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Case Report

Not the Usual Suspects: Challenges of Detecting Nonfunctioning Adrenal Cortical Carcinoma – A Case Report

Sivoravong J, Ly TM, Nejtek VA* and Talari D
Department of Family Medicine, University of North Texas Health Science Center, USA

***Corresponding author:** Nejtek VA, Department of Family Medicine, University of North Texas Health Science Center, 3500 Camp Bowie Blvd., PCC 2.290, Fort Worth, TX 76107, USA, Tel: 817-735-0640; Fax: 817-735-0643; Email: Vicki.Nejtek@unthsc.edu

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Abstract

Adrenal Cortical Carcinomas (ACC) are rare affecting about 1 out of 1,000,000 persons in the general population with the median age of 46 years old at the time of diagnosis [1,2]. A tumor of the adrenal cortex may be functioning or nonfunctioning. A functioning adrenocortical tumor may produce excessive cortisol, aldosterone, testosterone, or estrogen that can be used to help clarify a diagnosis. Here, we report a case of nonfunctional adrenal cortical carcinoma in a middle-aged patient seeking treatment for severe low back pain. The patient had no documented past medical history, was not on any prescription medications, and had no abnormal screening laboratory values. An abdominal ultrasound showed an enlarged solid isoechoic mass in the upper medial pole of the left kidney. The workup found a Stage IV nonfunctioning ACC that had metastasized to the lumbar spine. This case is especially helpful in reminding family physicians to consider looking beyond typical ACC hormone dysfunction and consider investigating nonfunctioning ACC in the differential for intractable low thoracic and/or lumbar back pain.

Keywords: Adrenal Cortical Carcinomas; Atypical; Non-functional

Case Presentation

Physical findings

A 58-year old Caucasian male presented to the Emergency Room (ER) complaining of progressively severe left flank pain during the previous week. The pain radiated from his left flank across in a band like fashion to the anterior part of his abdomen. The patient had no documented past medical history, was not taking any prescription medications, had no fever or obvious signs of infection, no external injuries or muscle trauma. The patient denied headache, recent weight changes, chest pain, joint stiffness, swelling, nausea, and vomiting, neurologic or psychiatric difficulties.

The patient was initially treated with Intravenous (IV) saline fluids, IV dexamethasone 6 mg every six hours, and IV morphine drip were given for pain control. Break-through pain was managed using 60 mg of hydrocodone bitartrate with acetaminophen as needed every four hours. The patient also received 4 mg of oral ondansetron as needed every four hours for nausea-and ducosate sodium 100 mg twice daily for opioid-induced constipation. For Deep Venous Thrombosis (DVT) prophylaxis, the patient received a daily 40 mg subcutaneous injection of enoxaparin. A sudden onset of hypertension (presumably due to increasing pain) was controlled with 10 mg of Lisinopril and 25 mg of metoprolol XL. Subsequent urinary retention secondary to obstructive uropathy required catheterization and the addition of 50 mg of oral bethanechol plus 0.4 mg of tamsulosin hydrochloride (Table 1).

Laboratory results, imaging studies, differential diagnosis

Table 1 shows hospital admission laboratory results. Table 2 illustrates additional chemistry and endocrine studies conducted on days 1-7 of inpatient stay. Plasma metanephrine, normetanephrine, and dexamethasone suppression tests ruled out pheochromocytoma and Cushing's syndrome [3,4]. Radiographs showed lower spine degenerative disc disease (not shown). Ultrasound of the abdomen showed an enlarged solid isoechoic mass slightly anterior to the upper medial pole of the left kidney which provided physicians enough diagnostic justification to order additional imaging tests. Non-contrast Magnetic Resonance Imaging (MRI) of the lumbar spine showed arthrosis, moderately severe neural foramina narrowing, spondylosis, arthropathy, canal stenosis, broad-based Lumbar (L) and Sacral (S) disc bulges from L1, 2, L5 - S1 and a large mass involving L2 and L3. Abdominal Computed Tomography (CT) scan without contrast showed a large adrenal mass which was confirmed on MRI (Figure 1) and suggested metastasis to the lumbar spine. A CT-guided needle biopsy initially suggested ACC and the respected tissues from the subsequent adrenoectomy confirmed the ACC diagnosis (Figure 1 and 2).

Confirmatory diagnosis and patient course

The patient underwent adrenoectomy. The tumor was 13.5 cm in length, and weighed 236 grams and obliterated the left adrenal gland and has areas of vascular invasion. Tissue immunostain studies were negative for renal cell carcinoma Ag, chromogranin A, S-100 Ag, and leukocyte common antigen, but were positive for inhibin-α, melan A, synaptophysin, pan keratin and calretinin. Histological report revealed nested, trabecular, and thick columns of elongated or ovoid cells divided by a delicate vascular network with diffuse growth patterns indicative of ACC (Figure 2). Based on overall morphology, clinical presentation and immunostaining pattern, the pathologist classified this highly malignant neoplasm as a poorly

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Table 1: Admitting Vital Signs and Laboratory Test Results.

