Adrenocortical Carcinoma - A Case Report

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Abstract :

Introduction : Adrenocortical carcinomas are very rare but highly aggressive tumors, accounting for 0.05 to 0.2% of all malignancies (1-2 cases per million population).Adrenocortical carcinomas have a bimodal age distribution, a small peak in first two decades and a larger one in fifth decade. While facing adrenocortical carcinomas, main 3 issues are: (i) To differentiate adrenocortical primaries from metastases and other primary tumors of adrenal, (ii)To distinguish adenoma from carcinoma and (iii)To predict clinical behavior.

Key words : Adrenocortical carcinoma, Metastasis

Introduction :

The pathological diagnosis of adrenocortical carcinomas is still a challenge because of its rarity and its morphological variants (oncocytic, myxoid and sarcomatoid). The presence of distant metastasis at the time of diagnosis is very common. 28 years ago, Weiss proposed the scoring system based on evaluation of nine parameters (nuclear grade, mitoses, atypical mitoses, clear cells, diffuse architecture, confluent necrosis, venous invasion, sinusoidal invasion and capsular invasion) and it is still widely applied with modifications and other approaches like immunochemistry.[1]

Case report :

In 2017, a 24 years old female presented to out-patient department with complaints of headache with confusion and diminution of vision in left eye since 1 month, associated with fever.

In 2013, patient had presented with mass in right adrenal gland and at that time, CT scan was done and it showed possibility of retroperitoneal mass with possibility of mesenchymal mass or malignant adrenal mass. Patient was operated and mass was removed and sent for histopathological examination and diagnosis given was, possibility of adrenocortical carcinoma. Immunohistochemistry was done and it showed positivity for Vimentin, Melan-A and Inhibin.

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Recent MRI brain showed well-defined lobulated, heterogenous; intensely enhancing space occupying lesion, suggestive of high grade neoplastic lesion, possibility of Meningioma or Metastasis was established. Recent PETSCAN showed no evidence of recurrent disease at the operated site in right adrenal gland and heterogeneously enhancing lesions in left parieto- occipital lobe of brain.

Patient was operated for the removal of left fronto-parietal space occupying lesion and it was then sent for histopathological examination.

On gross examination : Specimen consisted of multiple brownish soft tissue portions measuring 5×3×1.5 cm in aggregate.

On microscopy : Tumor was composed of solid sheets and papillary arrangement was seen. Tumor cells were pleomorphic with pink eosinophilic cytoplasm and prominent nucleoli. Atypical mitoses and necrosis were seen.

Figure 1: 10X magnification, H& E stain Showing sheets and papillary arrangement of tumor cells.

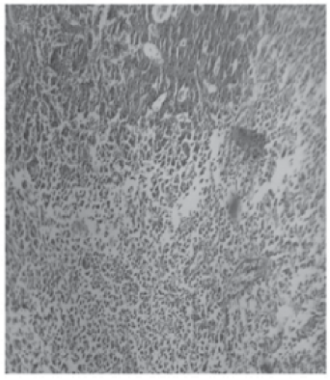
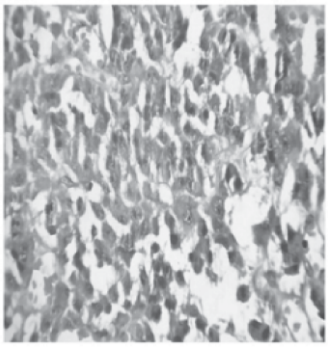


Figure 2: 40X magnification, H& E stain Showing pleomorphic tumor cells with eosinophilic cytoplasm and prominent nucleoli



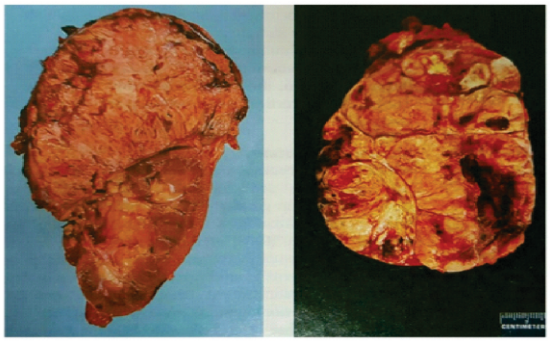
Discussion :

Clinical features: Non-functional, hormonally inactive adrenocortical carcinomas, accounting for approximately 40% of cases, typically present with any of the following: abdominal or loin pain, abdominal fullness, weight loss, fever or symptoms related to metastases. Hormonally active variants, constitute approximately 60% of cases; out of which 30-40% present with typical features of Cushing's syndrome, while 20-30% present with virilization syndromes.[2]

On gross examination: Tumor usually weighs more than 100 g, sometimes, more than 1000g.Capsule may/may not be present, and if present, often infiltrated by tumor. Areas of haemorrhage and necrosis are present. Tumor has a variegated pattern with solid and friable nodules. Invasion is frequent.[3]

Figure : 3(a)& 3(b): Gross appearance of adrenocortical carcinoma;showing areas of haemorrhage and necrosis.

Figure : 3(a) showing tumor destroying the upper pole of kidney.



3(a) **3(b)**

Fig 4: 40X magnification, H & E Stain,

Microscopic appearance of adrenocortical carcinoma; showing tumor cells with nuclear hyperchromasia, diffuse growth pattern and mitotic activity.

