

Fifteen-Year History of Virilization in a 17th-Century Woman

GLENN D. BRAUNSTEIN, MD

ABSTRACT

The Spanish artist, Jusepe de Ribera, painted a portrait of a virilized woman in 1631. He provided a brief clinical history on stone tablets, which indicates that the woman most likely harbored a benign, androgen-secreting ovarian tumor for 15 years.

KEYWORDS: hirsutism, virilization, ovarian adenoma, Jusepe de Ribera, androgens

INTRODUCTION

Currently residing in the Museo Nacional del Prado in Madrid, Spain, on loan from the Medinaceli Foundation, is a portrait of a virilized woman and her husband, along with a brief clinical history inscribed on a stone plinth (**Figure 1**). The artist, Jusepe de Ribera (1591–1652), was a Spaniard living in Naples, Italy, who was commissioned by his patron, Don Fernando Enriquez Afan de Ribera (1583–1637), the third Duke of Alcala and Viceroy of Naples, to paint the woman, Magdalena Ventura, in 1631. The Duke had an interest in individuals with medical abnormalities and had invited Magdalena to his palace to sit for Ribera.¹ Of interest, this painting had previously resided in the Hospital de Tavera in Toledo, which, after the Spanish Civil War (1936–1939), had been renovated and converted into an orphanage for girls. The portrait was housed by itself behind a closed door, presumably to not expose the young residents to the bizarre, realistic painting.²

La Mujer Barbuda (The Bearded Woman)

The painting, *La Mujer Barbuda* (The Bearded Woman), used the Caravaggio tenebrism style of contrasting light and dark shades to highlight the central figure.³ Magdalena, in a finely embroidered dress, is clearly virilized with a luxurious beard and mustache, coarse skin, masculinized hands, as well as prominent frontal balding. She is holding an infant who is in a position to nurse from an engorged midline breast that is not covered with coarse, terminal hair. Her husband is standing behind her and also possesses a beard, mustache and frontal balding, but not nearly as well demarcated as that of his wife. To the right of Magdalena sit stone tablets with the following text translated from the Latin: “A great miracle of nature. Magdalena Ventura from the town of Accumulus

Figure 1. *La Mujer Barbuda* by Jusepe de Ribera in the Museo Nacional del Prado, Madrid, Spain, on loan from the Medinaceli Foundation.

[COURTESY OF THE MEDINACELI FOUNDATION]



in Samnium, in the vulgar tongue Abruzzo in the Kingdom of Naples, aged 52, and what is unusual is when she was in her 37th year she began to go through puberty and thus a full growth of beard appeared such that it seems rather that of a bearded gentleman than a woman who had previously given three sons to her husband, Felici de Amici, whom you see next to her. Joseph de Ribera, a Spaniard, marked by the Cross of Christ, a second Apelles of his own time, by order of

Duke Ferdinand II of Alcala, Viceroy at Naples, depicted in a marvelously lifelike way. 16 February 1631.”

The veracity of these events was confirmed by the Ambassador of Venice in Naples, Marc’ Antonio Padovanino, who wrote on February 11, 1631: “In the rooms of Your Excellency, a very famous painter was making a portrait of a married Abruzzo woman and mother of many children, who has a totally virile face, with more than an inch of beautiful black beard, and a very hairy chest. His Excellency’s pleasure in showing it to me, as a marvelous thing, and truly so.”³

Thus, we have a 52-year-old woman who had given birth to three sons and then, at age 37, started to become virilized (“go through puberty”). We can assume that Ribera did not appreciate the physiology of the hypothalamic-pituitary-ovarian axis, as that was not described until the 20th century.⁴ He may have been unaware that it would be very likely that a 52-year-old woman in the 17th century would have undergone menopause and therefore be unable to conceive the infant she was holding.^{5,6} Although the association of the testes and virilization in men was known since antiquity, the concept of the testes secreting a substance was firmly established in 1849 by Berthold’s studies of castration and reimplantation of testicles in roosters, followed by Brown-Sequard’s classical human studies in 1889.⁷

