

Sažetak: Adrenokortikalni karcinom predstavlja retku malignu bolest, koja se javlja u 0,5-2/1.000.000 slučajeva godišnje. Klinički znaci mogu nastati kao posledica autonomne hormonske hipersekrecije tumorske promene, ali takođe i zbog lokalnih kompresivnih smetnji u stomaku.

Uspeh lečenja, zavisi od momenta ranog postavljanja dijagnoze, a preporuke za lečenje su definitivna adrenelektomija. Pored hirurgije, neizostavnu strategiju u daljem lečenju ovako kompleksnih maligniteta je hemioterapija mitotanom. Daljim istraživanjima o nadbubrežnim žlezdama doprineće bolji pristupu u otkrivanju i lečenju adrenokortikalnih carcinoma.

Prikazali smo pacijentkinju kod koje je tokom praćenja zbog operisanog adenokarcinoma kolona CT-om uočena promena desne nadbubrežne žlezde koja je zbog veličine i rezultata hormonskih analiza, su odgovarali supkliničkom Cushing-u operisana, a histopatološki nalaz je pokazao da se radi o adrenokortikalnom karcinomu. S obzirom na dokazani adrenokortikalni karcinom uvedena je terapija mitiotanom.

Uvod:

Adrenokortikalni karcinom (ACC) predstavlja redak maligni tumor nadbubrežnih žlezda sa nepovoljnom prognozom i često letalnim ishodom. Javlja se svega u 0,5-2/1.000.000 slučaja godišnje. Uobičajena prezentacija ovog tumora je u vidu hiperkorticizma, virilizacije i kompresivnih smetnji, te se u 45% slučajeva može da

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se manifestuje kao Kušingov sindrom, a u 10% slučajeva samo sa prezentacijom virilizacije. Ove tumorske mase mogu da se šire lokalno i da zahvate okolne krvne sudove, a retko mogu da formiraju trombne tumorske mase, putem kojih dolazi do udaljenih komplikacija od primarnog mesta lokalizacije. Uspeh lečenja zavisi od trenutka postavljanja dijagnoze.

Prikaz slučaja:

Pacijenkinja OM, 46 godina bila je hospitalizovana na Klinici za endokrinologiju, dijabetes i bolesti metabolizma u cilju ispitivanja tumorske promene desnog nadbubrega. Od aprila 2022.g. učinjena je resekcija sigmoidnog kolona, *PH Adenocarcinom coli*, koji je bio umereno diferentovan uz naknadno sporovođenje hemoterapijske senase. U toku radiografskog stejdžinga, CT jun-decembar 2022. godine je bio uredan. Na CT-u abdomena iz jula 2023. godine na desnoj nabubrežnoj žlezdi opisana je ovalana jasno ograničena promena vel. 28x46x46 mm, a poređenjem sa prethodnim CT nalazom promena je postojala ali nije opisana, vel. 25x18x25mm. Kasnije je promena ultrazvučno praćena, a veličina se kretala od 7x5,6mm do 9,2x8,5mm sa suspektnim poljima nekroze. Tokom hospitalizacije na Klinici u novembru 2023.g, učinjen je CT na kom je opisana heterodenzna centalno nekrotična promena desne nadbubrežne žlezde, vel. 92x98x122mm, koja se utiskuje u desni lobus jetre, ali očuvanog okolnog masnog plana, bez CT znakova aktivne ekstravazacije kontrastnog sredstva. Leva nadbubrežna žlezda je b.o. Funkcionalnim testiranjem je zaključeno da postoji autonomna kortizolska sekrecija (ACTH: 10; Bazni kortizol: 419, **dex screening, kortizol: 113.0**) uz nešto više vrednosti testosterona i DHEA-s (Testosteron U: 2.61...4.5; Testosteron F: 3.51; DHEA-S: 12.0...16.5). Nije bilo kateholamisnkog ekscesa, dok su aldo i PRA u referentnom opsegu (aldo/PRA 5,26). Hromorganin je bio pozitivan (CGA 111.8 ng/mL).

