Clinicomorphological study on endocrine gland neoplasms excluding thyroid

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Abstract

Introduction: Although endocrine cancers are relatively uncommon, they represent an important group of potentially treatable cancers.

Materials and Methods: This clinicomorphological study on endocrine neoplasms excluding thyroid had total of 26 cases of endocrine neoplasms. Clinically suspected patients were histopathologically studied.

Results: Among the 26 cases, most cases belonged to tumours of parathyroid [10 cases (38.46%)], followed by adrenal gland neoplasms [8 cases (30.77%)], tumours of pituitary [6 cases (23%)] and pancreatic endocrine neoplasms [2 cases (7.69%)]. Majority of the patients were between 20–60 yrs age group except for pancreatic endocrine neoplasms, were it was < 20 years of age. Tumours of pituitary and parathyroid showed female predominance while both adrenals and pancreas showed an equal male: female ratio. Clinical presentations were different for each tumour, except for the constitutional symptoms like fatigue and weakness.

Conclusion: In this present study more number of incidence of tumour cases observed higher in parathyroid followed by Adrenal, Pituitary and Pancreas.

Keywords: Endocrine gland neoplasms, Histopathological types, Hematoxylin and eosin staining.

Introduction

Endocrine system refers to the collection of glands of an organism that secrete hormones directly into the circulatory system to be carried towards distant target organs.[1]The major endocrine glands include the pineal gland, pituitary gland, pancreas, ovaries, testes, thyroid gland, parathyroid gland, hypothalamus, gastrointestinal tract and adrenal glands. Special features of endocrine glands are, in general, their ductless nature, their vascularity, and commonly the presence of intracellular vacuoles or granules that store their hormones. The endocrine system is a complex mode of communication between the body's tissues, involving complex feedback loops, mediated by secreted hormones, between glands and organs around the body. The information conveyed by these secreted hormones is critical for good health and well-being, as these feedback systems control normal development, growth, reproduction, metabolism, and fluid balance. Several processes can disturb the normal activity of the endocrine system, including impaired synthesis or release of hormones, abnormal interactions between hormones and their target tissues, and abnormal responses of target organs.[2] Endocrine diseases can be generally classified as: diseases of underproduction or overproduction of hormones and their resulting biochemical and clinical consequences and diseases associated with the development of mass lesions. Such lesions might be non-functional, or they might be associated with overproduction or underproduction of hormones.[3] Endocrine tumours are defined as neoplastic lesions resulting from the proliferation of cells engaged in an endocrine differentiation pathway, as shown by their expression of a set of specific markers, including true endocrine markers (such as chromogranin A) and neuro-endocrine markers, shared between neurons and endocrine cells (such as synaptophysin).[3] Before the new WHO classification, the tumours of the disseminated endocrine system were referred to as "carcinoids".[4] This term was used for the first time in 1907 by Oberndorfer, for those epithelial tumours with relatively monotonous structure and less aggressive behaviour than carcinomas.[5] Because an endocrine tumour arises from cells that produce hormones, the tumour itself can produce hormones and cause serious illness. Majority of the endocrine tumours are benign with some being malignant.

The risk factors for development of these tumours include age, gender, race, and positive family history of multiple endocrine neoplasia type 1, immunosuppression and exposure to sun, arsenic and radiation. The study of endocrine diseases requires integration of morphologic findings with biochemical measurements of the levels of hormones, their regulators, and other metabolites.

However, it is often difficult to obtain an epidemiological perspective for endocrine tumours, either because of asymptomatic disease which results in incomplete case ascertainment or the rarity of individual tumours.[6] Tumours of endocrine glands, although rare in the context of the overall burden of oncological disease, have provided important insights into the mechanisms of sporadic and familial tumour formation, with an overt incidence of 0.6–1.5 per 100 000 per year.[7] Other malignant endocrine tumours, including adrenocortical carcinoma, carcinoid and other neuroendocrine tumours are extremely rare, with incidence figures of <0.5 per 100 000 per year.[6] Parathyroid tumours giving rise to hyperparathyroidism are more common, with a minimum incidence of 28 per 100000 per year but the tumours are rarely malignant.[8]

This study has been designed to evaluate the incidence of endocrine neoplasms excluding thyroid along with

clinical manifestations, demographic variables and histopathological types of different tumours of pituitary, parathyroid, pancreas and adrenal glands that were received in the department of Pathology of Narayana Medical College.

Materials and Methods

The present study was conducted in the department of Pathology, Narayana Medical College, Nellore, during the tenure of 2 years. From the total 50 cases of endocrine neoplasm received in our department, this study focuses on 26 specimens of endocrine neoplasms involving Pancreas, Pituitary, Parathyroid and Adrenal glands. The remaining cases belonged to thyroid gland.