The first descriptions of adrenal or ovarian pathology and virilization in women took place after Ribera’s death.⁸ Ribera also would not have been aware of the fact that androgen levels sufficient to fully virilize a woman would not only suppress ovulation, and hence pregnancy, but also lactation.⁹ So, the infant and the misplaced breast were undoubtedly Ribera taking “artistic license” to make sure that the viewer knew that Magdalena, indeed, was a woman. The fact that her breast did not display the hirsutism that the Ambassador commented upon adds credence to this interpretation. In addition, he painted two items on top of the stone tablets. One is clearly a spindle of wool with a metal hook (i.e., a bobbin), a symbol of femininity. The other is less clear, but may be a container with unspun wool threads, which would also signify femininity. However, some authors have interpreted this as a snail or mollusk shell.³ Since snails and some mollusks are known to be hermaphrodites, it has been proposed that Ribera was suggesting that Magdalena was a hermaphrodite (i.e., intersex), which would not be unreasonable, considering that she was clearly a woman with masculine features.^{3,10} However, the first demonstration that snails are hermaphrodites was made by John Ray in 1660, a full 29 years after Ribera completed his painting.¹¹

Despite there being no information concerning an abdominal exam for adrenal masses; a pelvic exam to look for clitoromegaly, ambiguity of her external genitalia such as fusion of labioscrotal folds, or ovarian masses; measurement of sex steroid hormones and gonadotropins; chromosomal analysis or imaging studies, we can use the information contained in the painting to arrive at a reasonable diagnosis.

DIFFERENTIAL DIAGNOSIS OF VIRILIZATION

The differential diagnosis of virilization in an adult female is listed in **Table 1**.

Exogenous androgens can be excluded since neither purified testosterone, testosterone precursors nor anabolic steroids were discovered nor available in the 17th century. Although an intersex disorder (hermaphroditism) with Magdalena having an ovary and a testis or ovotestes is possible, the three prior pregnancies and onset of virilization at age 37 makes this a very unlikely possibility. Hirsutism or virilization in individuals with hermaphroditism tends to appear during adolescence and young adulthood and pregnancies are rare.¹² Late-onset congenital adrenal hyperplasia generally manifests with mild hirsutism in adolescence and infertility, neither of which were present here.^{13,14} Similarly, polycystic ovarian syndrome is found in adolescents and young adults and results in oligo- or anovulation, infertility, and hirsutism, but rarely is associated with virilization.¹⁴ Hyperthecosis may cause hirsutism and virilization but is a condition that occurs in postmenopausal women whose ovarian theca cells produce excessive testosterone under the influence of elevated levels of luteinizing hormone.¹⁵ Although it is conceivable that Magdalena went through a premature menopause and also developed hyperthecosis, this is less likely than other sources of pathological androgen secretion.

Adrenocortical carcinoma may cause virilization but usually in association with excessive production of glucocorticoids and mineralocorticoids. She does not have the physical

Table 1. Causes of Virilization in Adult Women

Exogenous Androgens
Intersex (Disorder of Sexual Development; hermaphroditism)
Adrenal Disorders
• Late Onset Congenital Adrenal Hyperplasia
• Neoplasms
Adenoma
Carcinoma
Ovarian Disorders
• Polycystic Ovarian Syndrome
• Hyperthecosis
• Hyperreacto luteinalis
• Neoplasms
Luteoma of pregnancy
Sex Cord tumors
Sertoli Cell tumor
Granulosa Cell tumor
Stromal Cell tumor
Thecoma
Leydig Cell tumor
Sertoli-Leydig Cell tumor
Mixed Ovarian and Testicular (gyandroblastoma)
Metastatic mucinous carcinoma (Krukenberg tumor)

stigmata of Cushing syndrome and the 15-year history of virilization is a vanishing rare duration of life for a woman with an adrenocortical carcinoma or an androgen-secreting ovarian carcinoma.¹⁵ Similarly, excessive androgen secretion and virilization may be found in a patient with a mucin-producing adenocarcinoma that has metastasized to the ovary (Krukenberg tumor), but again, a 15-year survival of a Stage IV untreated breast or gastrointestinal carcinoma would be quite unlikely.¹⁶

Thus, four diagnoses remain. On the surface, a portrait of a virilized woman nursing a newborn brings to mind the possibility that the virilization occurred during pregnancy from either hyperreactio luteinalis with cystic enlargement of the ovaries from multiple theca-lutein cysts or a luteoma, both of which may produce sufficient androgens to cause hirsutism or virilization.^{16,17} However, the virilization improves or disappears following delivery. Neither of these disorders fit the clinical history of virilization occurring 15 years before the portrait was painted.

