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Case Report Open Access

Type II Pityriasis Rubra Pilaris Associated with Grave's Disease-Case Report

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Abstract

Introduction

Pityriasis Rubra Pilaris (PRP) is a chronic inflammatory dermatological disease with no definite underlying cause to date, but many reports have linked it with autoimmune disorders, HIV infection, internal malignancies, streptococcal infections, hypothyroidism, and genetic mutation in a familial form.

The relation to hypothyroidism is partially established. This link has been reported in medical literature; researchers suggested assessing the thyroid status as part of the PRP workup. We are reporting, for the first time, a case of PRP in association with Grave's disease, which subsided after gaining control of the hyperthyroid status.

Case presentation: A 24-year-old Syrian female presented with symptoms and signs of hyperthyroidism, as well as extensive skin dryness, hyperkeratosis, and skin breaks at the hands and feet associated with widespread squamous plaques over the extensor surfaces of the joints, which were not responding to any type of emollients. She was diagnosed with Grave's disease and PRP and subsequently treated with anti-thyroid medications followed by radioactive iodine therapy, after which the PRP features improved remarkably.

Conclusions: This is the first report of PRP in association with Grave's disease. This link needs to be confirmed with more case reports. We agree with the previous suggestion of having thyroid function assessed cases of PRP refractory to traditional therapies. In those patients whose PRP is associated with thyroid dysfunction, in addition to topical agents, normalization of thyroid status should be attempted and might be beneficial.

Keywords: Pityriasis rubra pilaris; Grave's disease; Papulosquamous disease; Hypothyroidism; