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HIRSUTISM IN A WOMAN ON SULPIRIDE: A CASE REPORT.

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ABSTRACT

Antipsychotic medications are used to manage psychosis, principally in schizophrenia. There are many side effects of antipsychotic medications including hyperprolactinemia. The common presentations of hyperprolactinemia in pre-menopausal woman are many but hirsutism is a rare presentation. We report a case of a 47-year-old Malay lady who was noticed to have hirsutism two years after changing to oral sulpiride. She was on oral sulpiride for 7 years. Diagnosis of hirsutism secondary to hyperprolactinemia, induced by antipsychotic medication was made after excluding other causes of hirsutism. It is important for all physicians to understand that antipsychotic medication causes hyperprolactinemia and can potentially induce hirsutism.

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Keywords: Antipsychotic agents, Hirsutism, Hyperprolactinemia, Schizophrenia, Sulpiride.

INTRODUCTION

Hirsutism is defined as excessive male-pattern hair growth, in area of upper lips, chin, ears, cheeks, lower abdomen, back, chest and proximal limbs and affects about 5 to 10% of women. [1,2] The common causes of hirsutism are polycystic ovarian syndrome, acromegaly, Cushing disease, pathology arising from pituitary-gonadal axis, and adrenal tumours and drugs.[3]

Antipsychotic medications such as sulpiride, block dopamine D_2 receptors in the hypothalamic tuberoinfundibular tracts that removes the inhibitory effects of dopamine on the pituitary causing increased release of prolactin into the blood stream. The clinical manifestations of hyperprolactinemia in women are infertility, oligomenorrhea or amenorrhea and galactorrhea.[4] Hirsutism as a consequence of hyperprolactinemia due to antipsychotic medications is rare. Here we present a case report of a 47-year-old Malay lady who was noticed to have hirsutism two years after changing to oral sulpiride.

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CASE REPORT

A 47-year-old single, Malay lady with hypertension and dyslipidemia presented to the hospital for relapse schizophrenia. She was diagnosed with schizophrenia thirty-one years ago and was under the care of community psychiatric clinic. She was initially on oral

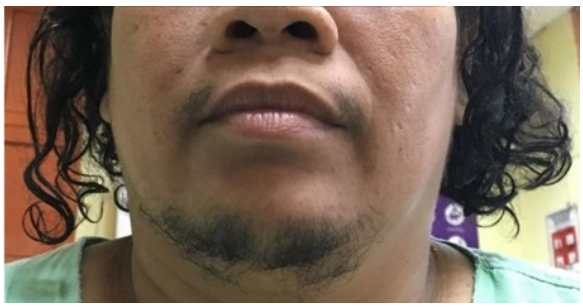

Figure 1: Excessive hair growth over upper lip and chin. (Click on image to enlarge)

haloperidol, chlorpromazine and intramuscular fluphenazine injection. Her medications were changed to oral sulpiride seven years ago after she developed neuroleptic malignant syndrome.

Her family members noticed excessive hair growth over her upper lip, chin and upper chest two years after taking oral sulpiride. These changes were only noticed by the doctors during her recent admission for relapsed schizophrenia. Further history revealed that she had changes in her menstrual cycle as the duration of her menstruation period was shortened and was irregular. She did not have breast engorgement, galactorrhoea, headache, blurring of vision or other neurological complaints.

On physical examination, there was excessive hair growth over the upper lip, chin, upper chest and inner thigh. Figure 1 shows the facial hair distribution in this patient. There were no signs of virilisation such as frontal balding, clitoromegaly, or deepening of voice. She scored 8 on Ferriman-Gallwey hirsutism scoring system indicating abnormal results. Score of 7 or above is considered abnormal in Asian populations.[5] Cranial nerve and other examinations were unremarkable. The abdominal and pelvic ultrasound was done and revealed no adrenal or ovarian masses. Table I shows the results of the endocrine blood investigations of our patient.

Polycystic ovarian syndrome is the commonest cause of hirsutism. At the same time, we entertained the possibility of androgen-secreting tumour and adrenal hyperplasia. Having exhausted our efforts ruling out other possible causes, it was safe to state that hirsutism was the side-effect of the chronic sulpiride therapy. Following the discussion with the patient and her family members, the decision was reached to continue with sulpiride as her antipsychotic treatment as she was doing well while on it. The cosmetic part would be dealt with later, with regular shaving as an option.

DISCUSSION

This patient's testosterone and prolactin levels were elevated while levels of other hormones were normal. The causes of elevated

Table I: Endocrine blood investigation results.

