

Usefulness of imaging modalities in providing timely optimal treatment in atypical clinical course of ectopic Cushing syndrome caused by pheochromocytoma

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Cushing syndrome (CS) due to ectopic adrenocorticotrophic hormone (ACTH) secretion (EAS) is a rare endocrine condition responsible for approximately 5% to 20% of all cases of CS.¹⁻⁴ In this group, pheochromocytoma is the source of ACTH only in about 5% of cases.⁵ We present 2 clinical cases of EAS caused by pheochromocytoma.

Patient 1 was a 70-year-old woman with a history of hypertension, hyperlipidemia, and ischemic heart disease as well as type 2 diabetes mellitus. The patient had been experiencing fatigue and muscle weakness for several months. She also reported decreased appetite and weight loss of 10 kg within 3 to 4 months. About 2 months earlier she had been hospitalized with suspected acute coronary syndrome. Coronary angiography had not revealed significant abnormalities, but it had been complicated by postcontrast acute kidney injury (AKI).

Because of mental confusion, head imaging was performed. Empty sella syndrome was suspected based on computed tomography (CT), which was confirmed by magnetic resonance imaging (MRI) of the pituitary gland. On admission, the patient was confused, with disturbed auto- and allopsychic orientation and blood pressure of 115/70 mm Hg. Edema of the legs, muscle atrophy, thin, dry skin with a diffuse hyperpigmentation as well as multiple petechiae and ecchymosis on the skin were present. Laboratory results are presented in Supplementary material, *Table S1*. Based on the clinical outcomes and the diagnostic workup to date, EAS caused by pheochromocytoma was suspected. Because of the recent episode of AKI, the patient was not referred for abdominal

CT scan as first-line imaging examination. Somatostatin receptor imaging (SRI) with gallium-68 labelled somatostatin analog was performed and an accumulation of the tracer in the right adrenal gland was observed (*FIGURE 1A*). Abdominal MRI confirmed a tumor (measuring 44 × 41 × 36 mm) in the right adrenal gland (*FIGURE 1B*). After pharmacological preparation, the patient underwent right-side laparoscopic adrenalectomy. Histological examination confirmed pheochromocytoma with chromogranin A and focal expression of ACTH-secreting cells (*FIGURE 1C* and *1D*). Unfortunately, on the ninth day after surgery the patient died of acute respiratory distress syndrome.

Patient 2 was a 61-year-old woman with a 2-month history of weight gain, proximal myopathy, depressive disorders, abdominal pain, diabetes mellitus of recent onset, and worsening control of hypertension. Physical examination revealed facial and leg edema, plethoric face, dermal and muscle atrophy and moderate central obesity. Laboratory results are presented in Supplementary material, *Table S1*. Abdominal CT scan and SRI showed a 30-mm mass in the right adrenal gland, with radiological suspicion of pheochromocytoma (*FIGURE 1E* and *1F*). After pharmacological treatment of the patient, the tumor was removed laparoscopically without complications. Histological examination confirmed pheochromocytoma with focal expression of chromogranin A and ACTH-secreting cells (*FIGURE 1G* and *1H*). Currently, the patient is in complete remission and does not require any treatment.

Ectopic ACTH syndrome caused by pheochromocytoma is extremely rare, but should be

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Received: February 18, 2021.

Revision accepted: March 15, 2021.

Published online: March 15, 2021.

Pol Arch Intern Med. 2021;

131 (5): 476-478

doi:10.20452/pamw.15877

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FIGURE 1

A–D – Patient 1;
A – somatostatin receptor imaging (SRI) with gallium-68 labelled somatostatin analog; accumulation of the tracer in the right adrenal gland (arrow); **B** – magnetic resonance imaging of the abdomen (coronal image) demonstrating right adrenal pheochromocytoma: a large heterogeneous mass measuring $44 \times 41 \times 36$ mm (arrow); **C, D** – histological examination showing diffuse expression of chromogranin A using anti-chromogranin A antibody (Ventana; LK2H10) (**C**) and focal reaction to adrenocorticotrophic hormone (ACTH) using ready-to-use primary antibody Anti-ACTH AM487-5M mouse monoclonal (clone AH26) (**D**) (magnification $\times 10$);
E–H – Patient 2;
E – abdominal computed tomography showing a 30-mm mass in the right adrenal gland (arrow) with radiological suspicion of pheochromocytoma; **F** – SRI with ^{99m}Tc labelled somatostatin analog; accumulation of the tracer in the right adrenal gland (arrow)