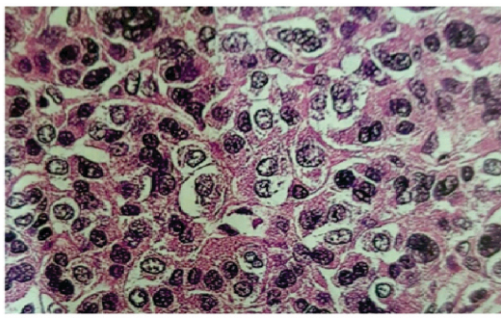


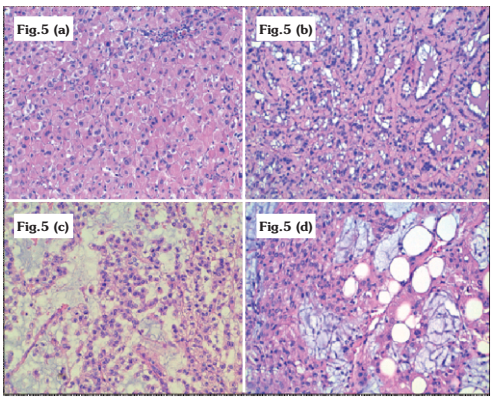
Fig.5 : (a)The oncocytic variant, with predominant solid pattern.*

Fig.5 : (b)The oncocytic variant, pseudo-glandular growth pattern.*

Fig.5 : (c)The myxoid variant with predominant deposits of myxoid material.*

Fig.5 : (d) The myxoid variant with focal lipomatous changes.*

***(10X magnification, H & E stain.)**



On microscopy: Foci of necrosis and haemorrhages are seen. Alveolar, trabecular or solid patterns of growth or admixtures of these patterns are seen. In some, foci of myxoid change, pseudoglandular patterns and spindle- cell growth patterns are seen. Cytoplasm may vary from vacuolated to eosinophilic, depending on their lipid content. In some, nuclei are small and uniform while in others, pronounced atypia-pleomorphism, coarse chromatin granularity and

Differential diagnosis :

Tumor	CK	VIM	NF	S-100	EMA	CEA	CG	SYN	BGI	AFP	MEL-A	CAL	INH
ACC	+/-	+	+/-	+/-	-	-	-	+/-	-	-	+	+	+
Pheochromocytoma	-	+/-	+	+	-	-	+	+	-	-	-	-	-
RCC	+	+	-	+/-	+	-	-	-	+	-	-	-/+	-/+
HCC	+	+/-	-	+/-	+/-	+	-	-	+/-	+	-	-	-/+
Met ACC	+	+/-	-	+/-	+	+	-	-	+/-	-	-	-/+	-
Lipo-sarcoma	-	+	-	+	-	-	-	-	-	-	-/+	-	-

CK- Cytokeratin, **VIM**- Vimentin, **NF-** Neurofilament, **EMA-** Epithelial membrane antigen, **CEA-** Carcinoembryonic antigen, **CG-** Chromogranin, **SYN-** Synaptophysin, **BGI**- Blood group isoantigen, **AFP-** Alfa- fetoprotein, **MEL-A-**Melan-A, **CAL-** Calretinin, **INH-** Inhibin

-EMA and CEA Positive for Metastatic adrenocortical carcinomas and negative for adrenocortical carcinomas.

-Positivity for NSE and Synaptophysin suggests Neuroendocrine feature of adrenocortical carcinomas.[4]

multiple prominent nucleoli are seen. Atypical mitotic figures and nuclear pseudo-inclusions often predominate.[4]

Gross and microscopic appearance of tumor

Gross appearance: In Fig. 3(a) & 3(b), both specimens show large areas of haemorrhage and necrosis. In figure 3(a), tumor has destroyed the upper pole of kidney.

Microscopic appearance: In Fig. 4, tumor shows nuclear hyperchromasia, diffuse pattern of growth and mitotic activity. Morphological variants: Three variants are seen. (i) Oncocytic (ii) Myxoid & (iii)Sarcomatoid. Oncocytic variant is most common. ACCs (Adrenocortical Carcinomas) very frequently display the mixture of different patterns either in terms of architecture or cytological features. So more often, all morphological variants are considered commonly as "CONVENTIONAL CARCINOMAS".[4]

Metastatic potential : The chances of metastases in ACCs to different organs in a decreasing order of occurrence is liver, lungs, retroperitoneum, IVC, serosa of intestine, lymph nodes(abdominal more than thoracic), bone, peritoneum, kidney, diaphragm, heart, spleen, pancreas, thyroid ,brain & skin.

Features found only in metastasizing/recurring adrenocortical tumors: Mitotic rate > 6/ 50 HPFs, atypical mitoses, invasion of venous structures.[4]

Treatment and prognosis of adrenocortical carcinomas: Most respond poorly to treatment. Complete surgical excision is the mainstay of treatment. Tumor is extremely resistant to chemotherapy. ACCs are having poor prognosis, mortality in adults' ranges from 70% to 90 %. Prognostic parameters involve tumor stage, mitotic rate and invasion of adjacent organs. Tumors with $\geqslant$ 20 mitoses/ 50 HPFs are High grade ACCs with mean survival of 14 months. Tumors with $\leqslant$ 20 mitoses/ 50 HPFs are Low grade ACCs with mean survival of 58 months.[4]

Conclusion:

Histopathological evaluation of adrenocortical carcinomas is interesting, and a challenge because of its rarity, morphological variants, high aggressiveness and poor prognosis. Genetic studies are continuously introducing novel molecular markers useful for IHC profiling.

References :

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