New onset of alopecia in a young woman with end-stage renal disease

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Background

Hair loss is a common complain of women receiving renal replacement therapy. Apart from its emotional impact on the patient, hair loss might allude to several underlying diseases. Differential diagnoses include malnutrition, adverse effects of drugs, endocrine, inflammatory or autoimmune disorders, abnormal behaviour (trichotillomania) or tinea capitis [1]. Therefore, a thorough exploration of affected patients is constitutional.

Case

A 30-year-old woman (see Figure 1) complained about a progressive hair loss within the preceding 5 months. Past medical history included end-stage renal disease (ESRD) due to IgA nephropathy; she received CAPD in our institution for 6 years. Furthermore, mentionable are arterial hypertension, normochromic anaemia and secondary hyperparathyroidism. Menarche was at the age of 12. The patient reported amenorrhea since 1 year after the withdrawal of oral contraceptives that she had taken before since she was 16 years old. Yearly gynaecological examinations were without pathological findings. Prescribed medications included ACE inhibitor, beta-blocker, furosemide, erythropoietin beta, cholecalciferol, calcium carbonate, sevelamer and iron(III) gluconate.

On physical examination the patient showed a nonscarring hair loss involving the central and temporal area of the scalp as well as hirsutism (modified Ferriman–Gallwey Score: 12) [2]. There was no evidence of galactorhea. Body mass index was 24.2 kg/m²; systolic and diastolic blood pressure ranged between 150 and 95 mmHg. Further physical examination remained unobtrusive.

The combination of hirsutism, alopecia and amenorrhea was highly suspicious for an underlying androgen excess. Differential diagnoses included gonadal or adrenal hyperandrogenism, Cushing’s syndrome, hyperprolactinaemia, hypothyroidism and acromegaly [3]. We accomplished a hormonal evaluation (in serum and plasma) that confirmed androgen excess (Table 1). These results were reconcilable with gonadal hyperandrogenism. Normal DHEAs, ACTH and 17 hydroxyprogesteron levels made different forms of adrenal hyperandrogenism such as adrenal neoplasm or congenital adrenal hyperplasia unlikely. Polycystic ovary syndrome (PCOS) is the most common cause of ovarian androgen excess and can be diagnosed after exclusion of other conditions if two of the following are present: oligo- or anovulation (usually represented as oligo- or amenorrhea), hyperandrogenaemia or hyperandrogenism [4]. Our patient in fact fulfilled all criteria. For diagnosis of PCOS polycystic ovaries need not to be present; however, an ultrasound examination of our patient showed enlarged ovaries with multiple cysts. PCOS may be associated with impaired glucose tolerance in up to 50% of patients [5]. A normal 75 g OGTT excluded this condition in the present case.
Table 1. Selected laboratory results

|                      | Actual value | Reference range |
|----------------------|--------------|-----------------|
| Testosterone (nmol/l) | 6.1          | 0.5–2.6         |
| Free testosterone (pmol/l) | 13.7        | 0.2–8.9        |
| Androstenedione (nmol/l)  | 9.0         | 1.6–9.3        |
| Sulfated dehydroepiandrosterone (µmol/l) | 5.3         | 1.2–7.3        |
| LH (U/l)              | 20.9         | n.d.            |
| FSH (U/l)             | 4.8          | n.d.            |
| 17 beta estradiol (pmol/l) | 144         | n.d.            |
| Prolactin (µg/l)      | 22.9         | 3.9–29.5       |
| ACTH (pmol/l)         | 7.8          | 2.6–10.1       |
| TSH (mU/l)            | 0.59         | 0.27–4.2       |
| 17 hydroxyprogesterone (nmol/l) | 11.6      | n.d.            |
| Cortisol (nmol/l)     | 272          | 119–618        |
| IGF 1 (ng/ml)         | 201          | 109–324        |
| Iron (µmol/l)         | 10.3         | 4.1–29.5       |
| Ferritin (µg/l)       | 272.1        | 15–150          |

We initiated a combined estrogen–progesterone therapy that improved hirsutism, reversed alopecia and resulted in regular menstrual bleeding. Since ESRD per se is associated with a low rate of conception and a high rate of spontaneous abortion we discouraged the patient to initiate a treatment with clomiphene citrate that induces ovulation and was shown to increase pregnancy rates in patients with PCOS [6]. However, clomiphene might be a treatment option after successful renal transplantation.

Discussion

About 30% of women will suffer from hair loss throughout their lifetime [1]. The two major forms of alopecia are scarring and nonscarring. Our patient had nonscarring alopecia that excludes diseases such as lupus erythematoses or lichen planus as underlying causes. Data about uraemia- and dialysis-related alopecia are limited. It might be associated with malnutrition—especially iron and zinc deficiency, anticoagulation with heparin during haemodialysis or in response to a major illness. However, affected women typically show telogen effluvium that abruptly begins ~3 months after the trigger event and is characterized by diffuse and prominent shedding [1]. Our patient neither reported a major illness nor received heparin or had nutritional deficiency. The distribution of hair loss made other forms of nonscarring alopecia such as alopecia areata, tinea capitis or traumatic alopecia unlikely. Female-pattern alopecia is the most common form of alopecia; the causative conditions often remain uncertain.

The prominent finding in our patient was the female pattern of hair loss in combination with hirsutism and amenorrhea that indicated androgen excess. However, it should be considered that the majority of premenopausal women with ESRD and long-term dialysis experience anoovulation, often associated with oligo- or amenorrhea [7,8]. Furthermore, hirsutism affects ~10% of women of reproductive age and is often idiopathic [9]. Uraemia-related amenorrhea is typically associated with supranormal LH levels and an increased LH/FSH ratio but normal testosterone and estradiol levels [8].

Symptoms of PCOS usually become evident around menarche yet a later onset may occur [3]. Our patient reported the intake of an estrogen–progestin contraceptive since the age of 16. This suppressed ovarian androgen excess and might have prevented the development of hirsutism and alopecia at an earlier date.

Treatment options for PCOS in general include control of hyperandrogenism, treatment of metabolic abnormalities and management of oligomenorrhea [3]. The latter condition might be associated with endometrial hyperplasia and an increased risk of endometrial carcinoma. The estrogen–progesterone combination as used in the present case is a very potent treatment for hirsutism, alopecia and the restoration of regular menstrual bleeding. However, this treatment is controversial due to its adverse metabolic effects, e.g. deterioration of insulin resistance [3]. There are currently no data available about possible cardiovascular complications after long-term treatment.

The best therapy for metabolic abnormalities in PCOS is lifestyle modification that includes the increase of physical activity and—if necessary—the induction of a diet. Recent data demonstrated favourable effects of metformin for women with PCOS. In addition to the improvement of glucose tolerance, metformin reduced serum androgen levels and improved menstrual cyclicity [10]. Thiazolidinediones might serve as an alternative therapeutic option if metformin is contraindicated (as in ESRD). However, their known spectrum of side effects—as the paucity of data about long-term effects available—discourages most physicians from its use in PCOS.

Conflict of interest statement. None declared.

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