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HISTOPATHOLOGICAL SPECTRUM OF ADRENAL GLAND LESIONS – TWO YEAR EXPERIENCE IN A TERTIARY CARE CENTRE OF NORTH EAST INDIA

Pathology

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ABSTRACT

Introduction – Adrenal gland tumours are quite uncommon. They are asymptomatic and most of the times, discovered incidentally. They are more common in adult age with a female sex predilection. They can be either benign or malignant with a diverse and overlapping morphologic spectrum. This study has been undertaken with the following aims and objectives : 1) To analyze the spectrum and frequency of adrenal lesions. 2) Application of the "Pheochromocytoma of the Adrenal gland Scaled Score" to separate benign from malignant Pheochromocytoma . **Materials And Methods –** This study is conducted for a period of 2 years from January 2021 to December 2022 in the Department of Pathology of Gauhati Medical College and Hospital. All cases of adrenal lesions are included in the study. **Results –** Our study population consisted of 10 females and 8 males. There were 18 adrenal gland lesions, 13 (72.22%) benign and 5 (27.78%) malignant. The different adrenal gland lesions in decreasing order of frequency are Pheochromocytoma (38.89%), Myelolipoma (27.78%), Adrenal adenoma (22.22%); Adrenocortical sarcomatoid carcinoma and Epithelial cyst each (5.56%) respectively. **Conclusion –** Approach to the management of Adrenal gland lesions should be multidisciplinary based on clinical picture, biochemical, radiological, histopathological diagnosis and if necessary ancillary investigations like immunohistochemistry.

KEYWORDS

adrenal adenoma, adrenocortical carcinoma, adrenal myelolipoma, pheochromocytoma

INTRODUCTION

Tumours of the Adrenal gland are in general rare. They may originate either from the adrenal cortex or medulla. Adrenal cortical adenomas are common with an approximate prevalence of 6% according to a summary of 25 autopsy studies.[1-2] More than 85% of adrenal neoplasms which are discovered incidentally by imaging techniques are adenomas.[3] Adrenocortical carcinoma is a rare endocrine malignant neoplasm with an estimated incidence of 0.5–2.0 cases per million per year[4-6]. It is more common in adults (females) with a peak in the fifth decade of life. The sarcomatoid variant of ACC was first reported in 1987 by Okazumi et al.[7] Pheochromocytoma is an uncommon neuroendocrine tumour that originates from the adrenal medulla. It is more common in adult (females) in the fourth decade.[8-10]

AIMS AND OBJECTIVES

1) To analyze the spectrum and frequency of adrenal lesions.
2) Application of the "Pheochromocytoma of the Adrenal gland Scaled Score" to separate benign from malignant Pheochromocytoma .

MATERIALS AND METHODS

This study is conducted for a period of 2 years from January 2021 to December 2022 in the Department of Pathology of Gauhati Medical College and Hospital. Cases of adrenal gland lesions were sent to the Pathology Department from Urology and Endocrinology Department. Clinical history with relevant biochemical and radiological investigations were gathered and specimen grossed and processed according to the standard operating procedure of the Department. The sections were stained in Haematoxylin and Eosin and mounted with DPX. Slides were screened, analysed and reports dispatched. Data was entered in Excel spreadsheet and statistical analysis done.

RESULTS

Our study population consisted of 10 females and 8 males. The mean age was 39.76 years with maximum age of 65 years and minimum of 17 years. There were 18 adrenal gland lesions, 13 (72.22%) benign and 5 (27.78%) malignant; 66.67% on the right side and 33.33% on the left side. The different adrenal gland lesions in decreasing order of frequency are Pheochromocytoma, Myelolipoma, Adrenal adenoma, Adrenocortical sarcomatoid carcinoma and Epithelial cyst.

