Cushing’s syndrome and bone metastases as the manifestation of adrenocortical carcinoma

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Article type: Clinical image

Received: January 6, 2021.

Accepted: February 14, 2021.

Published online: February 24, 2021.

ISSN: 1897-9483
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Short title: CS and bone metastases as the manifestation of ACC

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Conflict of interest: none declared
A 61-year-old woman was referred to an orthopedic clinic due to severe nontraumatic back pain. Lumbosacral computed tomography (CT) revealed compression vertebral body fractures Th11-L4, bone loss, and right adrenal tumor. Treatment with buprenorphine was initiated and the patient started using an orthopedic corset and a wheelchair. Additionally, the patient presented symptoms of Cushing’s syndrome (CS): abdominal obesity with thin limbs, a round red face, thinned skin, hypertension, diabetes requiring insulin, without hirsutism.

Clinical symptoms and the laboratory tests (increased cortisol levels without typical circadian rhythm 26.1 μg/dl at 6.00 AM, 29 μg/dl at 12:00 PM, decreased adrenocorticotropic hormone (ACTH) level (<5 pg/ml), hypokalemia 3.1 mmol/l) confirmed ACTH-independent CS. Abdominal CT verified a large right adrenal tumor, 60x47x51 mm, with heterogeneous contrast enhancement, delayed contrast washout, and compression vertebral body fractures. Dual-energy X-ray absorptiometry of the lumbar spine and the femoral neck revealed low bone mass.

The patient was referred to the Surgery Department for adrenalectomy. The histopathological examination documented adrenocortical adenomatous hyperplasia. Directly after surgery, clinically and hormonally persistent hypercortisolemia was observed. Thus, the control abdominal and thoracic CT were performed. The irregular hypodense lesion 51x28x26 mm on the post-adrenalectomy site with no contrast enhancement, and osteolytic lesions in the thoracic vertebral body, were shown. As the patient denied another operation, the metyrapone treatment was started and her condition improved. The third abdominal CT (after 4 weeks) presented the previously seen soft tissue lesion, with likely invasion of the surrounding tissues without any pathological lymph nodes, and multiple osteolytic lesions in bones. The second histopathology assessment also did not confirm adrenocortical carcinoma (ACC) (2/9 Weiss score). Due to the negative histopathological report and the rarity of bone metastases in ACC,
a $^{18}$F-fluorodeoxyglucose positron emission tomography ($^{18}$FDG-PET/CT) was performed to search for another malignancy. The $^{18}$FDG uptake was observed in postoperative site lesion SUV$_{max}$=3.1 and generalized osteolytic skeletal lesions SUV$_{max}$=5.2. It did not reveal any metastases to lymph nodes, lungs, liver or another malignancy. Studies strongly suggested ACC with bone metastases, further confirmed by surgical adrenal biopsy. Due to apparently metastatic disease, therapy with mitotane was initiated. Unfortunately, despite this therapy the patient died soon.

ACC is a very rare condition (0.7 to 2.0/million/year). About 50-60% of patients have clinical hormone excess, predominantly CS [1]. A bone loss in CS leads to fractures in approximately 30-76% of patients, especially at the vertebral site [2]. CT scans in these cases make the recognition of bone metastases difficult. ACC is usually metastatic at the time of diagnosis. The lung and liver are the most common metastatic locations [1]. Bone metastases are observed in up to 14% of patients with advanced ACC [3, 4]. The bone is the single metastatic site in only 9% of these patients [3].

Although CT and MR are the basic methods evaluating stage of ACC, and enabling adequate treatment, $^{18}$FDG-PET/CT can help localize all metastases. Nevertheless, despite typical clinical and radiological features, obtaining the histopathological confirmation of ACC is still a challenge and leads to a delay in chemotherapy.
References


Figure 1.

A – Lumbosacral computed tomography revealed right adrenal tumor

B – Computed tomography of the abdomen after right adrenalectomy revealed irregular hypodense lesion on the post-adrenalectomy site
C.D – MIP images showed multiple hypermetabolic bone metastases

E.F – $^{18}$FDG PET/CT showed high uptake of $^{18}$FDG in adrenocortical carcinoma

G.H – $^{18}$FDG PET/CT showed hypermetabolic osteolytic bone metastases in pelvic bones

Abbreviation: MIP: Maximum intensity projection; PET/CT: Positron emission tomography/Computed tomography; $^{18}$FDG: $^{18}$F-fluorodeoxyglucose; SUVmax, Maximum Standardized Uptake Value