INTRODUCTION

Trichotillomania (TTM) and Polycystic Ovarian Syndrome (PCOS) are common among young females. TTM, also known as Hair Pulling Disorder, is characterized by repetitive pulling of one’s hair commonly the scalp, eyebrows, and eyelashes but could also involve other parts of the body [1]. Majority of patients started hair pulling in between ages of 11 and 15 years [1]. Polycystic ovarian syndrome (PCOS) is a common metabolic-endocrine disorder characterized by menstrual irregularity, clinical hyperandrogenism, and ultrasound appearance of polycystic ovaries according to Rotterdam criteria [2]. It presents in 12-21% of women of reproductive age. Clinical symptoms of PCOS such as acne, hirsutism, obesity, and alopecia may cause psychological problems and body image issues, whereas psychiatric problems such as depression and anxiety, are common comorbidities seen in people with TTM [2].

Scientific evidence linking TTM and PCOS is insufficient. Our current understanding suggests the important roles of stress in both TTM & PCOS [3, 4]. There is also growing evidence of the effectiveness of N-acetylcysteine (NAC) in the treatment of both TTM & PCOS [5, 6]. How common is the co-occurrence between TTM and PCOS and what is the possible explanation?

CASE PRESENTATION

A 16 years old female secondary school student was diagnosed with trichotillomania (TTM) and Polycystic Ovarian Syndrome (PCOS) at 13 years old. She had been having repeated hair-pulling behavior, for three years prior to referral to psychiatric service. The behaviour was triggered by academic and family related stressors. There was ongoing marital disharmony between her parents, which had negatively affected her emotion. She was close to her mother who was supportive while her father was not involved and
emotionally absent. The hair-pulling behaviour increased when she felt stress and anxious. She repeatedly pulled one hair at a time to its roots. The hair pulling was mainly over the frontal scalp and axillary areas resulting in localised alopecia. There was no other associated behaviour such as trichophagia, trichotympsis, skin picking, and nail-biting. The alopecia had caused low self-esteem and distress but there were no significant depressive or anxiety symptoms.

Mental state examination revealed an anxious teenager who appeared sad when talking about her stressors. However, there were no persistent depressive affects. She also did not have any suicidal thoughts. Physical examination revealed a teenage girl with BMI of 24.7 kg/m². There was acne on her face, but no hirsutism. She had a patch of frontal alopecia with multiple patchy areas of baldness with hair follicles on her scalp.

She was treated with psychotherapy (i.e., relaxation and breathing technique) and habit reversal therapy. She was referred to the Gynaecologist for irregular menses. She reached menarche at 12 years old and had been having irregular menses ever since. Her laboratory findings revealed normal FSH level (6.1 IU/L), Estradiol level (90 pmol/L), Testosterone level (0.710 nmol/L), and androgen level (DHEA Sulfate) (4.47 umol/l) but high LH level (16.8 IU/L). Thyroid Function Test was normal (TSH: 2.61uIU/ml, Free T4: 12.86 pmol/L). Transabdominal ultrasound showed polycystic ovaries. She was diagnosed with PCOS and treated with Loette, a combined oral contraception therapy (COCP) for three months to regulate her menses. She was also advised to reduce her weight. She responded to treatment and had regular withdrawal bleeding following the treatment. She was also referred to dermatology for alopecia.

She progressed fairly well with treatments. She responded well with psychotherapy and was symptom-free for a month but the hair pulling behaviour started again due to the ongoing stressors. In relation to that, her menses became irregular again, and she was given progesterone challenge i.e. Tablet Provera 5 mg twice daily for five days followed by a continuation of her COCP. Her menstrual cycle became regular and COCP was discontinued. With continuous psychotherapy, the TTM symptoms improved but unfortunately, she had defaulted treatments since then.

**DISCUSSION**

The patient was diagnosed with TTM and PCOS at the age of 13 years old. Few stressors at the time possibly act as precipitating factors, triggering TTM and PCOS in the patient during her adolescent stage. This case highlights the co-occurrences of TTM and PCOS, but there is insufficient scientific evidence to suggest a possible link between the two conditions.

**What are the possible mechanisms to suggest the co-occurrences of TTM & PCOS?**

Stress plays significant roles in both TTM and PCOS, most probably as a trigger to people with biological vulnerabilities to develop the conditions. An individual with TTM has a higher level of emotional dysregulation [7] hence exposure to stress creates a sense of tension or an urge to pull hair that precedes an episode of TTM [8]. Individuals with TTM also show decrease of emotional states immediately after hair pulling [7].

Females with PCOS had stronger Hypothalamic-Pituitary-Adrenal axis (HPAA) response to a stressor and showed significantly greater increase in the HPAA axis mediators i.e. ACTH and cortisol compared to those without PCOS. Stress may increase testosterone level and lead to exacerbation of PCOS symptoms. Hyper-responsiveness of HPAA to stress may increase various health risks associated with PCOS including metabolic syndrome and cardiovascular disease. Stress-induced cortisol also plays a role in the development of depression among females with PCOS [3, 9, 10].

The other possible mechanism to explain the co-occurrences of the two illnesses is the involvement of oxidative stress. Oxidative stress, which is the imbalance accumulation of free radicals within the body that can interfere with normal functions, were found in both illnesses [11, 12]. There are several abnormal biomarkers in PCOS patient suggesting oxidative stress as one of its pathophysiology [12]. For instance, recent studies show that glutathione level is low in patients with TTM [11] and PCOS [12]. Lower glutathione level
has been correlated with higher motor impulsivity in TTM [11].