Table 1 – Spectrum of Adrenal Lesions

Adrenal Lesion	Number	Percentage
Adrenal Adenoma	4	22.22
Adrenal Myelolipoma	5	27.78
Adrenocortical sarcomatoid carcinoma	1	5.56
Pheochromocytoma	7	38.89
Adrenal Epithelial cyst	1	5.56

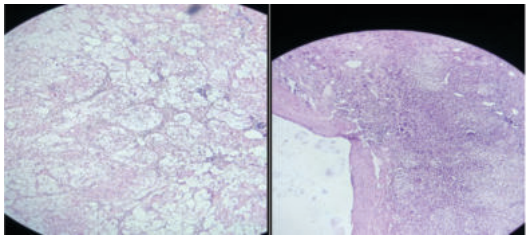

Figure 1 (A) H&E (100X) of a case of Adrenal cortical adenoma showing sheets and nests of cells that are large, polyhedral with admixture of clear and compact cytoplasm with distinct cell borders. Nuclei are round, uniform with occasional prominent nucleoli.Scattered foci of lymphocytic infiltration are also noted. (B) H&E (100X) of a case of Adrenal epithelial cyst showing flattened epithelium lining fibrocollagenous wall overlying the normal adrenal cortex.

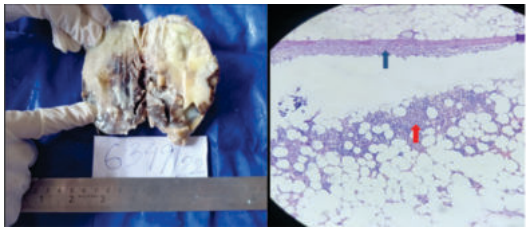

Figure 2 (A) Gross image of a case of Adrenal Myelolipoma : cut section showing an encapsulated mass which is solid, yellowish with few brownish areas (B) H&E (100X) of a case of Adrenal Myelolipoma showing sheets of trilineage haematopoietic cells (myeloid, erythroid and megakaryocytes - red arrow) admixed with mature adipocytes. A rim of adrenal cortical cells is seen in the upper half – blue arrow.

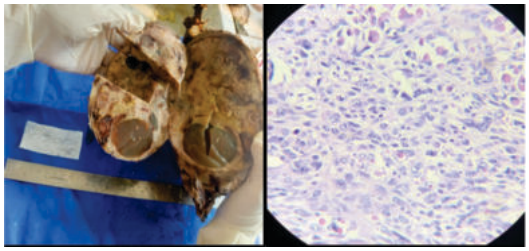

Figure 3(A) Gross image of an adrenal gland tumour: on cut section, it is encapsulated and solid with variegated appearance containing areas

of haemorrhage and necrosis. A uniloculated cyst containing gelatinous material is also noted in the lower half. (B) H&E section (400X) showing a tumour composed of dual population of epithelial component in the upper one fourth and mesenchymal component in the lower three fourth. The mesenchymal component consists of highly pleomorphic atypical spindle cells with enlarged bizarre nucleus and atypical mitotic figures. The epithelial component consists of sheets of atypical epithelial cells with moderate to abundant eosinophilic cytoplasm and eccentrically placed hyperchromatic nuclei with prominent nucleoli.

Table 2 – Table showing the PASS for all the cases of Pheochromocytoma

Histologic feature	Score	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
Periadrenal adipose invasion	2	-	-	-	-	-	-	2
>3 mitoses/10HPF	2	-	-	-	-	-	-	-
Atypical mitoses	2	-	-	-	-	-	-	-
Necrosis	2	-	2	2	-	-	-	2
Cellular spindling	2	-	2	2	-	-	2	-
Marked nuclear pleomorphism	1	1	-	1	1	-	-	-
Cellular monotony	2	-	-	2	-	-	-	-
Large nests/diffuse growth	2	-	2	2	-	2	2	2
High cellularity	2	-	-	-	-	-	-	-
Capsular invasion	1	-	-	-	-	-	-	1
Vascular invasion	1	-	-	-	-	-	-	-
Hyperchromasia	1	1	-	-	-	-	1	-
Total	20	2	6	9	1	2	5	7

