CLINICAL IMAGE

Giant uterine fibroid and adrenal tumor in a patient who ceased congenital adrenal hyperplasia treatment

Dorota Leszczyńska[1], Agata Tuszyńska-Meissner[1], Michał Ciebiera[2,3], Marta Włodarczyk[4,5], Wojciech Zgliczyński[1]

1 Department of Endocrinology, Centre of Postgraduate Medical Education, Warsaw, Poland
2 Warsaw Institute of Women's Health, Warsaw, Poland
3 Second Department of Obstetrics and Gynecology, Centre of Postgraduate Medical Education, Warsaw, Poland
4 Department of Biochemistry and Pharmacogenomics, Faculty of Pharmacy, Medical University of Warsaw, Warsaw, Poland
5 Centre for Preclinical Research, Medical University of Warsaw, Warsaw, Poland

Congenital adrenal hyperplasia (CAH) refers to a group of disorders characterized by genetic defects in steroidogenic enzymes. The most common cause of CAH is a mutation in the gene encoding 21-hydroxylase.[1] In patients with CAH, impaired negative feedback loop for inhibiting the release of adrenocorticotropic hormone by cortisol leads to adrenal hyperplasia, adrenal tumors, accumulation of cortisol precursors, and androgen excess, resulting in various forms of virilization in female patients.[2]

We report a rare case of a 51-year-old woman (karyotype 46,XX) with postnatally confirmed 21-hydroxylase deficiency in the steroid profile, severe virilization, and a large suspicious abdominal tumor (FIGURE 1A). The patient had been treated with prednisone and fludrocortisone as a child for a few years. She eventually stopped the treatment, which led to the development of full-blown CAH. The patient had a short stature, advanced male-pattern alopecia, significant hirsutism, clitoral hypertrophy, as well as primary amenorrhea (FIGURE 1A). Hormonal evaluation revealed abnormalities typical of CAH (Supplementary material, *Table S1*).

Computed tomography (CT) of the abdomen showed a giant, well-defined tumor (400 mm × 280 mm × 400 mm) that displaced and pressed all abdominal contents. Moreover, the scan yielded an image of enlarged adrenal glands and a heterogenous left adrenal tumor (92 mm × 70 mm) with calcifications and hemorrhagic areas (FIGURE 1B). Thanks to the collaboration of surgeons and gynecologists, hysterectomy with bilateral salpingo-oophorectomy and left adrenalectomy were successfully performed (FIGURE 1C). Histopathologic examination revealed a uterine fibroid and adrenal adenoma. Postoperatively, treatment with hydrocortisone (15 mg per day) and dexamethasone (0.25 mg once daily at bedtime) was prescribed. A significant decrease in the androgen level was observed; however, the degree of masculinization changed only slightly.

There is strong evidence that estrogens play a crucial role in development and growth of leiomyomas. In untreated women with CAH, the excess of estrogen results from androgen aromatization. Studies showed that in such patients, both aromatase (CYP19A1) and 17β-hydroxysteroid dehydrogenase type I (HSD17B1) were overexpressed in the fibroid tissue, as compared with the myometrium. This finding suggests that leiomyoma cells convert circulating androstenedione into estrone (via aromatase), and then into the active form of estrogen, estradiol (via HSD17B1).[3]

It has been demonstrated that, in addition to estrogen, progesterone action via progesterone receptor (PGR) increases fibroid volume through cell proliferation and extracellular matrix (ECM) accumulation.[4]

Considering the influence of estrogens, progesterone metabolites, and aromatizing activity on the development of leiomyomas, we assessed the expression of estrogen receptor (*ESR*), *PGR*, *CYP19A1*, and *HSD17B1* genes on the surface and in the center of the fibroid tissue.

Tissue gene expression was determined using TaqMan assays (Thermo Fisher Scientific, Waltham, Massachusetts, United States): *CYP19A1* (Hs00903413_m1), *HSD17B1* (Hs00166219_g1), *PGR* (Hs01556701_m1), *PGRB* (Hs04419616_s1),