Histopathology

An attempt was made to diagnose the lesion on gross visualization and to correlate them histopathologically. After adequate fixation entire tissue was routinely processed and embedded in paraffin. Four micron thick sections were cut perpendicular to this surface, three to four sections were prepared on each slide and were stained using Hematoxylin and Eosin staining procedure.

Inclusion Criteria

Organs studied – pituitary gland, parathyroid gland, endocrine pancreas and adrenal gland.

Exclusion Criteria

Other Endocrine organs and neuroendocrine tumours were exempted from this study.

Methodology

Specimens received were analysed and the occurrence of each subtypes were tabulated and its % ages were calculated and compared with other studies. Similarly, demographic variables like age and sex of the patient and the clinical presentations of these tumours were also tabulated and compared with other studies.

Photography

The digital images of the selected slide preparations were photographed using a SONY cyber-shot digital camera attached to Olympus BX31 Microscope.

Results

The total of 26 cases were obtained during the two year tenure of the current study. The incidence of pituitary, parathyroid, pancreas, and adrenal tumours observed as 6, 10, 2, and 8 cases respectively.

Pituitary Neoplasms

In the present study, all the 6 cases of pituitary neoplasm belonged to pituitary adenoma (100%). Incidence of pituitary neoplasm in different age groups was studied, by dividing the cases into four groups i.e. 0-20 years, 21-40 years, 41-60 years and 61-80 years respectively. More number of cases belonged to 21-40 years and 41-60 years (3 cases each; 50%), with mean age of 45.3 years, while the remaining age groups of 0-20 years and 61-80 years had no cases.

Frequency of pituitary neoplasm in males and females were assessed among the 26 diagnosed cases. Out of the 6 cases of pituitary neoplasm, all the 6 cases were diagnosed pituitary adenoma and our study shows female predominance, (4 cases, and 66.67%), with male: female ratio of 1: 2.

Among the 6 cases of pituitary adenomas studied, majority of the patients presented with visual disturbances (5 cases, 83.33%) followed by headache (4 cases, 66.67%). 1 case each (16.67%) of abnormal hormone effects like Hyperprolactinemia, in form of amenorrhoea and galactorrhoea, and Cushing's syndrome.

Parathyroid Neoplasms

Among the 10 cases of parathyroid neoplasms studied, 9 cases (90%) had parathyroid adenoma, accounting for maximum number of cases and 1 case (10%) had parathyroid carcinoma.

In the present study the age groups were divided into four categories, ranging from 1 – 80 years of age. 1 case was in age group 0-20 years. 2 cases each in 21-40 years and 61-80 years. 5 cases in 41-60 years, accounting for maximum number of cases (50%). Mean age was found to be 46.9 years.

For all the 10 cases of parathyroid neoplasms encountered, their frequency of distribution was studied in both males and females. Among them, maximum number of cases belonged to female gender 6 cases (60%) and 4 cases were seen among males (40%), accounting for male: female ratio of approx 1:1.5.

From the total of 10 cases of parathyroid neoplasm, majority had bone pains (90%), followed by fracture and hypercalcaemia (8cases, 80%). 2 cases (20%) had palpable neck mass, also fatigue and weakness (5 cases, 50%) as their presenting complaint. On further investigation, 8 cases had nephrolithiasis (80%) and one case had Brown tumour.

Adrenal Gland Neoplasms

Histological types

Among the 8 cases studied, 5 cases (62.5%) had pheochromocytoma, 2 cases (25.00%) had adrenal cortical adenoma and 1 case (12.5%) had adrenal cortical carcinoma. Maximum number of cases belonged to Pheochromocytoma (5 cases, 62.50%)

The incidence of adrenal gland tumours in different age groups were studied by dividing them into four categories i.e. 0-20 years, 21-40 years, 41-60 years and 61-80 years. 1 case was in age group 0-20 years, 2 cases in age group 21-40 years and 3 cases in age group 41-60 years. Majority of the cases were in the age group of 21-40 years (4 cases, 50.00%), with mean age being 30.3 years.

Frequency of adrenal tumours in males and females was assessed. Out of the total 8 cases studied, 4 cases each belonged to males and females, resulting in male: female ratio of 1:1.

Majority of the cases with Adrenal cortical neoplasm had cushing's syndrome, while all Adrenal medulla tumours had hypertension as their clinical manifestation. Adrenal cortical carcinoma had virilising syndrome and weight loss. Other symptoms like anorexia, fatigue, weakness were seen in few cases.

