CASE REPORT

Polycystic ovary syndrome due to the novel translocation 46XX t(2;9)(q21;p24)

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ABSTRACT

The etiology of polycystic ovary syndrome (PCOS) is not exactly known, but there are indications that genetic factors, exposure to androgen in early childhood, and obesity lead to a disruption of the hypothalamic-pituitary-ovarian axis and dysregulation of microRNAs. Chromosomal aberrations have rarely been described as a cause of PCOS. We present the case of a 20-year-old female diagnosed with PCOS at age 17 due to hyperandrogenism, obesity, polycystic ovaries, amenorrhoea, and emerging insulin resistance. A work-up for the cause of PCOS revealed a previously undescribed translocation 46XX t(2;9)(q21;p24). Alternative causes of PCOS were excluded. In addition, the patient had post-COVID syndrome. The patient was treated with contraceptive pills. PCOS can be caused by the translocation 46XX t(2;9)(q21;p24). The clinical manifestations of PCOS can be exacerbated by post-COVID syndrome.

KEYWORDS: PCOS; 46XX t(2; 9)(q21; p24); post-COVID; metabolic disease; hyper-androgenism

INTRODUCTION

Polycystic ovary syndrome (PCOS), also known as Stein-Leventhal syndrome, leads to infertility and affects up to 13% of females in childbearing age [1]. It is one of the most common endocrinopathies and the leading cause of unovulatory infertility in females [1]. The etiology of PCOS is not exactly known, but there are indications that genetic factors, exposure to androgen in early childhood, and obesity lead to a disruption of the hypothalamic-pituitary-ovarian axis and dysregulation of microRNAs [1-3]. Chromosomal abnormalities have been only rarely described as the cause of PCOS [4-6].

CASE PRESENTATION

The patient is a 20-year-old female, height 150.5cm, weight 68kg, sitting height of 82cm, body mass index (BMI) 27, who was diagnosed with PCOS at age 17 manifesting with hyperandrogenism with testosterone level of 0.6-0.7ng/ml (normal <0.45ng/ml), extensive acne vulgaris (which only marginally responded to the contraceptive pill), obesity, amenorrhoea, and emerging insulin resistance. Work-up for the cause of PCOS revealed the previously undescribed translocation 46XX t(2;9)(q21;p24). In addition to PCOS, the history was positive for intrauterine growth retardation (small for gestational age (SGA) child, birth weight 1160g in the 34th week of gestation, length 37cm (both <3rd percentile)), growth retardation from age 5 resulting in short stature, early puberty, menarche at age 12, and migraine since age 10. Since age 20 she changed to a vegan diet. In March 2022 she experienced a mild SARS-CoV-2 infection manifesting with coughing and powerlessness.

The family history was positive for attention deficit hyperkinesia syndrome (ADHS), Crohn's disease, schizoid personality, and myocardial infarction in her father, ADHS and Klinefelter syndrome in her brother, ankylosing spondylitis (morbus Bechterew) (grandfather from the mother's side), and arthritis (grandmother from the father's side). Her mother carried the same translocation as the index patient but did not manifest clinically.

Three months after a COVID-19 infection the patient additionally developed easy fatigability, exercise intolerance, and muscle cramps. She was referred to the neurologist for occasional dysarthria and chewing weakness, muscle cramps, leg stiffness, easy fatigability, exhaustibility, exercise-induced leg weakness, allodynia of lower limbs, and sore thigh muscles for five months.

Clinical neurologic exam revealed short stature, hypertelorism, facial acne, myopia, weakness for elbow extension and flexion (M5-) in the right, hirsutism of the linea alba, striae distensae on the thighs, knock knees, reduced Achilles tendon reflexes, but was otherwise normal including a negative Gower sign.

Cerebral magnetic resonance imaging (MRI) was non-contributive. Lumbar spine MRI only revealed a right L5 Tarlov cyst. Nerve conduction studies and needle electromyography were normal. Blood tests revealed hyperuricemia, low vitamin-D, vitamin B12, and folic acid, elevated copper, low selene, mild hypertriglyceridemia, hyperprolactinemia, very low luteic follicle stimulating hormones,

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elevated testosterone, elevated dihydro-epi-androstendione, and elevated sexual-binding hormone globulin. Transthoracic echocardiography only revealed atrial septum aneurysm. The HbA1c value was normal. Serum lactate was markedly elevated. Blood pressure was normal. Work-up for her complaints remained non-informative why mitochondrial disorder was ruled out as cause of PCOS and why post-COVID syndrome was additionally diagnosed.

She received vitamin D, B12, and folic acid substitution. For insulin resistance she was advised to reduce the intake of carbohydrates. Acne and hyperandrogenism were treated with ethinylestradiol 0.03mg/chlormadinonacetat 2mg. Migraine attacks responded to ibuprofen (600mg/attack).