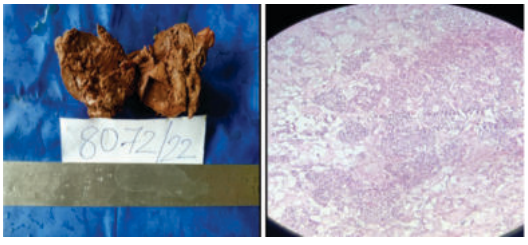

Figure 4 (A) Gross image of a Pheochromocytoma : cut section is solid and tan brown. (B) H&E(100X) showing circumscribed tumour mass with ill defined nests of tumour cells with moderate to abundant granular cystoplasm with predominantly uniform looking round vesicular nuclei with nucleoli. Intervening stroma is scanty. Mitotic figures <2/10HPF.

DISCUSSION

According to the WHO classification 2022, tumours of the adrenal cortex are divided into adrenal cortical carcinoma, adrenal cortical adenoma, sex cord stromal tumours, adenomatoid tumour, Mesenchymal and stromal tumours (Myelolipoma, Schwannoma), Hematolymphoid tumours and secondary tumours. Tumours of the adrenal medulla are divided into Pheochromocytoma, Extra-adrenal paraganglioma, Neuroblastic tumors of the adrenal gland, Composite pheochromocytoma and Composite paraganglioma. Adrenocortical nodular disease is classified into Sporadic nodular adrenocortical disease, Bilateral micronodular adrenocortical disease, Bilateral macronodular adrenocortical disease.[11]

ADRENAL CORTICAL ADENOMA – It is a benign tumour of the adrenal cortical cells. It is more common in females in the third to fifth decade of life.[12] In our study, there were 4 cases of adrenal adenomas, out of which 50% were in females and 50% in males. All the cases were in the third to fifth decade of life. Adenomas are generally small, well circumscribed and encapsulated with a solid homogeneous yellow to tan appearance. On microscopy, the tumour cells are clear to lightly eosinophilic and are filled with small lipid vacuoles and organized in nests or cords with a rich capillary vasculature or sinusoidal network.[13]

ADRENAL EPITHELIAL CYST – Adrenal cysts are rare with an incidence of 0.06%.[14] They occur in all ages with a peak in the fourth to fifth decade of life. The presence of adrenal tissue in the wall is diagnostic of adrenal origin. It is essential to rule out malignant adrenal neoplasm undergoing cystic change and also parasitic cyst whenever we come across an adrenal cyst. Large symptomatic cysts are treated by surgery or ultrasound guided percutaneous drainage.[15]In our study we found only 1 case of Adrenal epithelial cyst.

ADRENAL MYELOLIPOMA – Adrenal myelolipoma accounts for 3.3%-3.6% of all adrenal tumours with an equal incidence in both genders in the fifth to sixth decade of life. They are mostly discovered incidentally.[16] Grossly, they are either encapsulated or lack a capsule; cut section is solid yellowish with areas of haemorrhage. On microscopy, they consist of mature adipocytes and haematopoietic cells of all three lineages, erythroid, myeloid and megakaryocyte. Small asymptomatic masses are managed conservatively whereas large symptomatic myelolipomas are treated by surgical resection. In our study, they were the second most common adrenal lesions next only to pheochromocytoma.