Pancreatic Endocrine Neoplasm

Pancreatic endocrine tumours were the smallest group of endocrine neoplasm in the present study, accounting for 2 cases. Among these 2 cases, the frequency of pancreatic endocrine neoplasm was found to be more in 0-20 year's age group, with equal gender distribution. Majority of the patients presented with fatigue, weakness, sweating, epigastric pain, diarrhoea and diabetes mellitus.

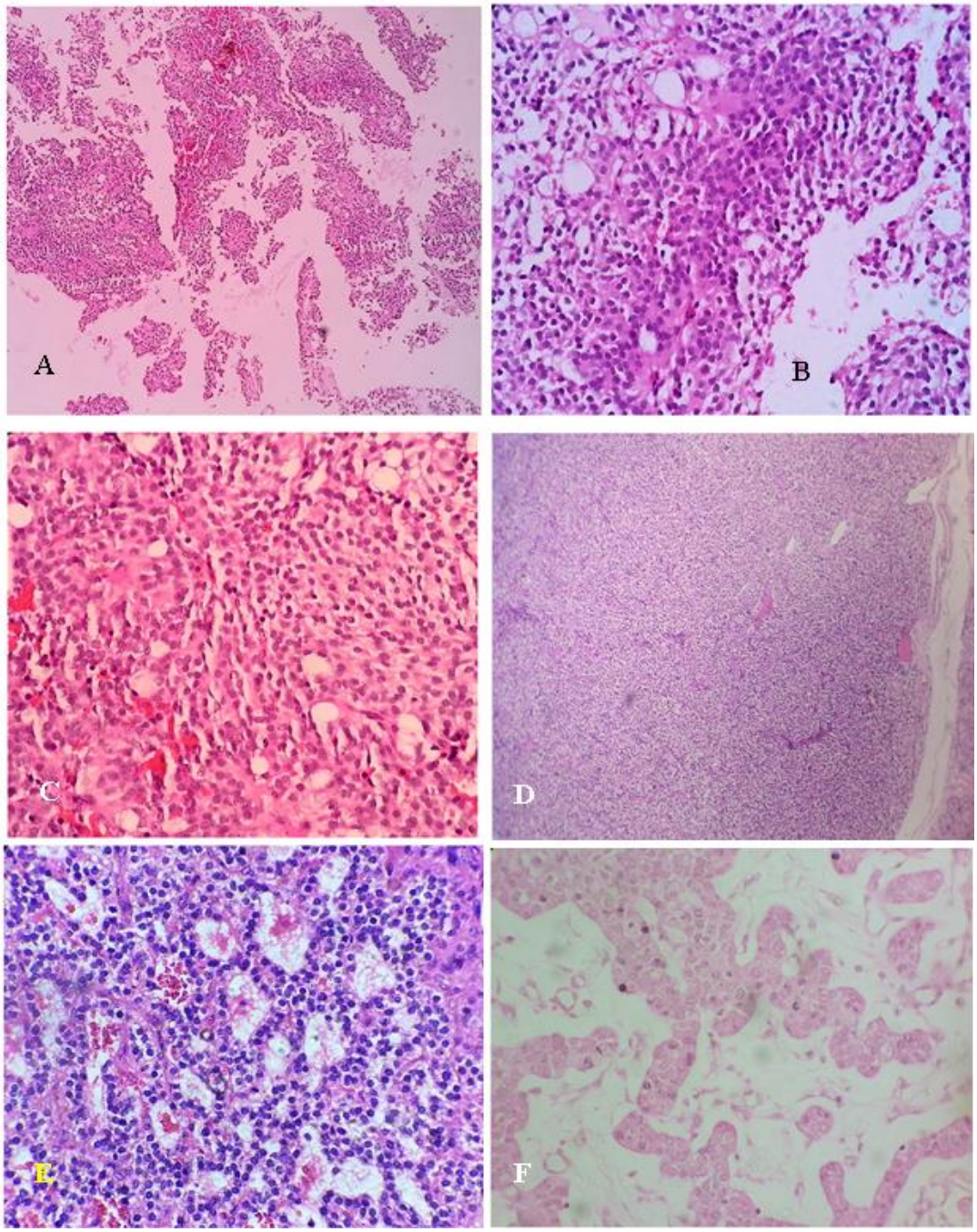

Fig. 1: A. Pitutary Adenoma. H& E. X100. B. Pitutary adenoma. Monomorphic pfoliferation of cells in uniform round nuclei, delicate strippled chromatin, inconspicuous nucleoli and moderate ctoplasm. H&E. X100. C. Pitutary adenoma. Diffuse arrangement of monotonous population of tumor cells. H&E. X400. D. Parathyroid adenoma. Tumor cells arranged in both nestin and diffuse pattern which are hypercellular, homogenous and well vascularised. H&E. X100. E. Parathyroid Adenoma composed of tumor cells arranged in follicular pattern H&E. X100. F. Parathyroid adenoma. Pseudopapillary arrangement with features of nuclear atypia and mitosis. H&E. X400.

