SECONDARY AMENORRHEA IN A PATIENT WITH ACROMEGALY: A CASE REPORT

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ABSTRACT. Acromegaly is a rare hormonal disorder with a prevalence of 40 to 60 individuals per million and incidence between 3 to 4 new cases per million annually. The diagnosis and treatment of acromegaly has undergone a paradigm shift in the past few decades. Its diagnosis may be missed as its initial presentation may overlap with other conditions associated with irregular menses, amenorrhea and hyperandrogenism. It has evaded diagnosis and can be mistaken for other pathologies until in its clinically obvious later stages when treatment is more difficult. Here we report a case of a 25 year old woman with acromegaly who was diagnosed after a bout of diabetic ketoacidosis, but had already presented with oligomenorrhea, acne and hirsutism at 19 years of age. She later presented with secondary amenorrhea after surgery and radiation therapy.

CASE REPORT

Patient profile: 25 years old G0 with no known comorbidities

Chief complaint: Amenorrhea

History of present illness: Patient had her menarche at 11 years old and since then had regular monthly menses until the age of 19, when intervals started to vary from 1 to 4 months. Two years prior, she had generalized body weakness and change in sensorium associated with increased thirst and hunger. Capillary blood glucose level was 500 and HbA1c was 16.2%. She was treated for diabetic ketoacidosis with insulin and Metformin. During this admission, the physician noted that she has prominent facial bones, enlarged nose and lips, as well as enlarged hands and feet. The patient was then worked-up and treated for acromegaly. Spontaneous menses did not resume for 10 months after transsphenoidal excision of a GH-secreting pituitary macroadenoma and radiation therapy hence the referral to our service.

Physical Examination: Internal examination was normal.

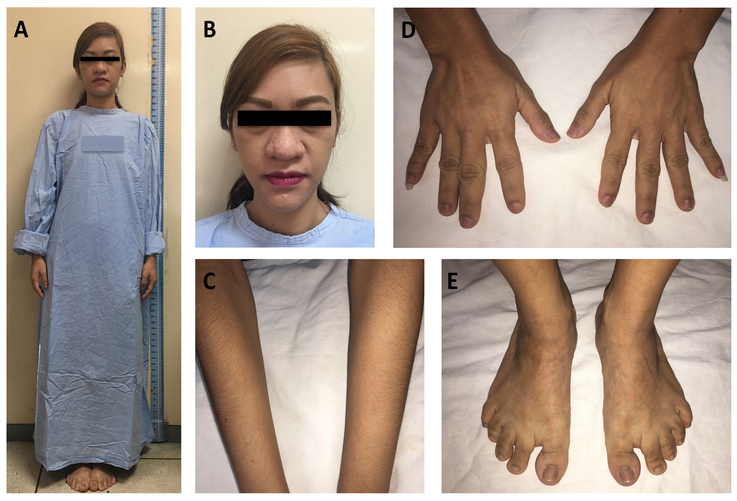

FIGURE 1.
A Height 170 cm, weight 61 kg (BMI 21.1)
B Coarse facial features, prominent mandible, protrusion of the lower jaw, eyebrow arch and cheekbones, enlargement of the nose and lips, acne
C Hirsutism
D, E Enlargement of hands and feet.

Cranial MRI:

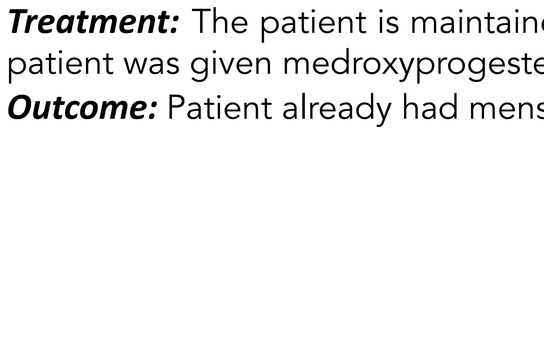

FIGURE 2. MRI with gadolinium enhancement after transsphenoidal excision and external beam radiation therapy.
A sagittal **B** coronal.

Red arrow indicates the heterogeneously enhanced macroadenoma in the sella tursica measuring 2.1 x 2.3 x 1.8 cm.

Transvaginal Ultrasound:

FIGURE 3. **A** Proliferative endometrium **B, C** Polycystic right and left ovaries

Hormonal Profile: Serum FSH 4.55 mIU/mL, LH 0.90 mIU/mL and estradiol 69.3 pg/ml. Prolactin normal at 9.68 ng/ml. TSH, FT4, FT3 are normal. IGF-1 is significantly increased to 1251 ng/ml.

Treatment: The patient is maintained on octreotide. To induce menses, the patient was given medroxyprogesterone acetate.

Outcome: Patient already had menses after medroxyprogesterone acetate.

DISCUSSION

The causes of amenorrhea in patients with GH-producing adenoma are:

- Hypogonadism from compression of the pituitary gonadotrophs
  Because the patient's serum LH and FSH levels were low, we suspect a hypogonadotropic hypogonadism state causing the amenorrhea. Among the hormone-secreting cells within the anterior pituitary, the reserve of the gonadotrophs that produce gonadotropins FSH and LH is limited. Therefore, hypogonadism can easily occur when over 50% of the pituitary gland is damaged by the tumor.
- Hyperandrogenism due to decreased sex hormone binding globulin levels and hyperinsulinemia
  Hyperandrogenism may also explain the patient's amenorrhea, acne and hirsutism. Furthermore, it has a correlation with hyperinsulinemia.
- From hyperprolactinemia, either due to concomitant production of prolactin by the tumor or stalk compression
  Not likely the cause in this case due to normal prolactin levels [1, 2, 3].

For patients who undergo sphenoidal surgery, new hypopituitarism may also develop in up to 20% of patients, reflecting operative damage to the surrounding normal pituitary tissue. Lastly, post-operative external beam radiation therapy may also have added to the hypogonadotropic hypogonadism state [4].

It remains unclear when the disease first manifested in this patient, and whether the oligomenorrhea is because of the polycystic ovaries or the pituitary macroadenoma. We cannot exclude the possibility that GH hypersecretion already existed before since its course is insidious. In our search of the literature, we found 3 cases of patients who have acromegaly, hirsutism and polycystic ovaries, 2 of which had menstrual irregularities. The polycystic ovary syndrome phenotype may occur in up to 50% of women with acromegaly, and there is increasing evidence that GH and IGF-1 themselves may directly affect ovarian morphology. First, GH-induced hyperinsulinemia may result in insulin acting directly on the ovaries increasing ovarian androgen production. Secondly, GH is also known to decrease SHBG leading to elevated free testosterone levels, which could also result in hirsutism[3].

CONCLUSION

There is a need to consider acromegaly as part of the differential diagnosis of menstrual irregularity, acne and hirsutism before diagnosing PCOS, as both can present initially as amenorrhea or oligomenorrhea.

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