Kasnije u decembru 2023.g, učinjena je desnostrana adrenalektomija, a histopatološka dijagnoza je bila adrenokortikalni karcinom (ACC), inkapsuliran tumor, *high grade* histološkog gradusa, vel. 115x82x85mm sa oskudnim fragmentima masnog tkiva na periferiji, na preseku sa velikim poljima neroze i krvarenja, tumor infiltriše kapsulu, ali je ne probija, limfovaskularna invazija prisutna, margine bez tumorskog tkiva. U periglandularnom masnom tkivu i tkivu jetre nije nađeno tumorsko tkivo (pT2NxMx. IHH: CK, CAM5 2 tehnički neuspeo, SF1+, Calretinin+, Inhibin+, Melanin A+, Synaptofizin+, NSE+, Vimentin+, INSM 1+). Postoperativno joj je uveden Hidrocortison 15+5mg. Prilaže hormone HPA (ACTH 1.4pmol/L; Kortizol 145nmol/L; Testosteron 0.29nmol/L; DHEA-S 0.4umol/L). U fizikalnom nalazu nisu nađeni značajni patološki klinički znaci. Rezultati laboratorijskih analiza ukazuju na granično niže vrednosti HGB i negativan zapaljenski sindrom. Nema poremećaja glikoregulacije ni retencije azotnih

materija, elektroliti i tumor marker su uredni (tabela 1). Nakon operacije uredne vrednosti su bile testosterona uz niže vrednosti DHEA-S (Testosteron, ukupan: 0.55; DHEA-S: 0.8). Uredne vrednosti baznog ACTH (ACTH: 2.42pmol/L), a profil kortizola ukazuje na adekvatnu supstituciju Hidrocortisonom (Kortizol: 256...932; 125...473; 129; <27,6nmol/L).

Tabela 1. Postoperativne analize

CRP	2,3
WBC	5,3
HGB	121
PLT	164
GLC	5
HB1C	5,9
Na	142
K	4,3
Testosteron	0,55
DHEA-S	0,8
AFP	< 2.00
CEA	3,1
CA 125	6
CA 19-9	11
NSE	4,4
CT	<0,5

Radiografija pluća, srca i ultrazvuk vrata su bili bez osobitosti, međutim subkapsularno u SVI jetre vidi se **hiper do heteroehogena promena 12x18mm**. Zbog specifične opisane promene, a i u svetlu postoperativnog radiografskog praćenja učinjen je kontrolni CT abdomena: Jetra je normalne veličine, KK promera desnog režnja 136mm, homogena, bez jasnog izdvajanja fokalnih promena. Na granici S7/S6 vidi se klips, uz koji se izdvaja hipodenzna zona 7x18mm, koja kroz preseke menja oblik (razvlači se) i ista je u svim fazama pregleda, najpre artefakt od klipseva. Desna nadburbežna žlezda operisana, lokalno nema znakova rest recidiva. Detektuju se jedan klipse u loži, pravi artefakte u S6 i S7 lobusu jetre. Leva nadbubrežna žlezda je normalne CT morfologije. Tokom hospitalizacije je učinjeno morfološko i funkcionalno ispitivanje nakon desnostrane adrenalektomije. Zbog ultrazvučno viđene fokalne promene

u jetri učinjen CT abdomena koji je pokazao da se radi o klipsu. U ličnoj anamnezi, histerektomija sa adneksektomijom (CA cervixa) 2018.g. Porodična anamneza je pozitivna za CA kolona. Prilikom hemioterapije javio joj se osip u predelu vrata sa gušenjem. Pušač je 20 cigareta po danu.

Diskusija:

Zahvaljujući tehnološkom razvoju i širokoj primeni vizuelizacionih tehnika abdomena, tumori ili mase nadbubrežnih žlezda poznati kao incidentalomi su postali uobičajni medicinski izazov u kliničkoj praksi. Slučajno otkrivene lezije treba morfološki i funkcionalno ispitati, odnosno proceniti da li su hormonski aktivne i da li imaju karakteristike maligniteta. Svega 10% incidentaloma je funkcionalno, dok 2% slučajeva je ACC.

Adrenokortikalni karcinom (ACC) je redak malignitet nadbubrežnih žlezda, koji se javlja u bilo kom uzrastu, ali sa najvećom prevalencom između 40 i 60 godina. Česće se javlja kod ženskog pola i može se manifestovati kao funkcionalno hormonski aktivna nadbubrežna žlezda kod 50-60% pacijenata. U najvećem broju slučajeva pacijenti mogu imati tipičan fenotipski izgled prekomerne autonomne sekrecije kortizola, tj. Kušingovog sindroma, dok u 30-40% pacijenata tegobe mogu biti u vidu nelagodnosti u stomaku uz bolove u leđima.