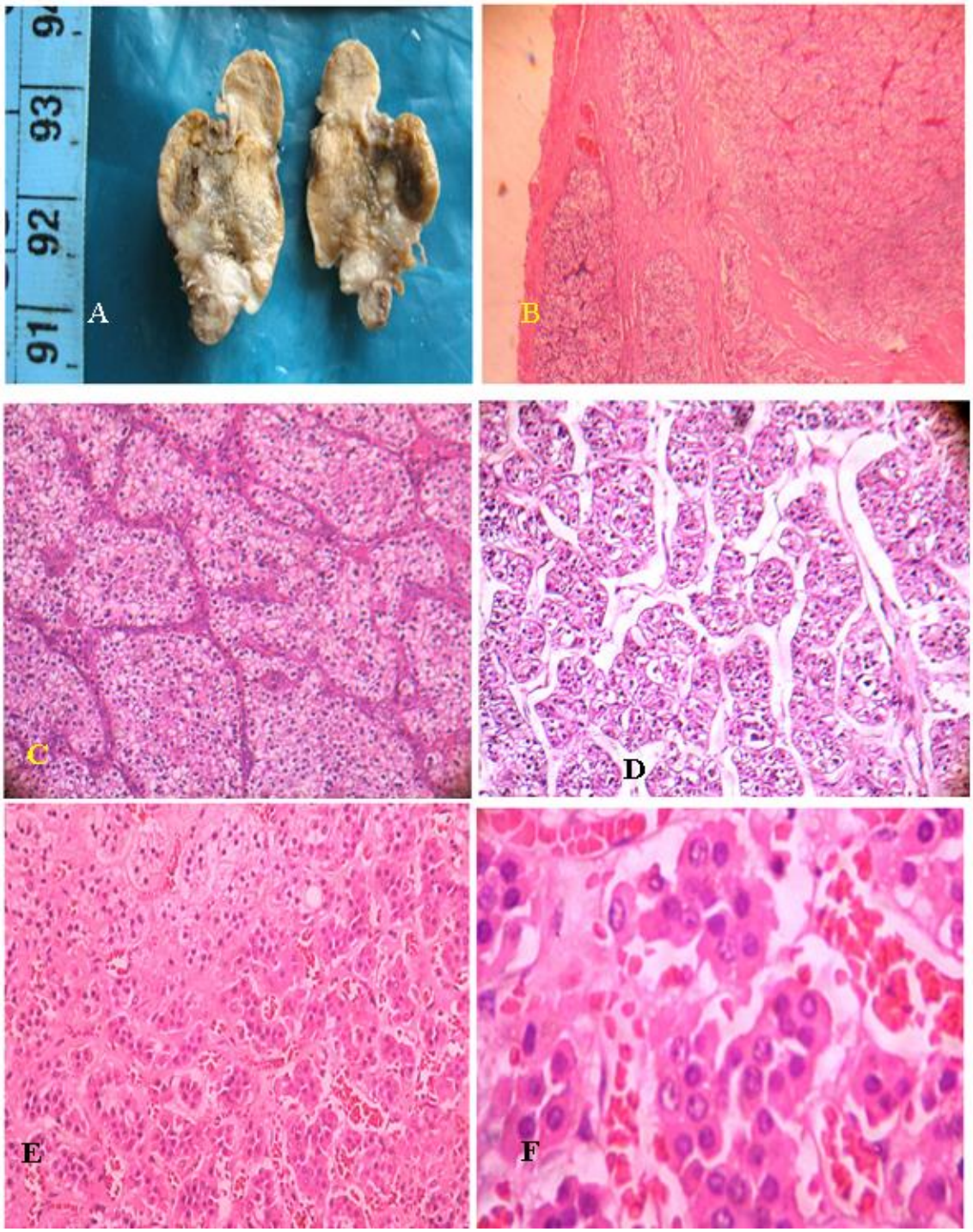

Fig. 2: A. Parathyroid carcinoma. B. Parathyroid carcinoma. Capsular infiltration by tumour cells. H&E. X100. C. Parathyroid carcinoma. lobules of tumor cells separated by thick fibrous bands. H&E. X100. D. Parathyroid carcinoma. Tumour cells with thick cytoplasm. H&E. X400. E. Adrenal cortical adenoma. sheets and nests of tumor cells. H&E. X100. F. adrenal cortical adenoma. Tumor cells having eosinophilic cytoplasm. H&E. X400.

