Brief conmmunication

Adrenocortical carcinoma: An extremely uncommon entity and the role of Immunohistochemistry in its diagnosis

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ABSTRACT

Adrenocortcal carcinoma is an extremely uncommon entity with an incidence of two in one millionth population. Here we present a 60 year gentleman with pain in abdomen, nausea, and backache, and weight loss. Contrast enhanced computed tomography (CECT) abdomen revealed a heterogenous well defined mass measuring (15 × 10.3 × 13) cm^3 on the left suprarenal region with central necrosis which extended medially up to the midline. Locally, the growth infiltrated the upper pole of left kidney. Initially, the differential diagnosis included that of renal cell carcinoma arising from upper pole of left kidney involving adrenal gland. The patient underwent left radical nephrectomy and left adrenalectomy. Histological evaluation could not differentiate it from of malignant pheochromocytoma, but immunohistochemistry confirmed it as adrenocortical carcinoma. This case highlights the crucial role of immunohistochemistry in establishing the diagnosis like tumors.

Key words: Adremanl mass, adrenocortical carcinoma, pheochromocytoma immunohistochemistry

Introduction

Adrenocortical carcinomas (ACC) are rare malignant tumors with poor prognosis. They show a bimodal age distribution occurring in childhood and in the 4th and 5th decades, with a slight female preponderance.[1,2]

Because of the juxtaposition of the adrenal gland to the kidney, it is not uncommon for ACC to involve the renal parenchyma. On the other hand, renal cell carcinoma (RCC) also frequently involves the adrenal gland.[1,3] Naturally, it is very difficult clinically and radiologically, and at times histologically, to differentiate between ACC and RCC. It is also difficult to differentiate ACC from lesions such as adrenal medullary neoplasms, adrenal adenoma, and secondaries to adrenals even in histological sections rendering immunohistochemistry essential.[4]

Access this article online	
Quick Response Code:	Website: www.ijem.in
	DOI: 10.4103/2230-8210.104098

Case Report

A gentleman aged 60 years presented with a moderate pain abdomen for 5 months and backache radiating to the hypochondrium for 1 month. He had nausea, low appetite, and mild weight loss (1.5 kg) during that period. He was treated for gastritis off and on with antacid, H2 blockers and proton pump inhibitors without significant relief of symptoms before coming to our center. On examination, a tender mass was palpable over left hypochondrium, left lumber region, and epigastrium crossing the midline. The central nervous system, cardio-vascular, and respiratory systems were clinically normal. He also did not have externally palpable lymphadenopathy in the cervical, supraclavicular and inguinal region. His complete blood count showed moderate anemia (hemoglobin 9.8 g/dL) and rather high erythrocyte sedimentation rate (135 mm at 1st h). Biochemical investigations showed venous plasma glucose, urea and creatinin electrolytes within biological

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reference range. Urinary VMA for 24 h was 2.60 mg/g creatinin (normal 1.8-6.7). On ultrasonography a solid, heterogeneous mass with central hypoechoic area measuring 14 × 13.1 cm seen in the left supra renal area. CECT abdomen revealed a heterogeneous well defined mass lesion with central necrosis measuring 15 × 10.3 × 13 cm in left suprarenal region medially extending upto the midline, and displacing or pressing on the nearby viscera in all directions. Radiological possibilites were two, namely: (i) ACC (left) infiltrating upper pole of left kidney and, (ii) RCC arising from upper pole of left kidney involving adrenal gland. The patient underwent left adrenelectomy and radical nephrectomy.

Results and Observations

Gross inspection of the surgical specimen revealed a glistening yellow-orange colored tumor measuring 12 × 10 cm, with areas of extensive hemorrhages, necrosis and cystic changes. It was infiltrating the upper pole of left kidney, rendering a demarcation between adrenal and kidney impossible. No definite capsule was noted. Cut section through the kidney neither revealed any tumor mass within renal cortex or medulla, nor any involvement of the renal vein. Microscopic examination of the mass showed a cellular tumor composed of cells arranged mostly in diffuse, and some trabecular, organoid pattern, supported by delicate fibrovascular stroma. Large areas of degeneration, necrosis, and hemorrhages were seen. Most of the cells were large, round, oval to polygonal with eosinophilic cytoplasm [Figure 1a]. Some of them showed clear cytoplasm. The nuclei, in general, were vesicular hyperchromatic and pleomorphic with some showing prominent nucleoli and abnormal mitotic figures (mitotic count 20-24/50 high-power field [HPF]) [Figure 1b]. A focus of vascular invasion by loose plug of tumor cells was seen [Figure 1c]. Immunohistochemistry for the tumor showed strong positivity for vimentin, granular positivity of synaptophysin, focal positivity for cytokeratin, negative for chromogranin A, ki67 labelling index was 21/50 HPF [Figure 1d].