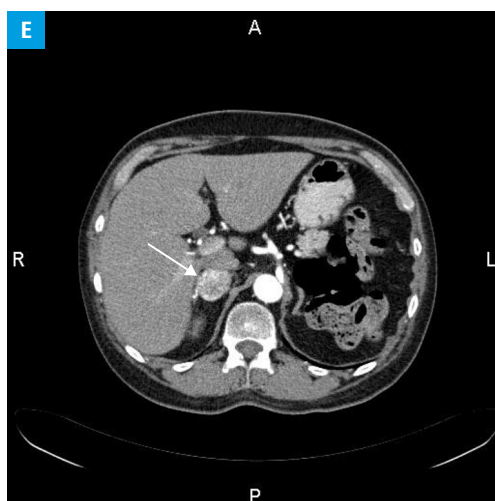
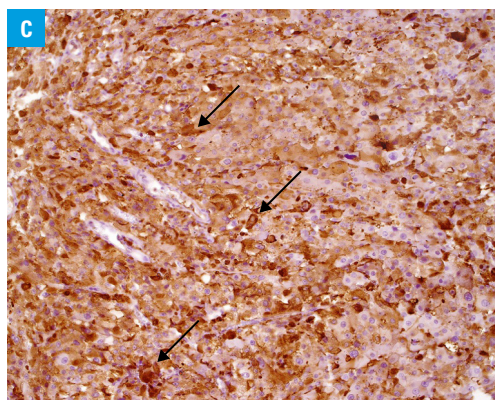
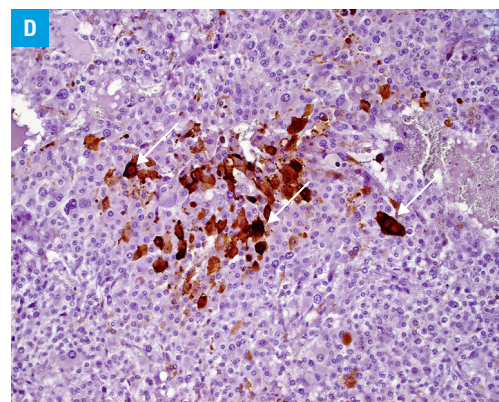
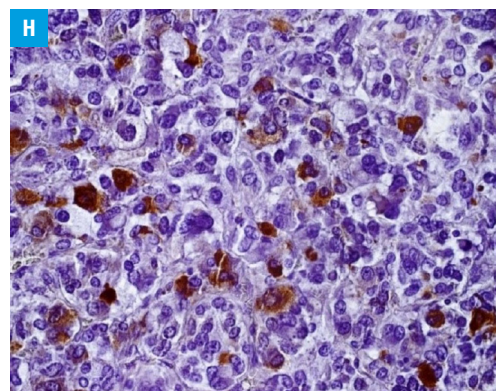
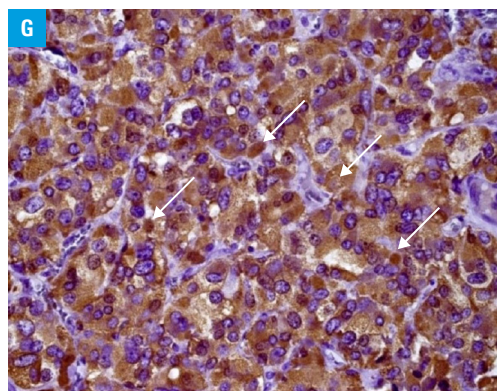


FIGURE 1

G, H – histological examination showing diffuse expression of chromogranin A using anti-chromogranin A antibody (Ventana; LK2H10) (**G**) and focal reaction to adrenocorticotrophic hormone (ACTH) using ready-to-use primary antibody Anti-ACTH AM487-5M mouse monoclonal (clone AH26) (**H**) (magnification $\times 20$)



considered as a possible source of ACTH production as it may be a life-threatening condition if not diagnosed early and treated properly. A longer history of CS and cardiac or renal burden are associated with worse prognosis.

SUPPLEMENTARY MATERIAL

Supplementary material is available at www.mp.pl/paim.

ARTICLE INFORMATION

CONFLICT OF INTEREST None declared.

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HOW TO CITE Kurzyńska A, Sowa-Staszczak A, Budzyński A, et al. Usefulness of imaging modalities in providing timely optimal treatment in atypical clinical course of ectopic Cushing syndrome caused by pheochromocytoma. *Pol Arch Intern Med.* 2021; 131: 476-478. doi:10.20452/pamw.15877

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