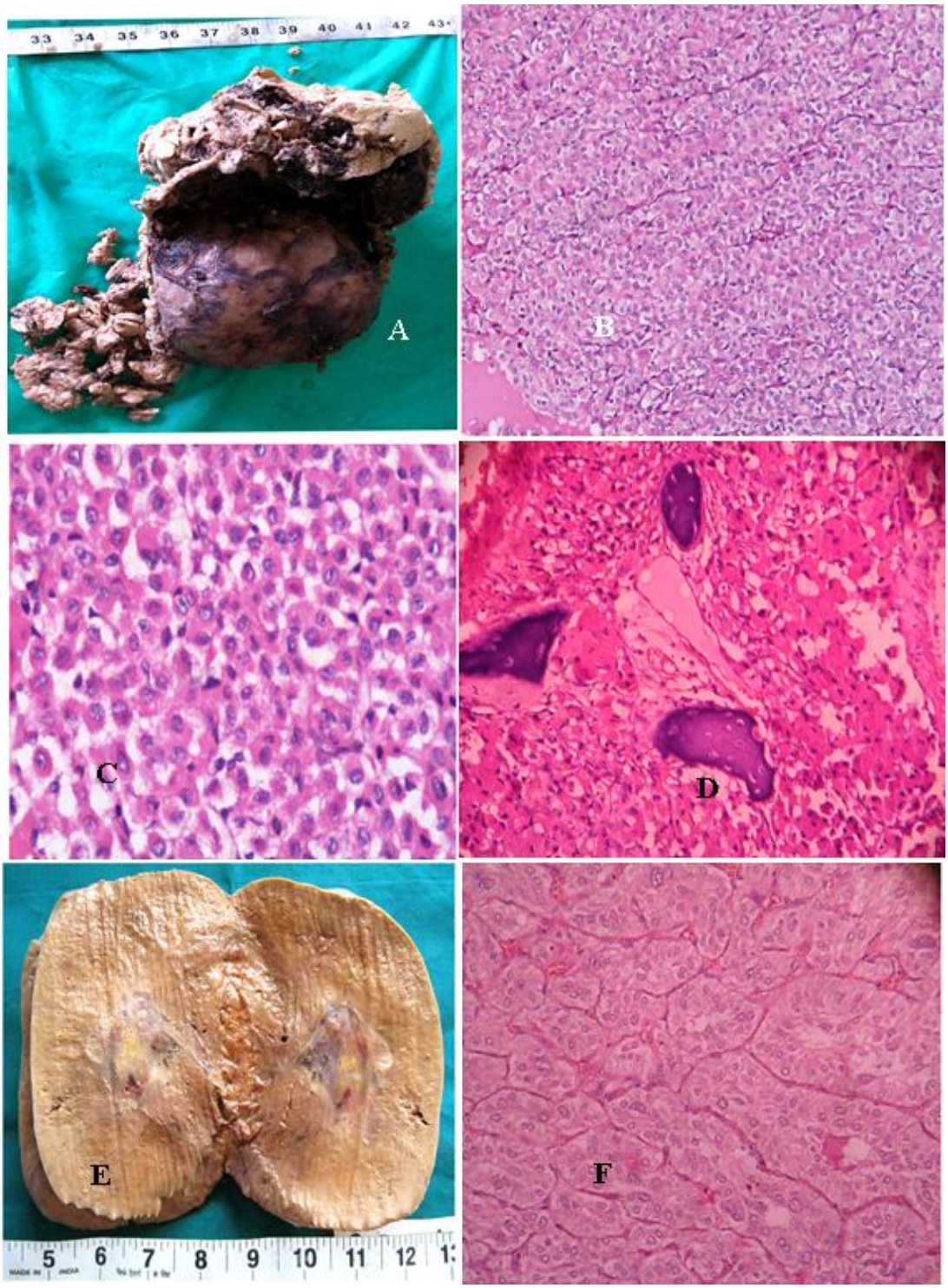

Fig. 3: A. adrenal cortical carcinoma. B. adrenal cortical carcinoma. Trabecular arrangement of tumor tissue. H&E. X100. C. adrenal cortical carcinoma. polygonal tumor cells. H&E. X400. D. adrenal cortical carcinoma. foci of calcification with bone formation H&E. X100. E. pheochromocytoma. F. Tumor cells arranged in Zellballen pattern. H&E. X100.