The final two possibilities are a benign adrenal or ovarian neoplasm. Androgen-secreting adrenal adenomas are less common than androgen-secreting ovarian neoplasms, and classically present with rapid onset of hirsutism, virilization and menstrual abnormalities in women in their mid-20s to mid-30s.^{15,18} Sertoli cell, Leydig cell, or combined Sertoli-Leydig cell ovarian neoplasms, which comprise the category of androblastomas, can occur in both reproductively-aged women and women who are post-menopausal and may lead to rapid virilization.¹⁵ Because these tumors are more common than pure androgen-secreting adrenal adenomas, it is likely that Magdalena harbored an androgen-secreting ovarian adenoma, although an androgen-secreting adrenal adenoma cannot be excluded based upon the clinical information that Ribera provided. Indeed, in his excellent analysis of the cause of Magdalena's virilization, W. Michael G. Tunbridge, MD, FRCP, Emeritus Physician, Nuffield Department of Medicine, Oxford, UK, also concluded that Ribera's subject suffered from a Sertoli-Leydig cell ovarian tumor.¹⁹

Although we do not have biochemical, imaging, or pathological confirmation of the diagnosis, Ribera's painting and brief clinical history provide sufficient information to arrive at a probable diagnosis. Today, we would measure testosterone and dehydroepiandrosterone sulfate, perform imaging, and, if necessary, a venous catheterization study of the ovarian and adrenal veins with testosterone measurements to confirm the diagnosis and recommend treatment.

References

1. Brown J, Kagan RL. The Duke of Alcalá: His collection and its evolution. *The Art Bulletin*. 1987;69:231-255.
2. Sears JB. The bearded lady (from some travel notes). *N Engl J Med*. 1958;258:1099-2000.
3. <http://en.fundacionmedinaceli.org/coleccion/fichaafondo.aspx?id=la-mujer-barbuda>
4. Plant TM. The hypothalamo-pituitary-gonadal axis. *J Endocrinology*. 2015;226:T41-T54.
5. Post JB. Ages at menarche and menopause: some Mediaeval authorities. *Population Studies*. 1971;25:83-87.
6. Amundsen DW, Diers CJ. The age of menopause in Medieval Europe. *Human Biology*. 1973;45:605-612.
7. Rostom M, Ramasamy R, Kohn TP. History of testosterone therapy through the ages. *Your Sexual Medicine J*. 2022;34:623-625.
8. Azziz R. A brief history of androgen excess. In *Contemporary Endocrinology: Androgen Excess Disorders in Women: Polycystic Ovary Syndrome and Other Disorders, Second Edition*. R. Azziz, et al. (eds). Humana Press, Inc., Totowa, NJ. 2006;3-16.
9. Duffy PV, Corsaro J. Suppression of lactation by testosterone. *JAMA*. 1941;116:33-36.
10. Valasco S. Hairiness in textural and visual culture in early modern Spain. *South Atlantic Review*. 2007;72:62-75.
11. Orstan A. John Ray's hermaphrodite snails on their 350th anniversary. *Mollusc World*. 2010;23:3-4.
12. Witchel SF. Disorders of Sex Development. *Best Pract Res Clin Obstet Gynaecol*. 2018;48:90-102.
13. Witchel SF. Congenital adrenal hyperplasia. *J Pediatr Adolesc Gynecol*. 2017; 30:520-534.
14. Cussen L, McDonnell T, Bennett G, et al. Approach to androgen excess in women: clinical and biochemical insights. *Clin Endocrinol*. 2022;97:174-186.
15. Hirschberg AL. Approach to investigation of hyperandrogenism in a postmenopausal woman. *J Clin Endocrinol Metab*. 2023;108:1243-1253.
16. Kanova N, Bicikova M. Hyperandrogenic states in pregnancy. *Physiol Res*. 2011; 60:243-252.
17. Masarie K, Katz V, Balderston K. Pregnancy luteomas. Clinical presentations and management strategies. *Obstet Gynecolog Surv*. 2010;65:575-582.
18. Cavlan D, Bharwani N, Grossman A. Androgen- and estrogen-secreting adrenal cancers. *Semin Oncol*. 2010;37:638-648.
19. Tunbridge WMG. *La Mujer Barbuda* by Ribera, 1631: a gender bender. *Q J Med*. 2011; 104:733-736.

Author

Glenn D. Braunstein, MD, Professor of Medicine, Cedars-Sinai Medical Center, Los Angeles, CA.

Disclosures

Conflicts of Interest: None

Funding Source: None

Acknowledgments

The author appreciates the helpful information provided by Ms. Matilde Fernandez Balsera and Ms. Andrea Perez of the Fundacion Medinaceli.

Correspondence

Glenn D. Braunstein, MD
9 Chatham Ct, Newport Beach, CA 92660
310-500-7675
Glenn.Braunstein@cshs.org