Rano postavljanje dijagnoze je važan prediktor za uspeh lečenja i prognoze ACC. Petogodišnje preživljavanje je 60-80% za ACC koji su ograničeni na nadbubrežne lože, dok je 35-50% za lokalno uznapredovalu bolest. Međutim, u slučaju metastatske bolesti, preživljavanje je još niže i u rasponu je 0-28%.

Dijagnoza i procena funkcionalnosti se postavlja na osnovu laboratorijskih analiza: 1. glukoza i elektroliti u serumu, 2. kortizol u serumu, 3. androgeni nadbubrežnih žlezda, 4. kateholamini i metaboliti u urinu, 5. *Screening i* potvrdnih testova, i na osnovu radioloških metoda kao što su CT i MR abdomena (Shema 1). Komplikacije su moguće kao i kod drugih maligniteta, u smislu lokalne invazije, kaheksije, bola u slučaju metastaza u kostima, i sistemskih efekata kao posledica hipersekrecije hormona, ili paraneoplastičkog sindroma. Nažalost, u trenutku postavljavnjanja dijagnoze ACC većina pacijenata ima uznapredovalu bolest, stoga je važno da se ispitaju incidentalomi odnosno mase nadbubrežnih žlezda.

U literaturi postoje jasna morfološka obeležija ACC, to su: nepravilan oblik, veličina preko 4cm, intralezijski kalcifikati i hemoragija ili nekroza, jednostrana lokalizacija, lokalna invazija i *CT Hounsfield* jedinica > 20 *HJ*. U cilju ispitivanja funkcionalnosti nadbubrežnih masa potrebno je uraditi screening-potvrdne testove, kao što su prekonoćni supresioni test sa 1 mg deksametazona i test izlučivanja kortizola u 24h urinu. U slučaju da su rezultati nekonkluzivni, evaluacija se može proširiti na merenje dnevnog ritma kortizola u serumu ili salivarnog kortizola uz

dodatne supresione testove. Adrenokortikotropni hormone (ACTH) može biti smanjen u slučaju autonomne produkcije kortizola. Takođe evaluacija mora da obuhvati ispitivanje u pravcu mogućeg feohromocitoma na osnovu merenja kateholamina i metabolita u 24h urinu, a obzirom da ove supstance u serumu imaju kratak poluživot, rutinski se ne određuju. Ponekad, u biohemijskim nalazima se registruju snižene vrednosti kalijuma, kao posledica prekomernernih vrednosti kortizola, koji svoj efekat ostvaruje i preko mineralokortikoidnih receptora. Za virilizacione i feminizacione sindrome se mere: serumski adrenalni androgeni, testosteron, estradiol i 17- ketosteroid u 24h urinu.

Lečenje nefunkcionalnih adrenalnih tumora se bazira na njihovoj veličini, te praktično svi tumori preko 6cm treba da budu uklonjeni. Međutim, hirušku sivu zonu predstavljaju tumori veličine između 3 do 6 cm, te neki autori smatraju da veličina za adrenalektomiju treba da bude 4 ili 5cm. U slučaju da klinička slika, morfološka i funkcionalna ispitivanja govore u pravcu karcinoma, terapija izbora je totalna hirurška resekcija.

Pored hirurgije, hemioterapija ima neizostavnu ulogu u lečenju ovih pacijenata. Mitotan predstavlja glavni hemoterapijski izbor za lečenje ACC, a koristi se kao primarna, adjuvantna terapija, ali i kod recidiva bolesti. Lečenje se započinje u dozi od 2 do 3 grama kod odraslih, koja se postepeno povećava do postizanja terapijskog okvira u serumu (14-20mg/L). Neophodno je praćenje mitotana u serumu obzirom na neurotoksičnost leka koja nastaje pri prelasku koncentracije leka preko 20mg/L. Terapijska koncentracija se dostiže nakon 3 do 5 meseci od početka primene leka. Ovaj potentan lek kontroliše kortizolsku hipersekreciju tako što inhibira sintezu holesterola i 11 beta oksidaciju. Meta-analizom koja je obuhvatila 1249 pacijenata je pokazala da adjuvantni mitotan predstavlja odličnu postoperativnu strategiju, odnosno da dovodi do dužeg preživljavanja bez recidiva i ukupnog preživljavanja. Neželjeni efekti tokom primene mitotana najčešće su uvidu gastrointestinalnih: mučnina, povraćanje, dijareja, depresija, slaba koncentracija, narušen hepatogram. S obzirom na adrenolitičko dejstvo, treba istaći da pacijenti lečeni mitotanom zahtevaju i egzogenu primenu steroida (Tabela 2).