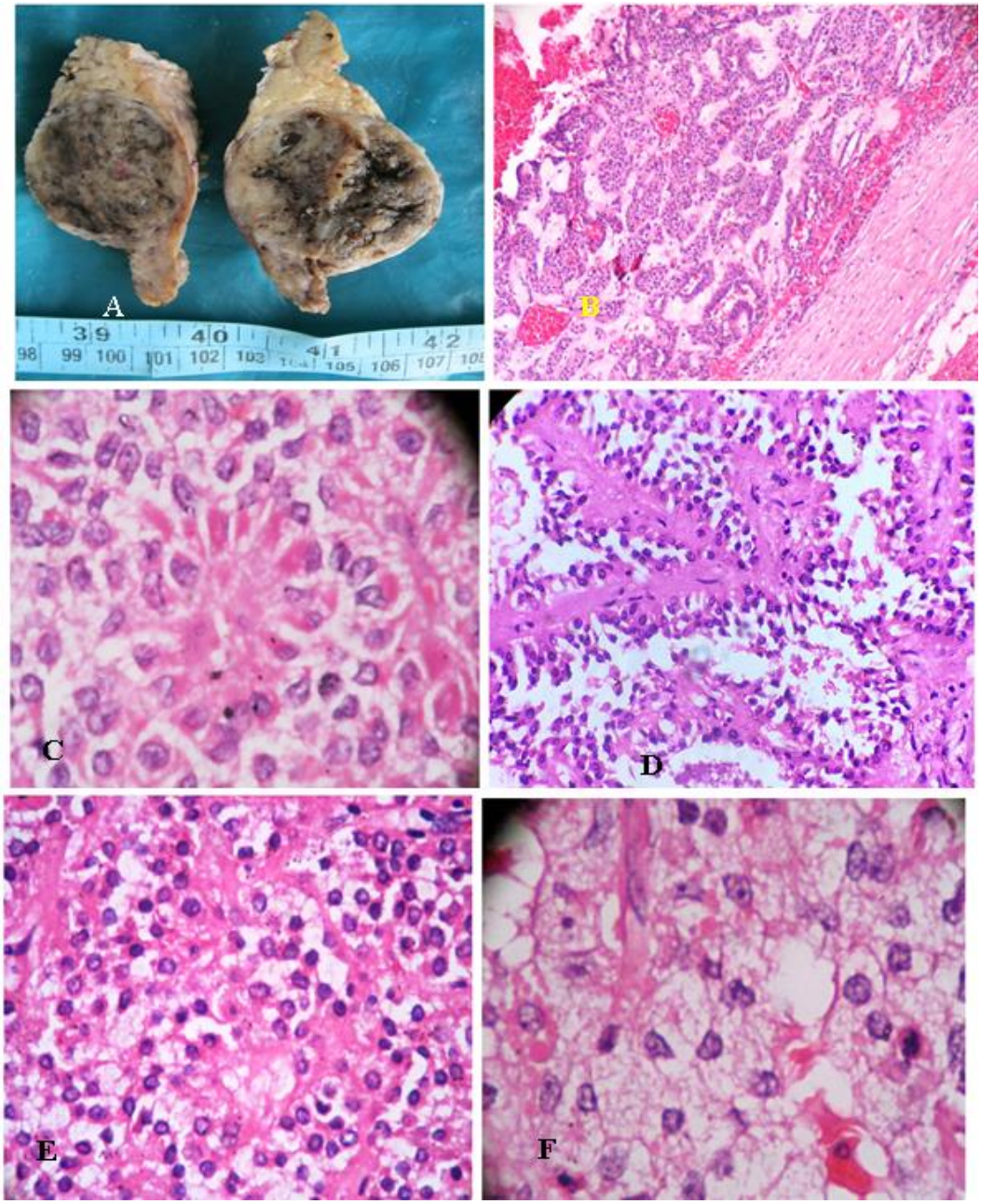

Fig. 4. A. pancreatic endocrine neoplasm. B. capsulated lesion with trabecular pattern. H&E. X100. C. acenar pattern. H&E. X400. D. papillary pattern. H&E. X100. E. tumor cells with clear cytoplasm and some having granular esonophilic pattern. H&E. x400 F. Tumor cells with clear cytoplasm and some having granular esonophilic pattern. H&E. x400

Discussion

Tumours of endocrine glands are rare in the context of the overall burden of neoplastic diseases. Endocrine cancer is a rare malignancy worldwide (1.5% in males and 3.5% in females).[9] The most commonly affected endocrine organ is the thyroid gland representing 80-92% of all endocrine malignancies.[10]

The present study was done from June 2012 to June 2014 and included a total of 26 cases of endocrine neoplasm of pituitary, parathyroid, pancreas and adrenal glands.