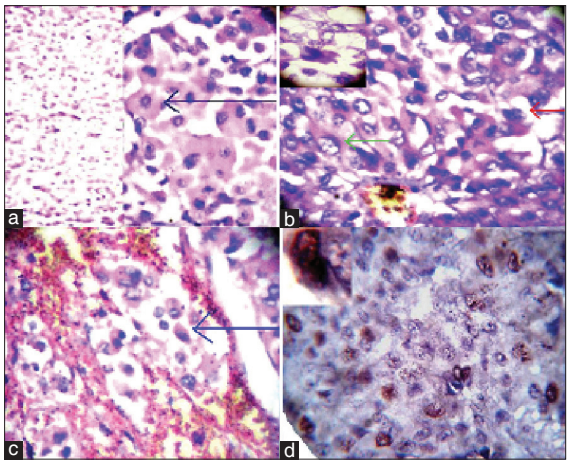

Figure 1: Light microscopic examination (a) showing a cellular tumor, composed of cells arranged mostly in diffuse pattern with some trabecular and organoid areas, supported by delicate and loose fibro-vascular stroma (left half). Variable areas of degeneration, necrosis, and hemorrhages are noted. Cells are large in size, round, oval or polygonal in shapes with bright eosinophilic cytoplasm (right half-light blue arrow). (H and E, ×10 and ×40), (b) showed the tumor cells with predominant eosinophillic cytoplasm (green arrow) and occasional cells with clear cytoplasm (red arrow). The nuclei are vesicular and pleomorphic with prominent nucleoli and abnormal mitotic figures (inset). Mitotic count 20-24/50 HPF. (H and E, ×100), (c) showing a focus of vascular invasion by loose plug of tumor cells (dark blue arrow), (H and E, ×100). (d) Immunohistochemistry showing high (21/50 HPF) ki67 labelling index, indicating mitotic activity.

Discussion

Certain histopathological parameters are useful in prognosticating ACC where mortality ranges from 70% to 92% within 12 months of diagnosis. Apart from advanced stage of disease, increased size and invasion of nearby structure, mitotic rate of more than 20/50 HPF heralds bad prognosis.[5,6] Because of anatomical proximity of adrenal glands and kidneys, it is possible that malignant lesion of adrenal cortex may involve the renal parenchyma and vice versa. It is therefore, necessary to make a systematic approach to inspect renal parenchyma in serial sections, and extensions.[3]

Morphologic distinction between adrenal cortical and medullary tumors can be difficult.[7] Macroscopic examination is the first important step toward diagnosis and should include accurate measurement of the specimens and description of the cut surface of the tumors. It is also essential to sample the specimens for histological diagnosis near foci of hemorrhage, and/or necrosis. Histological scoring systems evaluating multiple parameters, especially the criteria of Weiss, have been shown to be reliable in differential diagnosis.[4] There are nine histological criteria according to Weiss system of grading.[6] A tumor is labelled malignant when it meets three or more of these histological criteria.[8] In this case, seven out of nine criteria were fulfilled. Immunohistochemistry for nuclear proliferation associated antigen, Ki67 shown to be strongly correlated with malignant behavior was well documented in our case.

There are instances, where, an ACC can be very difficult to be differentiated from pheochromocytoma.[6] Presence of hyaline globules are very characteristic in pheochromocytoma, but it can sometimes be present in adrenocortical tumor as well.[7] Nuclear pleomorphism is comparatively higher in pheochromocytoma. In this particular case, higher nuclear pleomorphism, and

eosinophillic characteristic of cells and some cells with clear cytoplasm histologically made differentiation from pheochromocytoma difficult. However, application of the immunohistochemical marker leads to a definitive diagnosis of ACC. Negative reactivity of chromogranin A helps to exclude benign adrenal medullary tumor.

Conclusion

ACC which is an extremely rare entity, pauses diagnostic challenge in imaging due to its anatomic proximity and direct extension when sufficiently large to involve kidneys. Histological mimicry with adrenal adenoma, pheochromocytoma, RCC, and secondaries in adrenals should be categorically excluded by pathologists. The clinician as well as the pathologists should consider the application of immunohistochemistry as it has a crucial role in accurate diagnosis of the cases along with histology.

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Cite this article as: Gogoi G, Baruah MP, Borah P, Borgohain M. Adrenocortical carcinoma: An extremely uncommon entity and the role of Immunohistochemistry in its diagnosis. Indian J Endocr Metab 2012;16:S373-5.

Source of Support: Nil, **Conflict of Interest:** None declared