Admit Vital Signs	
Temperature	98.9
Respiration	18
Pulse	60
Oxygen saturation	95%
Blood pressure	
Systolic	152
Diastolic	99
Electrocardiogram	65 bpm
Admit Laboratory Studies (reference range)	---mEq/L--
Sodium (135-145)	144
Potassium (3.6-4.8)	4.2
Chloride (100-108)	104
Bicarbonate (22-29)	27
Magnesium (1.9-2.7)	1.9
----------	---Mg/dL--
Serum urea nitrogen (6-21)	15
Creatinine (0.8-1.2)	1.1
Blood glucose (70-100)	106
Ionized calcium (8.9-10.1)	7.9
Bilirubin (0.4-1.0)	0.4
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Hemoglobin (13.8-17.2 g/dL)	15.9
Hematocrit (38.8-50%)	45.6
Platelets (150-450 x 10^9/L)	209
White blood cell (3.8-10.8 x 10^9/L)	9.6
Mean corpuscular volume (81.2-95 fL)	88.7
Prothrombin (25-41 sec)	20.6
Phosphatase (50-160 units/dL)	72
Alanine (1-21 units/L)	38
Aspartate (7-27 units/dL)	24
Albumin (3.5-5.0 gm/dL)	3.6
Total protein (6.0-8.4 gm/dL)	6.1
Urinalysis	
Clear	
Negative	
Glucose, Ketones, Bilirubin, Protein, Blood, Nitrate, Leukocytes	

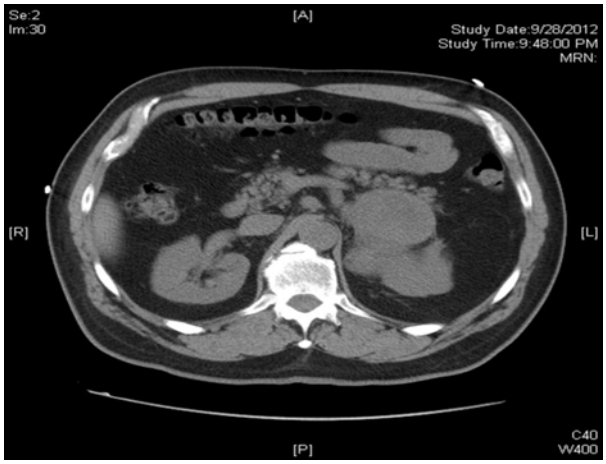

Figure 1: T2 weighted magnetic resonance image of ACC mass.

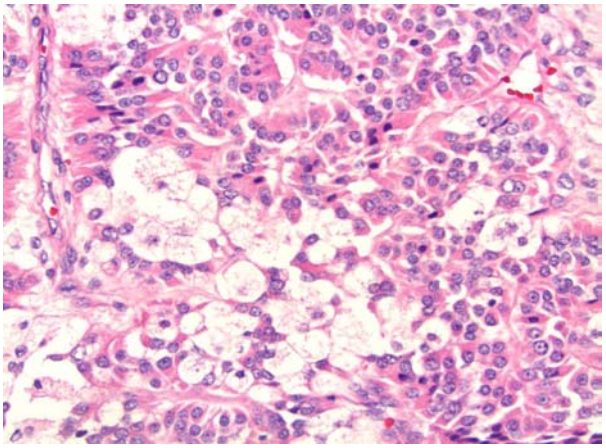

Figure 2: Histology shows diffuse growth patterns indicative of ACC.

differentiated adrenal cortical carcinoma. The invasion of the L2-3 lumbar spine and the size of the mass suggested the patient had stage IV metastatic cancer (McFarlane/Sullivan classification) [5]. After the adrenoectomy, the patient received follow-up treatment with oral mitotane (adrenal-specific pharmacotherapy) using a dosing strategy similar to Terzolo et al [6] and was given prednisone for prevention of hypocortisolism.

The patient was discharged to home with instructions to follow-up with the general surgeon and a hematology/oncology specialist in 2-weeks and a neurosurgeon within 1-week. Other discharge medications included oral 5 mg of hydrocodone bitartrate and 325 mg acetaminophen and oral 50 mg of morphine sulfate controlled-release taken as needed for pain plus 100 mg of ducosate taken twice daily for opioid-induced constipation. The prognosis for this patient is considered very poor. In line with the literature [3,7,8], this patient has an estimated post-surgery survival rate of about 14-months.