They were mainly classified into adenomas and carcinomas according to WHO classification. Pituitary adenomas are found to be more common when compared to pituitary carcinomas. In the present study, the % ages of adenomas were 100% when compared to carcinomas, as no cases were obtained. This study was found to be correlating with the studies of Villwock et al., who noted that pituitary tumours constitute 10-15% of all diagnosed intracranial tumours, 90% of which are adenomas.[11] The study done by Minouk J et al., found 97.7% cases to be adenomatous neoplasms.[12] In Cho HJ et al., study Pituitary adenomas

accounted for 83.4% from all the surgically resected pituitary lesions studied.[13]

Pituitary adenomas show somewhat of a predilection for women in the third to sixth decades of life. No age group is exempt, including childhood, a period wherein 2% of all adenomas occur.[12] In the present study Pituitary adenomas were found to be slightly more common in females when compared to males, having male: female ratio of 1:2 and majority of them presented between 30 years to 60 years, with mean age of 45.33 years. This was consistent with earlier documentations of Minouk J et al, Cho et al, Faglia G, Salami et al, and S Cawich et al.[12-16]

Pituitary tumours are a common type of intracranial neoplasm and, depending on the cell type of origin, have diverse endocrine and reproductive effects.[17] In the present study, most common symptom encountered was visual disorders, this was in correlation with the study of Cho et al., who proved that out of the 83.4% cases of pituitary adenomas, 37% had visual disorders accounting it to be the most common clinical manifestation.[13] Similarly, this study was also found to be correlating with study of S G Elkington et al.[18] According to the study done by Harpel et al., headache (97%) was found to be the most common presenting symptom followed by visual disturbances (71%).[19]

Prolactinomas and non-functioning adenomas are the most common types of pituitary adenomas. Patients with pituitary adenomas may present initially with symptoms of endocrine dysfunction such as infertility, decreased libido, and galactorrhea, or with neurologic symptoms such as headache and visual changes.[20] The abnormal hormone effect in the present study was galactorrhoea/amenorrhoea and Cushing's syndrome (1 case each, 16.67% each).This study was found to be correlating with the study of Cho et al.,[13] In the study by Elkington et al., three-quarters of the female patients aged 45 years and under suffered from amenorrhoea at the time of operation, while almost 90% had observed menstrual irregularity.[18]

The neoplasm was classified as adenoma, carcinoma and secondary tumours. In the present study we came across 9 cases of adenomas and 1 case of carcinoma.

Neoplasms of the parathyroid are common, but parathyroid carcinoma is exceptionally rare.[21] In this study, majority of the cases were benign adenomas, accounting for 90% and the remaining 10% was carcinoma, this study was found to be similar to the above mentioned studies.

Parathyroid neoplasms are responsible for approximately 85% of all cases of primary hyperparathyroidism and the vast majority are benign (>95%).[6] Primary hyperparathyroidism (P-HPT) is a common endocrine disorder that occurs as a result of adenomas (80–85%), hyperplasias (10–15%) or carcinomas (<1%) of the parathyroid glands.[22]

In the present study, more cases belonged to 40-60 years of age, with a mean age of 46.9years and female: male ratio for parathyroid neoplasm was found to be approximately 1.5:1. This was found to be correlating to the studies done by Surg Capt B Fanthome et al, and Ronald A Delellis.[21,22]

Similarly, according to Sathe et al., majority of the cases were between 21-30years, and had a female: male ratio of 2.5:1. This was also found to be comparable with the present study.[23]

In the present study every case of parathyroid neoplasm had clinical manifestations of hyperparathyroidism, including skeletal in form of bone pain and fracture, followed by renal manifestation in form of nephrolithiasis. This study was found to be comparable with the study of Surg Capt B Fanthome et al.[21] While the features secondary to hypercalcaemia like fatigue and weakness in the present study was found to be similar to the study of A. Bhansali et al.[24]

Other clinical presentations documented in the present study included palpable neck mass in 2 cases (20%). This was found to be correlating with the study of Sathe et al, where 2 cases (4.17%) of palpable neck masses were documented.[23]

Similarly, the present study had one case of Brown tumour (10%), while the study of Pradeep et al., had 233 cases (42%).[25]

The present study had 2 cases of adrenal cortical adenoma (25%), 1 case of adrenal cortical carcinoma (12.5%), and 5 cases of pheochromocytoma (62.5%), out of the total 8 cases. This was found to be correlating with the study of Rashmi D Patel et al in which out of the total of 29 adrenalectomies done for primary adrenal tumours, 4 cases had adrenal cortical adenoma (13.7%), 2 cases had adrenal cortical carcinoma(6.9%), and 20 cases had pheochromocytoma (68.9%).[26]

In the present study, majority of the patients were between 21-40 years, with a mean age of 30.3 years. This was found to be comparable with the study of Rashmi D Patel et al.[26] Similarly the frequencies of adrenal gland neoplasms were found to be equal in both sexes, this was also found to be comparable with the study done by Rashmi D Patel et al.[26]