Nakon lečenja savetuje se praćenje svakog meseca tokom prve dve godine zbog mogućih recidiva kao i pojava metastaza u plućima, što značajno poboljšava dugotrajno preživljavanje. Radiološko praćenje abdomena i najčešća mesta ACC metastaza, treba uraditi tokom prve dve godine na svaka tri meseca, treća i četvrta godina svaka 4 meseca, a u petoj godini na šest meseci.

Metastaze u nadbubrežne žlezde iz drugih organa su čest nalaz, obično su bilateralne, ali mogu biti i jednostrane. Najčešći primarni tumori koji daju metastaze u nadbubrežne žlezde su: 1. karcinom pluća, 2. kolorektalni karcinom, 3.

karcinom dojke i pankreasa; ostali ređi prijavljeni tumori: hepatocelurarni karcinom, maligni melanom, osteosarkom, itd. Zato je važno uzeti u obzir bilo koju adrenalnu promenu u celokupnom kliničkom kontekstu, naručito ako pacijent ima ličnu anamnezu o malignitetima.

Zaključak:

Istraživanjima je postignut značajan doprinos razumevanju patologije i patogeneze ACC. Međutim ACC ipak predstavlja komplikovanu bolest sa lošim ishodom. Ključ uspeha lečenja je rano postavljanje dijagnoze, a adrenelektomija predstavlja terapijsku opciju sa definitivnim izlečenjem. Do danas, mitotan kao adjuvantna terapija predstavlja najefikasniji lek. Prikazali smo pacijenkinju kod koje je tokom praćenja zbog operisanog adenokarcinoma kolona CT-om incidentalno uočena promena desne nadbubrežne žlezde koja je zbog veličine i rezultata, koji su odgovarali supkliničkom Cushing-u operisana, a HP je pokazao da se radi o ACC. S obzirom na dokazani ACC uvedena je terapija mitiotanom uz inicijalno povećanje doze hidrokortizona.