DISCUSSION

The presented patient is interesting for PCOS and a previously undescribed translocation that was suspected to be causally related to PCOS. The diagnosis of PCOS in this patient was based on the ''Rotterdam criteria'', which were established in 2003 [7]. According to these criteria PCOS is diagnosed if there is oligo-ovulation or anovulation, surplus androgen activity, and polycystic ovaries [7]. The most common presentation of PCOS includes hyperandrogenism, menstrual cycle abnormalities, disturbed follicular development, and anovulation [8]. Other manifestations include obesity, type-2 diabetes, and cardiovascular disease [8]. PCOS has a strong impact on fertility of females [9]. Treatment of PCOS is symptomatic and requires a multidisciplinary collaboration to address the physiological, psychological, and psychosocial aspects of PCOS [9].

Whether PCOS was truly due to the translocation remains questionable. Arguments for a causal relation are that PCOS was previously reported in association with chromosomal defects [4-6]. A further argument in favor of a causal relation is that thus far no plausible, alternative explanation could be provided. There was no history of androgen exposure in early life, obesity-related hypothalamic-pituitary-ovarian axis dysfunction, and dysregulation of miRNAs. An argument against a causal relation is that the mother carried the same translocation as her daughter but did not manifest with PCOS. A mitochondrial disorder in addition to the translocation was largely ruled out upon the normal neurologic exam and the normal instrumental investigations. Arguments in favor of a mitochondrial disorder are that PCOS has been repeatedly reported in patients with a mitochondrial disorder [10] and that the patient had some stigmata of a mitochondrial disorder, such as short stature, migraine, easy fatigability, exercise intolerance, hyperuricemia, hypercholesterolemia, and knock knees. Occasional dysarthria, chewing weakness, muscle cramps, leg stiffness, easy fatigability, exhaustibility, exercise-induced leg weakness, allodynia of lower limbs, and sore thigh muscles occurring after a SARS-CoV-2 infection were interpreted as long-COVID syndrome.

CONCLUSIONS

This case shows that PCOS may be due to the translocation 46XX t(2;9)(q21;p24). Clinical manifestations in addition of those attributable to PCOS require thorough work-up not to miss a double trouble. PCOS may be aggravated by post-COVID syndrome.

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Compliance with Ethics Guidelines

This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

Patients consent

Informed, written consent was obtained from the patient to publish the case in anonymous form.

REFERENCES

1. Joham AE, Piltonen T, Lujan ME, et al. Challenges in diagnosis and understanding of natural history of polycystic ovary syndrome. *Clin Endocrinol (Oxf)*. 2022;97(2):165-173. PMID: 35593530; PMCID: PMC9541175. doi: 10.1111/cen.14757.
2. Wang T, Liu Y, Lv M, et al. miR-323-3p regulates the steroidogenesis and cell apoptosis in polycystic ovary syndrome (PCOS) by targeting IGF-1. *Gene*. 2019;683:87-100. PMID: 30300681. doi: 10.1016/j.gene.2018.10.006.
3. Finsterer J. Mitochondrial Dysfunction in Polycystic Ovary Syndrome. *Reprod Sci*. 2023;30(5):1435-1442. PMID: 36221022. doi: 10.1007/s43032-022-01100-z.
4. Kuznetzova T, Baranov A, Ivaschenko T, et al. X;Y translocation in a girl with short stature and some features of Turner's syndrome: cytogenetic and molecular studies. *J Med Genet*. 1994;31(8):649-651. PMID: 7815426; PMCID: PMC1050031. doi: 10.1136/jmg.31.8.649.
5. Georgieva V, Ganev V. Familen sluchaĭ na balansirana khromozomna translokatsiia (7;8) (q11;p23) kato prichina za reproduktivni neblagopoluchiia [Familial case of a balanced chromosomal translocation (7;8) (q11;p23) as a cause of reproductive failure]. *Akush Ginekol (Sofiia)*. 1983;22(5):409-414. Bulgarian. PMID: 6687104.
6. Frederic J, Lennès G, Rongé-Collard E, et al. Mise en évidence par analyse statistique d'une petite translocation chez un sujet atteint du syndrome de Stein-Leventhal [Demonstration, by statistical analysis, of a small translocation in a patient with Stein-Leventhal syndrome]. *J Genet Hum*. 1967;16(1):25-41.
7. Rotterdam ESHRE/ASRM-Sponsored PCOS consensus workshop group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). *Hum Reprod*. 2004;19(1):41-47. PMID: 14688154. doi: 10.1093/humrep/deh098.
8. Azziz R, Carmina E, Chen Z, et al. Polycystic ovary syndrome. *Nat Rev Dis Primers*. 2016;2:16057. PMID: 27510637. doi: 10.1038/nrdp.2016.57.
9. Lathia T, Joshi A, Behl A, et al. A Practitioner's Toolkit for Polycystic Ovary Syndrome Counselling. *Indian J Endocrinol Metab*. 2022;26(1):17-25. PMID: 35662757; PMCID: PMC9162262. doi: 10.4103/ijem.ijem_411_21.
10. Finsterer J. Photosensitive Epilepsy and Polycystic Ovary Syndrome as Manifestations of MERRF. *Case Rep Neurol Med*. 2020;2020:8876272. PMID: 33062354; PMCID: PMC7542499. doi: 10.1155/2020/8876272.