In Rashmi D Patel et al., study on primary adrenal tumours, from the total 20 cases of pheochromocytoma, 75% (15 cases) had hypertension.[26] Out of the 4 adrenal cortical adenoma, 25% (1 case) had Cushing's syndrome and from the 2 adrenal cortical carcinoma cases, 50% (1case) had virilisation. The present study was almost similar to the above mentioned study, as it also had 75% cases with hypertension, 37.5% with Cushing's syndrome, which was slightly higher and 12.5% with virilising syndrome which was lower, when compared to the study of Rashmi et al.[26]

From the study done by Bernardo Leo W et al., on Adrenocortical carcinoma, a total of 47 cases were studied, in both children and adults.[27] Among them, 6.3% (3 cases) had Cushing's syndrome, which was significantly low when compared to the present study which comprises 37.5% cases. Virilising syndrome was found in a total of 36.17% (17 cases), this was found to be high when compared to the present study which has only 12.5% cases with virilising

syndrome. 51% cases had mixed Cushing-Virilising syndrome (CVS), while the present study did not have any such cases. But hypertension was found to be the common symptom in both Bernardo Leo W et al., and present study, accounting for 81% and 75% each.[27]They has also mentioned that majority of cases presented with abdominal pain and mass but exact number was not given, while in the present study 37.5% cases presented with abdominal pain and 25% had abdominal mass.

According to the study done by Henk V Slooten et al., on adrenal cortical tumours, out of the total 60 cases (45 carcinoma & 15 adenoma). 57.14% patients had Cushing's syndrome, which is slightly higher when compared with the present study, which had Cushing's syndrome in 37.5% cases.[28] Whilethe % age for virilising syndrome was found to be comparable with, 11.4% in Henk V Slooten et al., study and 12.5% in the present study.[28]

The study of Richard E. Goldstein et al., on pheochromocytoma, revealed that majority of the cases had hypertension as their presenting symptom, accounting for about 82% cases.[29] This was found to be correlating with the present study where, 75% cases had hypertension. Only 6% of cases had abdominal pain and weakness and in 5% anorexia and weight loss were seen. But In the present study, 62.5% presented with weakness and fatigue while 37.5% came with abdominal pain and 12.5% had anorexia and weight loss.

According to the study done by Philip T Cagle et al., on adrenal cortical tumors, 47.82% of the cases had Cushing's syndrome, 43.48% had virilising syndrome and 4.3% presented with abdominal mass. This was different from the present study that had Cushing's syndrome in 37.5% cases, Virilising syndrome in 12.5% cases and abdominal mass in 25.00%.[30]

Endocrine tumours account for approximately 1–2% of all pancreatic neoplasm.[31] However, the precise incidence of pancreatic endocrine tumours is not known. Because of their generally rather favourable prognosis, the incidence rate is probably substantially lower than the prevalence rate, which has been estimated at less than 1 in 100 000.[32] The incidence is higher in autopsy studies, ranging from 0.8 to 10% suggesting that these tumours frequently go unnoticed.[33]

From the total 26 endocrine neoplasms of the present study, 2 cases (7.69%) had pancreatic endocrine tumours. This was slightly higher when compared to the studies documented by Cancer trends (4%) and Kimura et al (3%).[34,35] But due to the unavailability of specific Immunohistochemical markers in our institution, further classification of the pancreatic endocrine tumours could not be done.

In the present study, both cases of pancreatic endocrine neoplasms belonged to 0-20 year's age group, with male: female ratio of 1:1. This was found to be slightly different from other studies documented, for example, the study done by S Philips et al., states that pancreatic endocrine neoplasms are discovered most commonly in the fourth and fifth decades of life and demonstrate a slight female predominance.[36] But, the studies of Rachel B. Lewis et alas well as Simona Gronzinsky- Glasbergstates that they may manifest at any age, most often during the 4th–6th decades of life and overall, there is no significant gender predilection.[37,38]

In the present study majority of the patients presented with fatigue, weakness, sweating, epigastric pain, diarrhoea and diabetes mellitus. This was found to be correlating with the study of Simona Gronzinsky-Glasberg, where he stated that based on their secretory hormonal properties and related clinical picture, pancreatic neuroendocrine tumours are divided as functional(rare) and non-functional (>70%).[38] According to the study done by B Eriksson et al., the most frequent presenting features were dyspepsia and epigastric pain, which was found to be correlating with the present study.[39] Similarly, the present study also correlates with the study done by Pattou F et al.[40] According to the study done by Pannala Rabout 25% of patients with pancreatic cancer have diabetes mellitus at diagnosis, and roughly another 40% have pre-diabetes (higher than normal blood glucose levels).[41]

Conclusion

In this present study more number of incidences of tumour cases observed higher in Parathyroid followed by Adrenal, Pituitary and Pancreas.

Conflict of Interest: None.

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