Discussion

Observable versus non-apparent risks

Nonfunctional ACC is difficult to diagnose compare to functioning adrenal mass due to the lack of pathological hormonal presentation [3,8-10]. The differential diagnosis of the adrenal mass in this case includes adenoma, myelolipoma, cyst, lipoma, pheochromocytoma, adrenal cancer, metastatic cancer, hyperplasia, and tuberculosis [3, 8-10]. Generally, about 50% of ACC are identified late in the disease process with distant metastasis in the lungs, liver, peritoneum, lymph nodes, and/or bones arising from other sources such as bronchogenic carcinoma, renal cell carcinoma or melanoma [2-4,8,9]. Although the patient presented here may represent less than one-third of all ACC cases, these dismal statistics suggest that many more nonfunctioning ACC cases potentially go unrecognized and untreated. Kapoor et al report the forensic prevalence of nonfunctioning ACC is as high as 8% discovered during autopsy [11].

One reason why earlier detection was obscured in this particular patient may be that the lower back pain may have been considered common given his age, as risks for nonfunctioning ACC may increase with age [11]. Another possible reason is that this patient did not present with endocrine abnormalities or the usual symptoms associated with functioning ACC. Thus, in the absence of these warning signs patients of any age are unlikely to seek medical treatment for back pain unless the pain has a sudden onset or is severe and intractable. These diagnostic difficulties suggest the need for heightened awareness of the risks and atypical clinical symptoms that may point towards ACC.

The mean age of diagnosis, in adults, is 45 years and men with adrenocortical carcinoma tend to have non-functional tumors after

Table 2: Additional Chemistry and Endocrine Study Results on Inpatient Days 1-7.

Chemistry	Reference Units	Collection Date	Collection Time	Actual Units
Day 1		**9-28**	**2025**	
Calcium Ioniz	1.12-1.32 mmol/L	"	"	1.10
Anion Gap	5.0-19.0 mmol/L	"	"	18.0
Glucose	70-110 mg/dL	"	"	106.0
BUN	7-18 mg/dL	"	"	15
Creatinine	0.8-1.3 mg/dL	"	"	1.1
Day 2		**9-30**	**0527**	
CRP	<0.29 mg/dL			0.88
Days 3 -4				
Cortisol	undefined ug/dL	10-02	1804	7.18
		10-03	0928	0.78
Day 5		**10-05**	**1223**	
Plasma				
Normetanephrine	0-145 pg/mL	"	"	83.0
Metanephrine	0-62 pg/mL	"	"	31.0
Day 6		**10-08**	**0436**	
Prealbumin	20.0-40.0 mg/dL			23.4
Venus Blood Gases	mmHg			
PH	7.350-7.45	"	1413	7.357
PCO2	44.0-48.0	"	"	51.4
PO2	38.0-42.0	"	"	27.9
HCO2	20-30 mmol/L	"	"	28.9
BASE EXCE	- 2 to +2	"	"	2.4
O2 SAT	60.0-80.0 %	"	"	48.5
Total CO2	21-31 mmol/L	"	"	30.4
Day 7		**10-09**	**1523**	
Urine	ug/L			
Metanephrine	undefined	"	"	44
Metanephrine Catecholamine	45-290 / 24 hr	"	"	81
Normetanephrine	Undefined	"	"	203
Normetanephrine Catecholamine	82-500 / 24 hr	"	"	376

the age of 40 years [12]. The majority of adrenal cortical cancers are sporadic but up to 15% are linked to genetic defects especially when seen in children. Genetic syndrome that have been linked to adrenal cancer are Li-Fraumeni syndrome, Beckwith-Wiedemann syndrome, Multiple Endocrine Neoplasia (MEN1), Familial Adenomatous Polyposis (FAP), and Hereditary Nonpolyposis Colorectal Cancer (HNPCC) also called Lynch Syndrome (http://www.cancer.org/acs/groups/cid/documents/webcontent/003081-pdf.pdf). Physicians should be aware of the possible link between nonfunctional ACC and radiating back pain due to the anatomical placement of an adrenal mass impinging on adjacent spinal nerves as in this case report. In terms of gender risks, Ng and Libertino (2003) [9] reported that in four out of seven studies (n=602), nonfunctional ACC was predominantly found in 62% of the women examined.

Suggested screening strategies

Currently, there are no clearly defined outpatients screening protocols to help identify nonfunctioning ACC. Here, we recommend adding a three-step preliminary differential screening protocol to help detect early stage nonfunctioning ACC in the outpatient setting: (1) consider age, sex, and presence of high risk genetic syndrome, (2) be suspicious with unexplained radiating and/or intractable low thoracic or lumbar back pain proximal to the adrenal gland area, (3) conduct ultrasonography tests as a screening method when patients meet criteria for #1 and #2. Thus, a potential change in examination and screening strategies in outpatient settings may be warranted in addition to becoming aware of the risk factors and unusual symptoms of nonfunctioning ACC. Due to the morbidity of late stage ACC, it is important for physicians to be vigilant in their examinations and thorough with the laboratory workup in 'at-risk' yet asymptomatic patients. This case serves to remind clinicians to look beyond the usual suspects and consider investigating an adrenal mass as nonfunctioning ACC may present only with intractable thoracic or lumbar back pain.

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