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A Case Report on Primary Pigmented Nodular Adrenocortical Disease (PPNAD) Presenting as Cushing Syndrome in a 25 Yr Old Female

Dr. Praveena K P[1], Dr. Kalaranjini K. V.[2], Dr. Shashikiran M. S.[3]

[1]MD Pathology, Assistant Professor, Sree Gokulum Medical College and Research Foundation, Trivandrum, 695607

[2]MD Pathology, Professor, Sree Gokulum Medical College and Research Foundation, Trivandrum, 695607

[3]MS, MCH Gastrosurgery, Consultant and HOD, Sree Gokulum Medical College and Research Foundation, Trivandrum, 695607

Abstract: ***Aim: To describe the case of primary pigmented nodular adrenocortical disease (PPNAD) presenting as cushing syndrome in a 25 year old female. Background: Primary pigmented nodular adrenocortical disease (PPNAD) is a rare cause of Cushing's syndrome, which is adrenocorticotropic hormone-independent and involves both adrenal glands. The characteristic pathological features include multiple pigmented cortical nodules and atrophy of the internodular cortex. Case Vignette: A 25-year-old female presented with excessive weight gain with increased abdominal girth and abdominal striae. She is k/c/o ACTH independent cushing syndrome and hypertension. She underwent hemithyroidectomy 2 years back for papillary carcinoma thyroid. Treatment: Laparoscopic bilateral adrenalectomy under general anesthesia was done. The histopathology findings were consistent with PPNAD. Genetic studies for PRKAR1A, PDE11A gene was done and no mutation was detected. Conclusion: The early diagnosis and treatment allowing timely bilateral adrenalectomy will not only prevent severe complications of hypercortisolism, but may also preclude the development of adrenocortical carcinoma. The diagnosis of Carney complex can be made in our case as the patient has papillary carcinoma of thyroid and PPNAD.***

Keywords: Cushing's syndrome, primary pigmented nodular adrenocortical disease

1. Introduction

Primary pigmented nodular adrenocortical disease (PPNAD) is a rare cause of adrenocorticotropic hormone (ACTH)-independent Cushing's syndrome (CS) and is a bilateral disease that occurs due to autonomous cortisol hypersecretion from functional adrenal nodules.[1]

PPNAD is an important cause of hypercortisolism especially in the paediatric age group with characteristic gross multiple small and pigmented nodules, and microscopic features such as synaptophysin positive, lipofuscin pigmented nodules, atrophic cortex in between nodules of the adrenal glands. It may occur independently or associated with Carney complex[2]

Carney complex, is associated with many other lesions, including cardiac myxomas and other cutaneous tumors, breast myxomatosis, spotty skin pigmentation and other lesions, pituitary adenomas and acromegaly, large-cell calcifying Sertoli cell tumors , adrenocortical lesions, and Leydig cell tumors, psammomatous melanotic schwannoma, epithelioid blue nevus, and ductal adenoma of the breast and thyroid follicular neoplasms, both benign and malignant To make a diagnosis of Carney complex, a patient must either: (i) exhibit two of the manifestations of the disease listed above, or (ii) exhibit one of these manifestations and meet one of the supplemental criteria (an affected first-degree relative or an inactivating mutation of the PRKAR1A gene).[3]

The pathogenesis of PPNAD has recently been well established. nodules of PPNAD arise from the zona reticularis and demonstrate autonomous hypersecretion of cortisol, supporting the theory of abnormal development of the zona reticularis.[4] Recently, molecular studies have demonstrated inactivating mutations of the PRKAR1A gene on chromosome 17q22-23 or of the PDE11A gene, both of which are key components of the cAMP signaling pathway.[3]

Treatment options with proven clinical efficacy for PPNAD include adrenalectomy (bilateral or unilateral adrenalectomy) and drug treatment to control hypercortisolemia. Previously, the main treatment of PPNAD is bilateral adrenal resection and long-term hormone replacement after surgery. In recent years, cases reports suggest that unilateral or subtotal adrenal resection can also lead to long term remission in some patients without the need for long term hormone replacement therapy.[5]

2. Case Report

A 25-year-old female presented with excessive weight gain with increased abdominal girth and abdominal striae. She also complains of hirsuitism. She is k/c/o ACTH independent cushing syndrome and hypertension on amlodipine for 3months.