1. Shematski prikaz evaluacije adrenalne mase:

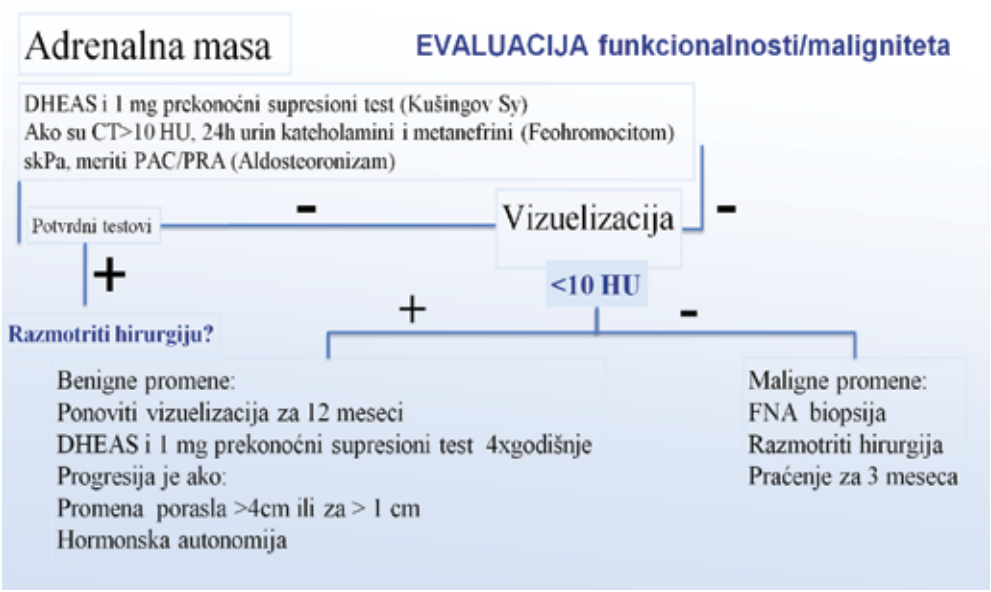

Tabela 2. Preporučeno praćenje kod pacijenata na mitotanu

Parametar	Vremenski interval	Komentar
Preporučeno praćenje		
Nivo mitotana u krvi	Svakih 3-4 nedelje, čim se postigne nivoa u krvi, svakih 2-3 meseca	Cilj nivoa u krvi > 14 mg/L
AST, ALT bilirubin, (gGT)	U početku svakih 3-4 nedelje, nakon 6 meseci svakih 2-3 meseca	Ako su drugi jetreni enzimi naglo povišeni (> 5 puta od osnovne vrednosti) i postoji rizik od insuficijencije jetre: prekinuti mitotan
Krvna slika	U početku nakon 3-4 nedelje, zatim svakih 3-4 meseca	Leukopenija, trombocitopenija i anemija
Predloženo praćenje		
ACTH	Adrenalna insuficijencija	Cilj: ACTH u normalnom rasponu ili blago iznad
TSH, fT4	Na 3-4 meseca	Nadoknada se preporučuje kod kliničkih simptoma hipotiroidizma
Renin	Na 6 meseci	Ako je renin ↑ i prisutni su klinički simptomi hipoaldosteronizma, uvesti fludrokortizon
Holesterol (HDL, LDL)	Na 3-4 meseca	Ako je LDL / HDL ↑↑ razmotriti lečenje statinima u odabranim slučajevima
Testosteron i SHBG kod muškaraca	Na 3-4 meseca	Ako je testosteron nizak i prisutni su klinički simptomi hipogonadizma, dodati testosteron

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RAPIDLY GROWING ADRENAL GLAND TUMOR IN A FEMALE PATIENT WITH A HISTORY OF COLON CANCER

Abstract: Adrenocortical carcinoma is a rare malignant disease, occurring in 0.5-2 per 1,000,000 cases annually. Clinical signs may arise due to autonomous hormonal hypersecretion by the tumor, but also due to local compressive symptoms in the abdomen. The success of treatment depends on early diagnosis, with the recommended treatment being definitive adrenalectomy. An essential strategy in the further treatment of such complex malignancies is chemotherapy with mitotane. Thanks to advancements in medical sciences and comprehensive research, there will be an improved approach in the detection and treatment of adrenocortical carcinomas.

We presented a female patient who, during follow-up for operated colon adenocarcinoma, was incidentally found on CT to have a lesion in the right adrenal gland. Due to its size and results consistent with subclinical Cushing's syndrome, the lesion was operated on, and histopathological findings indicated adrenocortical carcinoma. Given the confirmed adrenocortical carcinoma, therapy with mitotane was initiated.

Introduction:

Adrenocortical carcinoma (ACC) is a rare malignant tumor of the adrenal glands with a poor prognosis and often lethal outcome. It occurs in only 0.5-2 per 1,000,000 cases annually. Common presentations of this tumor include hypercorticism, virilization, and compressive symptoms, with 45% of cases manifesting as Cushing's syndrome and 10% presenting solely with virilization. These tumor masses can locally

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invade surrounding blood vessels, and rarely, tumor thrombus formation can occur. The success of treatment depends on the timing of diagnosis.

Case Report:

Patient O.M., a 46-year-old female, was hospitalized at the Clinic for investigation of a tumor lesion in the right adrenal gland. Since April 2022, she had undergone resection of the sigmoid colon due to moderately differentiated adenocarcinoma of the colon, followed by chemotherapy sessions. During radiographic staging, CT scans from June to December 2022 were normal. However, a CT scan of the abdomen in July 2023 revealed a well-defined oval lesion in the right adrenal gland measuring 28x46x46 mm. Comparison with a previous CT scan showed that the lesion had been present but not described, measuring 25x18x25 mm. Later, ultrasound monitoring indicated that the lesion size ranged from 7x5.6 cm to 9.2x8.5 cm, with suspected necrotic areas. During hospitalization at the Clinic in November 2023, a CT scan described a heterodense centrally necrotic lesion in the right adrenal gland, measuring 92x98x122 mm, impinging on the right lobe of the liver but preserving the surrounding fat plane without CT signs of active contrast extravasation. The left adrenal gland was normal.

Functional testing indicated autonomous cortisol secretion (ACTH: 10; Basal cortisol: 419; dex screening, cortisol: 113.0) with slightly elevated testosterone and DHEA-S levels (Total testosterone: 2.61...4.5; Free testosterone: 3.51; DHEA-S: 12.0...16.5). There was no catecholamine excess, while aldosterone and plasma renin activity (PRA) were within the reference range (aldo/PRA ratio: 5.26). Chromogranin was positive (CGA 111.8 ng/mL).