Correspondence to:
Agata Tuszyńska-Meissner, MD, Department of Endocrinology, Centre of Postgraduate Medical Education, ul. Cegłowska 80, 01-809 Warszawa, Poland, phone: +48 22 569 05 29, email: agata.tuszynska@wp.pl
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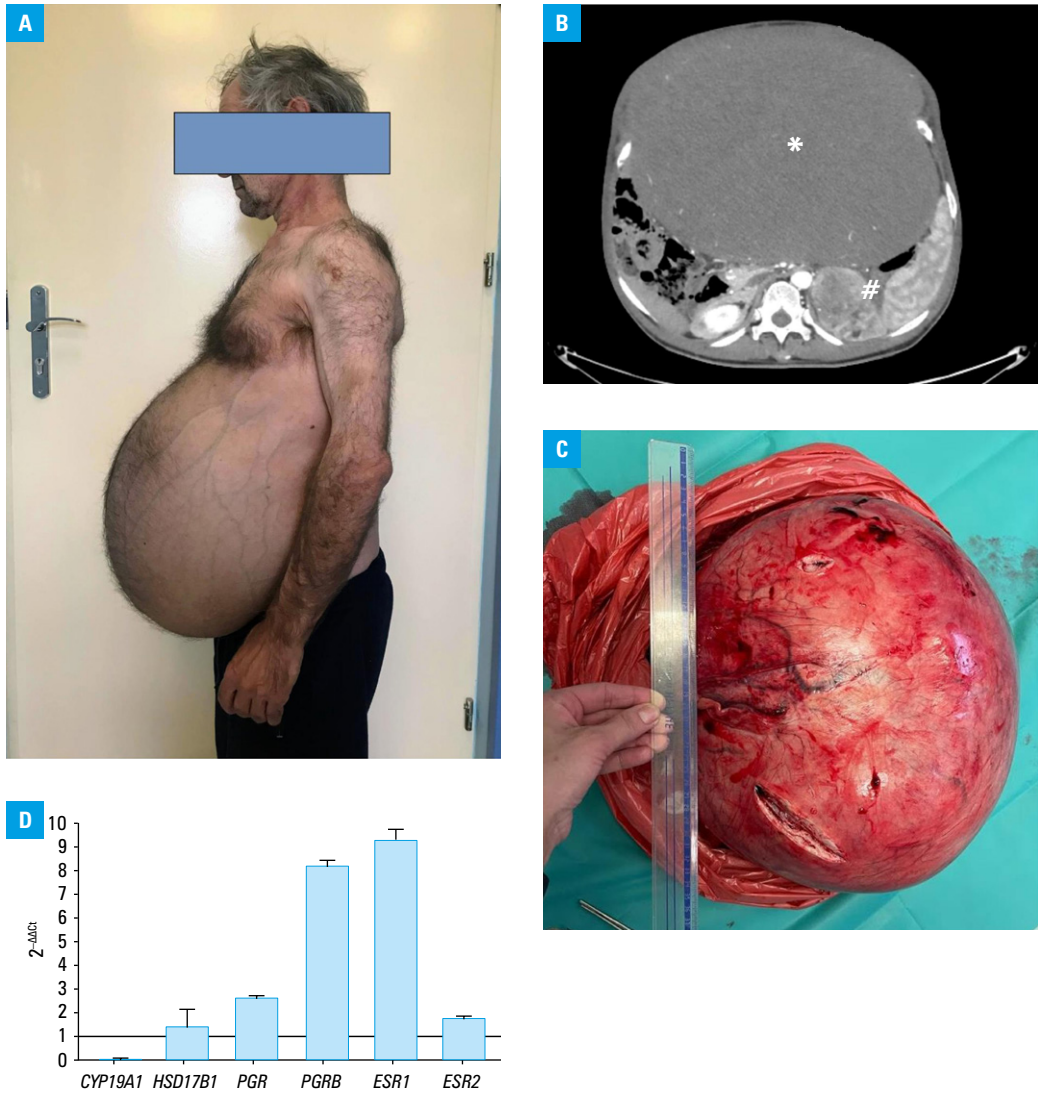

FIGURE 1 **A** – a 51-year-old woman with untreated congenital adrenal hyperplasia and a giant abdominal tumor; **B** – computed tomography scan showing the abdominal tumor (400 mm × 280 mm × 400 mm; asterisk) and the left adrenal tumor (92 mm × 70 mm; octothorpe); **C** – the resected uterine fibroid (44 cm × 38 cm × 88 cm); **D** – relative gene expression ($2^{-\Delta\Delta Ct}$ analysis) in the fibroid tissues (value of 1 refers to an equal expression, values >1 refer to higher expression, and values <1 refer to lower gene expression on the surface, as compared with the center part of the fibroid tissue); bars and whiskers represent the mean and SD obtained from the averages of 3 replicates of the samples.

ESR1 (Hs00174860_m1), *ESR2* (Hs01100353_m1), and *GAPDH* (Hs03929097_g1) as a reference gene. The $2^{-\Delta\Delta Ct}$ formula was used to assess the gene expression on the surface and in the center of the fibroid tissue.

Apart from *CYP19A1*, all the studied genes showed higher expression on the surface than in the center part of the fibroid (FIGURE 1D). The highest gene expression was observed for estrogen receptor 1 (*ESR1*) and progesterone receptor subtype B (*PGRB*). The higher expression of *PGRB* on the surface than in the center of the tissue may be related to the process of ECM accumulation and the fact that tumor development takes place faster in the outer layer of the fibroid tissue.[4]

In our opinion, untreated CAH, and consequently high concentrations of gestagens and androgens converted into estrogens, alongside with hormonal fibroid receptor status, may have created an appropriate environment for development of a giant uterine leiomyoma in the described patient. Such reasoning coincides with the current knowledge about the pathogenesis of uterine fibroids.[5]

SUPPLEMENTARY MATERIAL

Supplementary material is available at www.mp.pl/paim.

ARTICLE INFORMATION

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