International Journal of Research in Medical Sciences
Chittamuri S et al. Int J Res Med Sci. 2015 Jul;3(7):1807-1809
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20150278

Case Report

Leydig cell tumor of ovary with primary hyperparathyroidism: A rare association

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Received: 18 May 2015
Accepted: 05 June 2015

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ABSTRACT

Leydig cell tumors of ovary are extremely rare sex cord stromal tumors that account for <0.2% of ovarian cancers. Most of these tumors can cause hyperandrogenism. A 54 year old multiparous postmenopausal woman, known diabetic and hypertensive, presented with progressive virilization, bone pains and depressed mood for 2 years. Diagnostic evaluation revealed markedly elevated testosterone with normal dehydroepiandrosterone sulphate. Computerized tomography of abdomen showed right ovarian mass with multiple cysts in both kidneys. Biochemical investigations revealed hyperglycemia, hypercalcemia, hypophosphatemia and elevated parathormone (PTH) levels. Sestamibi scan for parathyroids was suggestive of right inferior parathyroid adenoma. Histopathology of the resected right ovarian tumor was consistent with leydig cell tumor of ovary. Postoperatively serum testosterone and blood glucose levels were normalized, but PTH levels remained high. PTH levels were normalized after resection of parathyroid adenoma

Keywords: Leydig cell tumor, Parathyroid adenoma, Virilization

INTRODUCTION

Leydig cell tumors of ovary are rare, benign tumors, commonly seen in postmenopausal women and are usually unilateral in location. They produce androgens and virilization is seen in 70-85% of cases. Parathyroid adenoma accounts for 75-80% of cases with hyperparathyroidism. Association of parathyroid adenoma with multiple endocrine neoplasia type 1, multiple endocrine neoplasia type 2A and hyperparathyroidism-jaw tumor was described. However, the association between leydig cell tumor and parathyroid adenoma is very rare.

CASE REPORT

A 54 year old postmenopausal hypertensive woman presented with a two year history of progressive virilization. Two years back she had noted progressive hair growth and coarsening of hair over arms, legs, thighs and abdomen. She also developed facial hair which prompted her to shave three times a week initially and then daily thereafter. There was no voice change or clitoral enlargement. She also gives history of bone pains and depressed mood for 2 years. There was a history of renal failure 2 years back which improved with treatment and evaluation showed bilateral renal cysts. She was also found to have elevated fasting plasma glucose levels during that evaluation and was started on glipizide. She is married, had two children and underwent hysterectomy 14 years back for fibroid uterus. There was no relevant past medical illness. Father had both diabetes and hypertension.

On physical examination she had a body mass index of 27 kg/m^2 with acanthosis nigricans and skin tags. Scoring for hirsutism done by modified Ferriman Gallaway method was 15/36 with temporal baldness (Figure 1).

There was no clitoromegaly. Pelvic examination had not revealed any masses or tenderness. There were no bony swellings or deformities.

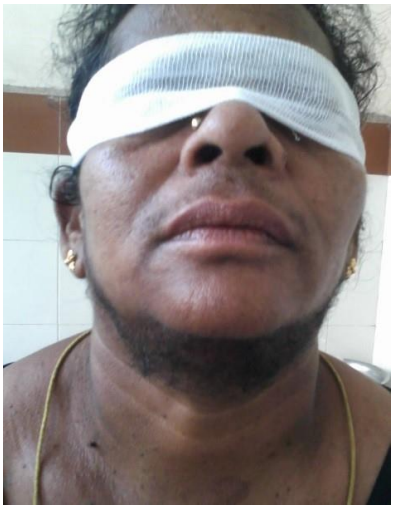

Figure 1: Clinical photograph of the patient with prominent hirsutism and skin tags.

Investigations revealed hypercalcemia with a corrected serum calcium of 12.44 mg/dl (normal 8.6 -10.5 mg/dl), hypophosphatemia of 2.25 mg/dl (normal 2.5 – 4.5 mg/dl), elevated PTH levels of 314.3 pg/ml (normal 15 – 65 pg/ml), increased serum testosterone of 676 ng/dl (normal 40 – 80 ng/dl) with normal 17-hydroxy progesterone of 1.6 ng/ml (normal <2 ng/ml), normal serum dehydroepiandrosterone of 67.3 ng/dl (normal 35 – 430 ng/dl) and nomal serum dehydroepiandrosterone sulphate levels of 100 µg/dl (normal 45 – 320 µg/dl). Serum creatinine was 1.6 mg/dl with an estimated glomerular filtration rate of 50.76 ml/1.73 m^2/min. Urinary calcium creatinine ratio was elevated to 0.38 (normal < 0.2) with an abnormal fractional excretion of phosphate of 46%. CA 125 levels were normal which were about 16.18 IU/ml (normal < 35 IU/ml). Computerized tomography of abdomen showed multiple cysts in both kidneys with a solid right ovarian mass measuring about 2.4x1.7 cm^2. Sestamibi scan for parathyroids showed retained tracer activity with in right lower pole of thyroid suggestive of right inferior parathyroid adenoma (Figure 2).