In December 2023, a right-sided adrenalectomy was performed, and the histopathological diagnosis was adrenocortical carcinoma (ACC), an encapsulated high-grade tumor measuring 115x82x85 mm with scant peripheral fat tissue fragments. The tumor had extensive areas of necrosis and hemorrhage, infiltrated the capsule without breaching it, showed lymphovascular invasion, and had clear margins. No tumor tissue was found in the pericapsular fat tissue or liver tissue. Pathological staging was pT2NxMx. Immunohistochemistry (IHH) was positive for CK, CAM5 2 (technically unsuccessful), SF1+, Calretinin+, Inhibin+, Melanin A+, Synaptophysin+, NSE+, Vimentin+, INSM 1+.Postoperatively, the patient was started on Hydrocortisone 15+5 mg. She feels well. Hormone levels are as follows: ACTH 1.4 pmol/L; Cortisol 145 nmol/L; Testosterone 0.29 nmol/L; DHEA-S 0.4 μmol/L. Physical examination showed no significant pathological clinical signs. Laboratory results indicated borderline low HGB levels and a negative inflammatory syndrome. There were no disturbances in glucose regulation or nitrogen retention, and electrolytes and tumor markers were normal (Table 1). Postoperatively, testosterone levels normalized with lower DHEA-S values (Total testosterone: 0.55; DHEA-S: 0.8). Baseline ACTH levels were normal

(ACTH: 2.42), and the cortisol profile indicated adequate substitution with Hydrocortisone (Cortisol: 256...932; 125...473; 129; <27.6).

Table 1. Laboratory

CRP	2,3
WBC	5,3
HGB	121
PLT	164
GLC	5
HB1C	5,9
Na	142
K	4,3
Testosteron	0,55
DHEA-S	0,8
AFP	< 2.00
CEA	3,1
CA 125	6
CA 19-9	11
NSE	4,4
CT	<0,5

Radiography of the lungs, heart, and ultrasound of the neck showed no abnormalities. However, a subcapsular hyper to hyperechoic lesion measuring 12x18 mm was observed in segment VI of the liver. On a follow-up abdominal CT scan, the liver was of normal size, with the craniocaudal diameter of the right lobe measuring 136 mm, homogeneous, without clear focal changes. At the S7/S6 boundary, a clip was seen, adjacent to which a hypodense zone measuring 7x18 mm was observed, changing shape across slices (stretching) and consistent in all phases of the scan, likely an artifact from the clips. The right adrenal gland was operated on, with no signs of local recurrence. One clip was detected in the surgical bed, causing artifacts in segments S6 and S7 of the liver. The left adrenal gland had a normal CT morphology. Post-left hemicolectomy status, otherwise unremarkable. During hospitalization, morphological and functional examinations were conducted following right adrenalectomy. Due to the ultrasound-detected focal liver lesion, an abdominal CT scan was performed, revealing it was a clip. The patient had a hysterectomy with adnexectomy (CA cervix) in 2018.

Family history is positive for colon cancer. During chemotherapy, she developed a rash in the neck area accompanied by choking. She smokes 20 cigarettes per day.

Discussion:

Recently, with the widespread use and technological advancement of abdominal imaging techniques, tumors or masses of the adrenal glands, known as incidentalomas, have become a common medical challenge in clinical practice. Incidentally discovered lesions need to be morphologically and functionally evaluated to determine if they are hormonally active and if they have malignant characteristics. Only 10% of incidentalomas are functional, while 2% are ACC.Adrenocortical carcinoma (ACC) is a rare adrenal malignancy that can occur at any age, with the highest prevalence between 40 to 60 years. It occurs more frequently in females and can manifest as hormonally active adrenal glands in 50-60% of patients. Most patients may exhibit phenotypic features of excessive autonomous cortisol secretion, i.e., Cushing's syndrome, while 30-40% of patients may experience abdominal discomfort and back pain. Early diagnosis is a crucial predictor of treatment success and prognosis in ACC. Five-year survival is 60-80% for ACC confined to the adrenal bed, while it is 35-50% for locally advanced ACC. However, in the case of metastatic disease, survival is much lower, ranging from 0-28%.Diagnosis is based on laboratory tests: 1. serum glucose and electrolytes, 2. serum cortisol, 3. adrenal androgens, 4. catecholamines and metabolites in urine, 5. screening tests, and radiological methods such as CT and MRI of the abdomen (Scheme 1). Complications, as with other malignancies, may include local invasion, systemic effects from hormone hypersecretion, paraneoplastic syndrome, cachexia, and bone pain in cases of metastasis. Unfortunately, at the time of diagnosis, most ACC patients have advanced disease, making it essential to investigate incidentalomas or adrenal gland masses.