There were emerging evidence of literature on the effective roles of N-acetylcysteine (NAC) to treat both TTM [5] and PCOS [6]. NAC is a precursor to glutathione, through the generation of cysteine, and plays a role in the regulation of glutamatergic system [13]. Glutamatergic dysfunction has been implicated in the pathogenesis of obsessive-compulsive disorder, a disorder with phenomenology and possible neurobiological links to TTM. NAC is converted to cysteine causing reverse transport of glutamate into extracellular space, stimulating inhibitory metabotropic glutamate receptors and consequently reducing synaptic release of glutamate. The restoration of extracellular glutamate concentration in nucleus blocks reinstitution of compulsive behaviours. NAC, may, therefore, correct the underlying pathophysiological abnormalities and treat symptoms of TTM.

In PCOS, NAC effectively decreases levels of insulin, LH, leptin and malondialdehyde (MDA) in follicular fluid through antioxidant and anti-apoptotic actions [14]. NAC increases the cellular levels of antioxidant and reduces glutathione at higher doses hence, potentially improves insulin receptor activity in human erythrocytes and insulin secretion in response to glucose. Reduction in the levels of circulating insulin can lead to significant decline in testosterone levels and free androgen index in women responding to the treatment. NAC may provide a novel approach for increasing or inducing ovulation in patients with chronic anovulation, including PCOS [6, 14].

CONCLUSION

The pathophysiology of TTM and PCOS share some common mechanisms, which may explain the existence of both disorders in some patients. At present, there is inadequate scientific evidence to suggest a possible link between the two conditions. Further studies need to be done in this area to understand the common neurobiology and other aetiological factors, that would better explain the co-occurrences between TTM and PCOS.

Conflict of Interest

Authors declare none

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REFERENCES

1. Golomb R, Franklin M, Grant JE, Keuthen NJ, Mansueto CS, Mouton-Odum S, Novak C, Woods D. Expert Consensus: Treatment Guidelines for Trichotillomania, Skin Picking And Other Body-Focused Repetitive Behaviors. California: Trichotillomania Learning Center, Inc. 2011. https://www.bfrb.org/storage/documents/Expert_Consensus_Treatment_Guidelines_2016w.pdf. Accessed 10 July 2017.
2. Boyle J. Polycystic ovary syndrome. Aust Fam Med. 2012; 41(10): 752–756.
3. Benson S, Arck PC, Tan S, Hahn S, Mann K, Rifaie N, Janssen OE, Schedlowski M, Elsenbruch S. Disturbed stress responses in women with polycystic ovary syndrome. Psychoneuroendocrinology. 2009. 34(5): 727–735.
4. Walther MR, Snorrason I, Flessner CA, Franklin ME, Burkel R, Woods DW. The Trichotillomania Impact Project in Young Children ( TIP-YC ): Clinical Characteristics, Comorbidity, Functional Impairment and Treatment Utilization. Child Psychiatry Hum Dev. 2014. 45: 24-31
5. Grant JE, Odlaug BL, Won Kim S. N-Acetylcysteine, a Glutamate Modulator, in the Treatment of Trichotillomania. Arch Gen Psychiatr. 2009. 66(7): 756.
6. Thakker D, Raval A, Patel I, Walia R. N-Acetylcysteine for Polycystic Ovary Syndrome: A Systematic Review and Meta-Analysis of Randomized Controlled Clinical Trials. Obstet Gynecol Int. 2015. 2015: 1–13.
7. Arabatzoudis T, Rehm IC, Moulding R. Emotional regulation in individual with or without trichotillomania. J Obsessive Compuls Relat Disord. 2017. doi: 10.1016/j.jocrd.2017.01.003
8. Woods DW, Houghton DC. Diagnosis, Evaluation, and Management of Trichotillomania. Psychiatr Clin North Am. 2015. 37(3): 301–317.

9. Barry JA, Kuczmierczyk AR, Hardiman PJ. Anxiety and depression in polycystic ovary syndrome: A systematic review and meta-analysis. Hum Reprod. 2011; 26(9): 2442–2451.

10. Barry JA, Hardiman PJ, Saxby BK, Kuczmierczyk A. Testosterone and mood dysfunction in women with polycystic ovarian syndrome compared to subfertile controls. J Psychosom Obstet Gynecol. 2011; 32(2): 104–111.

11. Grant JE, Chamberlain SR. A Pilot Examination of Oxidative Stress in Trichotillomania. Psychiatry Investig. 2018; 15(12): 1130–1134.

12. Mora Murri, Manuel Luque-Ramírez, María Insenser, Miriam Ojeda-Ojeda, Hector F. Iscobar-Morreale, Circulating markers of oxidative stress and polycystic ovary syndrome (PCOS): A systematic review and meta-analysis. Hum Reprod Update. 2013; 19(3): 268–288.

13. Sansone LA. Getting a knack for N-Acetyl-Cysteine. Innov Clin Neurosci 2011; 8(1): 10–14.

14. Cheraghi E, Mehranjani MS, Shariatzadeh MA, Esfahani MHN, Ebrahimi Z. N-Acetylcysteine improves oocyte and embryo quality in polycystic ovary syndrome patients undergoing intracytoplasmic sperm injection: An alternative to metformin. Reprod Fertil Dev. 2016; 28(6): 723–731.