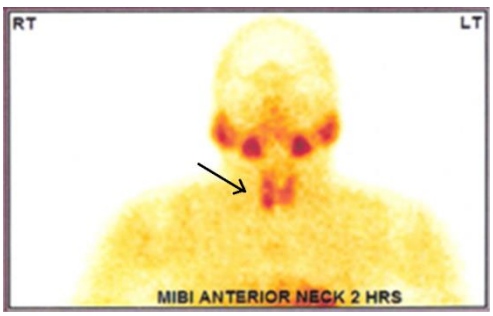

Figure 2: Sestamibi Scan: Delayed image showing tracer retention in the thyroid with relative increase in right lower pole suggestive of Right inferior Parathyroid adenoma.

Patient was treated for hypercalcemia with intravenous fluids and intravenous Zoledronate. Bilateral oopherectomy was done and histopathology of the resected right ovarian tumor was consistent with leydig cell tumor of ovary. Postoperatively serum testosterone and plasma glucose levels were normalized with persistent elevation of serum calcium and PTH levels. Two months later parathyroid adenoma was resected and there was normalization of serum calcium and PTH levels and histopathology was consistent with right parathyroid adenoma. Follow-up was uneventful for the past two years.

Final diagnosis was a leydig cell tumor of right ovary with right inferior parathyroid adenoma and bilateral renal cysts.

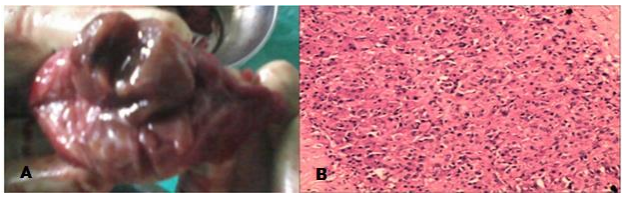

Figure 3: [A] Cut section of Right sided ovary measuring 5 × 4 cm with solid component of 3 × 2 cm. [B] Photomicrograph of leydig cell tumor of ovary showing Circumscribed tumor composed of round to polygonal leydig cells with abundant eosinophilic and granular cytoplasm with mild nuclear pleomorphisim & areas of collagenisation (H&E, ×100).

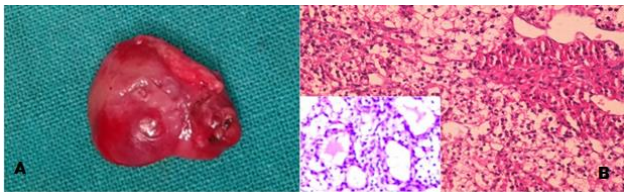

Figure 4: [A] Excised Right inferior parathyroid measuring 2.2x1 cm^2. [B] Photomicrograph of parathyroid adenoma showing both clear cell & oxyphilic components with predominant clear cell pattern (H&E, ×100). Inset showing cystic spaces filled with eosinophilic colloid like material resembling thyroid follicles (H&E, ×100).

DISCUSSION

Androgen secreting tumors are the least common of the androgen excess disorders in women, having a prevalence of 0.2%.[1] These tumors may arise from adrenals or ovaries. Leydig cell tumors of ovary are extremely rare sex cord stromal tumors that account for <0.2% of ovarian cancers. These are predominantly seen in postmenopausal women and most of them are benign, small (diameter < 3 cm) and solid. They can produce androgens and virilization is noted in 70-85%.[2] Ovarian tumors are known to elaborate factors which can cause hypercalcemia mainly parathormone related peptide (PTHrP) or rarely PTH.[3]

The increased PTH levels in this patient makes a PTHrP related hypercalcemia unlikely as two site immunoradiometric PTH assay does not cross react with PTHrP.

The co-existence of Parathyroid adenoma with a Virilizing ovarian tumor may be a chance association. The presence of bilateral renal cysts and history of uterine fibroids along with parathyroid adenoma raises the possibility of hyperparathyroidism-jaw tumor syndrome (HPT-JT). Previous case series have shown that jaw tumors are present only in 35% of cases and is associated with various other tumors like testicular mixed germ cell tumors, thyroid tumors, pancreatic tumors.[4,5] However, ovarian tumors have never been described previously. The confirmation of HPT-JT requires genetic analysis of HRPT2 or CDC73 gene which could not be done in this patient.

CONCLUSION

We are presenting this case because of rare association of virilizing leydig cell tumor of ovary with parathyroid adenoma resulting in symptomatic hypercalcemia and this is first such case reported in literature to the best of our knowledge. This case reiterates the concept that even in patients with tumor associated hypercalcemia, the traditional causes of hypercalcemia have to be ruled out.

Funding: None
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Suhitha C, Mythili A, Bhagyalakshmi A, Subrahmanyam KAV. Leydig cell tumor of ovary with primary hyperparathyroidism: A Rare Association. Int J Res Med Sci 2015;3:1807-9.