ADRENOCORTICAL SARCOMATOID CARCINOMA – In our study, a young male with left abdominal mass and pain with non-functioning adrenal glands was incidentally found on radiology as an adrenocortical carcinoma and on histopathology as a case of Adrenocortical sarcomatoid carcinoma with concomitant oncocytic features. Grossly, the tumour was encapsulated, solid and variegated with areas of haemorrhage and necrosis. On microscopy, the tumour was biphasic with both epithelial and mesenchymal components. The epithelial component consisted of sheets and nests of atypical epithelial cells with moderate to abundant eosinophilic cytoplasm and eccentrically placed hyperchromatic nuclei with prominent nucleoli. The mesenchymal component comprised of sarcomatous change with haphazardly arranged fascicles of atypical spindle cells with moderate to severe pleomorphism. Many bizarre cells and atypical mitotic figures were noted. Cystic degeneration and abundant necrosis were also noted. Following are the Weiss Scoring Criteria for the classification of Adrenal neoplasms : 1)Tumor necrosis 2)Mitotic rate >5 mitoses per 50 high-power fields 3)Atypical mitoses 4)High nuclear grade (Fuhrman criteria for grade III or IV) 5)Diffuse architecture >30% of tumour volume 6) < 25% clear cells 7)Invasion of venous structures 8)Invasion of sinusoidal structures 9)Invasion through the capsule. Each criteria is given a score of 1. The Modified Weiss Scoring System of Adrenal neoplasms is as follows : Mitotic count >5/50HPF -2, Clear cells <25% - 2, Atypical mitosis – 1, Necrosis -1, Capsular invasion – 1. The presence of > 3 of the above criteria points towards malignancy.[13]Treatment consisted of surgery. In cases of advanced disease, palliative treatment with Mitotane is given. Sarcomatoid Adrenocortical carcinoma has a very poor prognosis with frequent metastases, with the majority of patients dying within 3–12 months after surgical treatment.[17-21]

PHEOCHROMOCYTOMA – Pheochromocytoma is a tumour originating from the adrenal chromaffin cells with a tendency to secrete catecholamines; the hypertensive episodes depending on the secretion of the same. Approximately 90% of phaeochromocytomas arise in the adrenal gland, and 10% originate from extra-adrenal chromaffin tissue.[22] The typical triad of tachycardia, headaches and sweating attacks are present only in about 25% of the cases. Mutations in genes RET, NF1, VHL, SDHA, SDHB, SDHC, SDHD,SDHAF2, MDH2, PHD1/PHD2, IDH1, HIF2A/EPAS1/2, TMEM127, HRAS, MAX, MAML3 and SDE1 have been found in pheochromocytoma. Genetic conditions associated with pheochromocytoma are Multiple endocrine neoplasia 2 syndrome, types A and B, Von Hippel-Lindau syndrome, Neurofibromatosis type 1, Hereditary paraganglioma syndrome,Carney-Stratakis dyad (paraganglioma and gastrointestinal stromal tumor) and Carney triad (paraganglioma, GIST, and pulmonary chondroma).[13] Confirmation of diagnosis is by testing for the evidence of catecholamine production, by plasma free metanephrines or urinary fractionated metanephrines. Grossly, the tumour is solid and reddish brown.On microscopy, tumor cells are arranged in well-defined nests ("Zellballen") or trabeculae bound by a delicate fibrovascular stroma. Cells are pleomorphic with a granular basophilic to amphophilic appearance. Nuclei are round to oval with presence of nucleoli.[13]Pheochromocytoma of the Adrenal gland Scaled Score (PASS) is employed to assess the nature of Pheochromocytoma, whether benign or malignant. PASS score > 4 is considered concomitant with malignancy. The histopathological characteristics and PASS scoring of all 7 cases of pheochromocytoma are detailed in Table 2. Treatment of Pheochromocytoma is Surgery although it is challenging for large lesions because of the extensive vascularization, difficulties in mobilization and dissection of the adrenal gland.[23]

CONCLUSION

Tumours of the adrenal gland are uncommon and can occur in any age group with a predilection for elderly and the female gender. They can be either benign or malignant with variable size. Radiology and biochemical investigations aid in the diagnosis of adrenal tumours. Definitive diagnosis is by histopathology. Weiss score and Pheochromocytoma of the Adrenal gland Scaled Score are applied in the distinction of benign and malignant tumours. Treatment is by surgery unless asymptomatic or contraindicated.

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Conflicts Of Interest – None

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