Hormonal Test	Level	Normal range
Serum Testosterone	94.3ng/dL	15 – 70ng/dL *
Serum Prolactin	1053mIU/L	< 600mIU/L †
Dehydroepiandrosterone sulfate (DHEAS)	235ug/dL	<700ug/dL *
17-hydroxyprogesterone (17-OHP)	1.988nmol/L	<5.15 nmol/L *
Luteinizing hormone (LH)	15.89IU/L	3 - 16IU/L †
Follicular Stimulating Hormone (FSH)	8.04IU/L	2 - 8IU/L †
Morning serum Cortisol	342.1nmol/L	320 - 450nmol/L †
Free Thyroxine	21.93pmol/L	9 – 22pmol/L †
Thyroid Stimulating Hormone (TSH)	1.96mIU/L	0.5 – 4.2mIU/L †
HbA1c	5.7%	<6.5% †

* Based on Martin et al., 2018 [5].
† Based on Wilkinson et al. 2017 [15].

serum testosterone need to be identified. Although her testosterone level was higher than normal, it did not exceed 200ng/dL. Thus, the possibility of androgen-secreting tumour was excluded.[6] The normal level of 17-OHP and DHEAS also makes androgen-secreting tumour and congenital adrenal hyperplasia unlikely. Her normal pelvic ultrasound and HbA1c result ruled out ovarian hyperthecosis such as polycystic ovarian syndrome. The patient's drug history was further explored. Drugs that are associated with hirsutism include glucocorticoids, cyclosporine, phenytoin, diazoxide, minoxidil and some antipsychotic medications.[7]

The antipsychotic medication taken by our patient was sulpiride. Table II shows antipsychotic effect on prolactin level.[8] Compared to other antipsychotics, sulpiride has higher potency in elevating prolactin. This explained the hyperprolactinemia in our patient. At this point, we explored the relationship between hyperprolactinemia and hirsutism. Seppala et al., first described the association between hyperprolactinemia and hirsutism in 1975.[9] The study found that all women with amenorrhea-hirsutism syndrome had elevated prolactin levels without any evidence of a pituitary tumour. From later literature, few mechanisms had been proposed to explain hyperprolactinemia induced hirsutism. Hampel et al., suggested that prolactin inhibits the hepatic synthesis of sex hormone-binding globin, thereby raising the concentration of plasma-free testosterone.[10] Hatch et al., stated prolactin synergises with luteinizing hormone to stimulate testosterone synthesis.[11] In a latest review by Rosenfield et al., it is suggested that hyperprolactinemia stimulates adrenal formation of the prohormone dehydroepiandrosterone sulfate which is metabolised to testosterone in peripheral fat cells causing testosterone level to increase in blood.[12]

Table II: Antipsychotic medications effect on prolactin level.

Drugs	Effect on Prolactin Levels
Sulpiride	+++
Aripiprazole	-
Clozapine	-
Olanzapine	+
Quetiapine	-/+
Risperidone	+++
Chlorpromazine	+++
Haloperidol	+++
Flupentixol	+++

Simplified from Peuskens, J et al.[8]
Symbols: +++ high incidence/severity; ++ moderate; + Low; - Very low

In our patient, the temporal relationship between the introduction of sulpiride and the occurrence of hirsutism made it very likely that sulpiride induced the excessive hair growth. However, specific study about effects of sulpiride on hirsutism is lacking. It is possible due to advancement of atypical antipsychotic drugs that have lesser side effects, the use of sulpiride in schizophrenia management is less popular.

As for our patient, the management goal aims to normalise the prolactin level and prevent long term complications such as osteopenia and osteoporosis without risking another episode of relapse schizophrenia. Management options include reducing the antipsychotic dose or switching to an antipsychotic such as aripiprazole that is less likely to raise serum prolactin level.[13] If switching to other antipsychotic is chosen, cross tapering the antipsychotics is preferable to abruptly switching to new antipsychotics.[14] If the above option is not feasible, adding aripiprazole or a dopamine agonist to the concurrent treatment regime can be considered.[15] The choice of management should only be decided in conjunction with psychiatrist advice.

CONCLUSION

Antipsychotic medication Sulpiride can potentially cause hirsutism, as shown by this case. It is important for all physicians to under-

stand that antipsychotic medication causes hyperprolactinemia and can potentially induce hirsutism, through the inhibition of hepatic synthesis of sex hormone-binding globin by elevated prolactin level and thereby elevated free plasma testosterone level. More importantly we must exclude other serious diseases before considering antipsychotic as the cause of hirsutism.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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DECLARATION

Consent for publication including use of photo obtained from patient.

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