Past history: She underwent hemithyroidectomy 2 years back for papillary carcinoma thyroid. There was no significant family history. The systemic examination was normal. The magnetic resonance imaging showed minimal nodularity in bilateral adrenals. MRI of the pituitary fossa was normal. Serum electrolytes were normal. The serum cortisol level at 8 am was 9.8 µg/dl and late night serum cortisol was 0.34 µg/dl

3. Treatment

Multidisciplinary evaluation was done and she underwent laparoscopic bilateral adrenalectomy under general anesthesia. The right adrenal measured 4cm x 1 cm x 1 cm and the left adrenal measured 3.2 cm × 1.8cm × 0.6cm. The external surface of both adrenals was normal. The cut surface showed black nodules measuring 2–6 mm in diameter with intervening yellow areas [Figure 1]. Sections from both adrenals showed multiple well-circumscribed nodules composed of large polygonal cells with abundant granular eosinophilic to vacuolated cytoplasm with mild anisonucleosis variable golden-brown pigment [Figure 2].these nodules show positivity for synaptophysin. The findings were consistent with PPNAD. The postoperative period was uneventful. Other features of Carney's complex (CNC) were looked for. There were no skin lesions. Echocardiogram was negative for cardiac myxomas. Genetic studies for PRKAR1A , PDE11A gene was done and no mutation was detected.

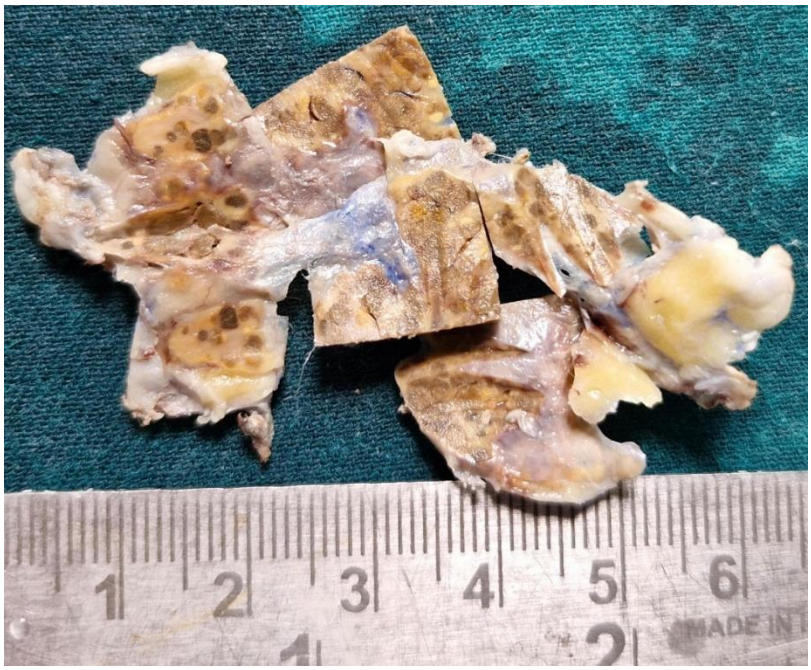
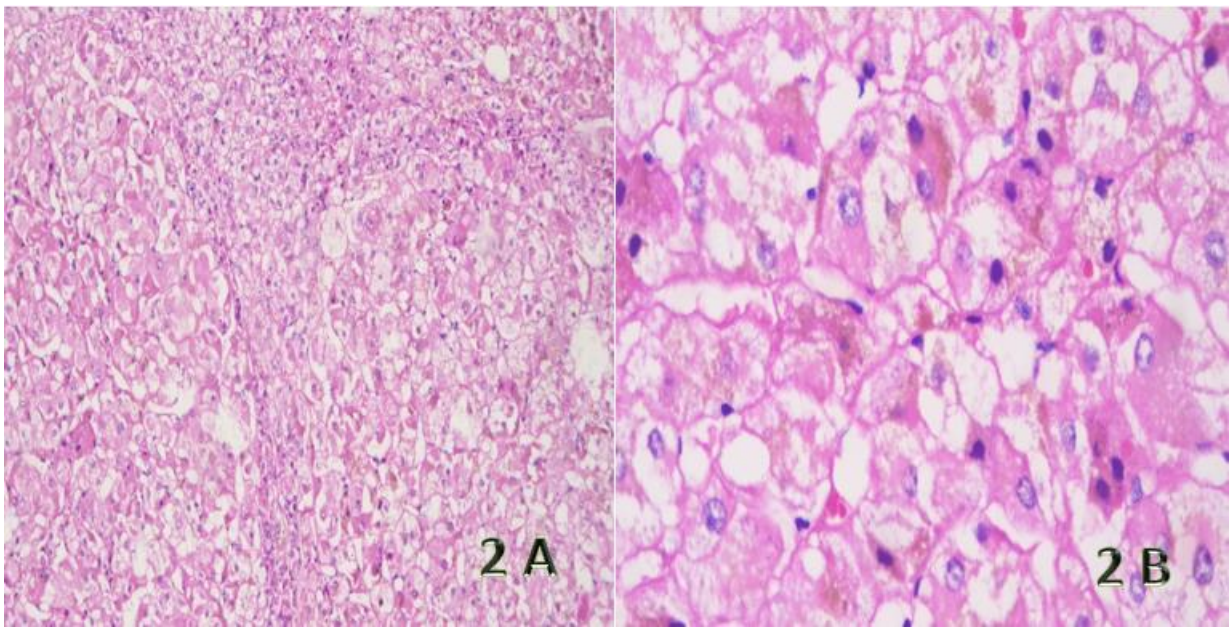