In the literature, the clear characteristics of ACC are: irregular shape, size over 4 cm, intralesional calcifications and hemorrhage or necrosis, unilateral localization,local invasion, CT Hounsfield units > 20 HU. To investigate the functionality of adrenal masses, screening-confirmatory tests should be performed, such as: Overnight dexamethasone suppression test with 1 mg dexamethasone, 24-hour urinary cortisol excretion test. If results are inconclusive, further evaluation can include measuring the diurnal rhythm of serum cortisol or salivary cortisol with additional suppression tests. Adrenocorticotropic hormone (ACTH) may be decreased in cases of autonomous cortisol production. Evaluation must also include testing for possible pheochromocytoma by measuring catecholamines and metabolites in 24-hour urine, as these substances have a short half-life in serum and are not routinely measured. Occasionally, biochemical findings may show decreased potassium levels due to excessive cortisol acting through mineralocorticoid receptors or hyperaldosteronism.

For virilization and feminization syndromes, serum adrenal androgens, testosterone, estradiol, and 17-ketosteroids in 24-hour urine are measured.Treatment of non-functional adrenal tumors is based on their size, with practically all tumors over 6 cm requiring removal. However, the surgical gray zone includes tumors between 3 to 6 cm, with some authors suggesting a threshold of 4 or 5 cm for adrenalectomy. If the clinical picture, morphological, and functional evaluations suggest a likely carcinoma, the treatment of choice is total surgical resection.

Besides surgery, chemotherapy plays an indispensable role in treating these patients. Mitotane is the main chemotherapeutic agent for ACC treatment, used as primary therapy, adjuvant therapy, and in case of disease recurrence. Treatment starts with a dose of 2 to 3 grams for adults, gradually increasing until the therapeutic range in serum (14-20 mg/L) is reached. Monitoring mitotane serum levels is necessary due to the drug's neurotoxicity, which occurs when concentrations exceed 20 mg/L. The therapeutic concentration is reached 3 to 5 months after the start of treatment. This potent drug controls cortisol hypersecretion by inhibiting cholesterol synthesis and 11-beta oxidation. A meta-analysis involving 1249 patients showed that adjuvant mitotane is an excellent postoperative strategy, leading to longer relapse-free survival and overall survival.Side effects during mitotane treatment are mostly gastrointestinal, including nausea, vomiting, diarrhea, depression, poor concentration, and disrupted liver function tests. Due to its adrenolytic effect, patients treated with mitotane require exogenous steroid administration (Table 2).

After treatment, follow-up is recommended every month during the first two years due to the risk of recurrence and the appearance of lung metastases, significantly improving long-term survival. Radiological monitoring of the abdomen and the most common metastatic sites of ACC should be performed every three months during the first two years, every four months in the third and fourth years, and every six months in the fifth year.Metastases from other organs are a common finding, usually bilateral but can be unilateral. The most common primary tumors that metastasize to the adrenal glands are: Lung carcinoma, colorectal carcinoma, breast and pancreatic carcinoma. Other less frequently reported tumors include: Hepatocellular carcinoma, malignant melanoma, osteosarcoma, etc.

Conclusion:

Research has significantly contributed to understanding the pathology and pathogenesis of ACC. However, ACC remains a complex disease with poor outcomes. The key to successful treatment is early diagnosis due to the overall poor prognosis, with adrenalectomy being the definitive cure. To date, mitotane represents the most effective drug as adjuvant therapy. We presented a patient who, during follow-up for resected colon adenocarcinoma, was incidentally found to have a lesion in the right adrenal gland on CT. Due to its size and results

consistent with subclinical Cushing's syndrome, the lesion was surgically removed, and histopathology confirmed it was ACC. The hydrocortisone curve indicates adequate substitution, and given the confirmed ACC, mitotane therapy was initiated alongside an initial increase in the hydrocortisone dose.

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