Figure 1: Cut section of adrenal showing multiple pigmented nodules



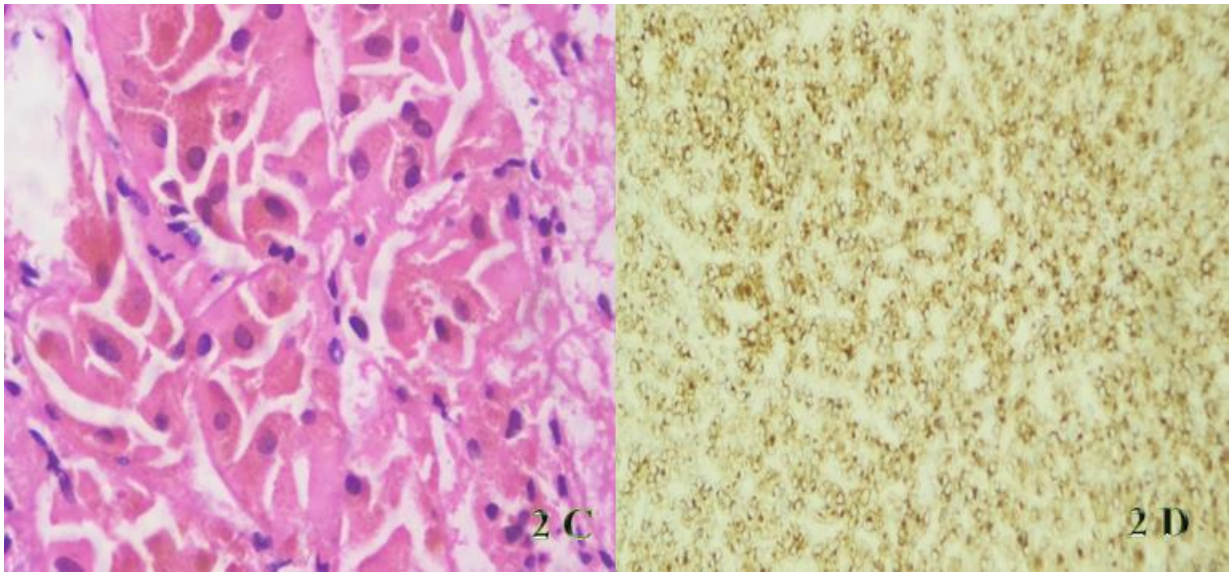


Figure 2: Section from adrenals showing multiple well-circumscribed nodules (fig2A). nodules composed of large polygonal cells with abundant granular eosinophilic to vacuolated cytoplasm with mild anisonucleosis variable golden-brown pigment (fig 2B,2C).Nodules are positive for synaptophysin.

4. Discussion

Cushing's syndrome is most often secondary to adrenocortical adenomas or carcinomas, and more rarely to bilateral adrenal hyperplasias. Corticotropin-independent cortisol-producing hyperplasia is caused by micronodular diseases, including primary pigmented nodular adrenocortical disease and nonpigmented micronodular hyperplasia and adrenocorticotropic hormone-independent macronodular adrenal hyperplasia.[6]

The early diagnosis and treatment allowing timely bilateral adrenalectomy will not only prevent severe complications of hypercortisolism, but may also preclude the development of adrenocortical carcinoma.

The diagnosis of Carney complex can be made in our case as the patient has papillary carcinoma of thyroid and PPNAD.

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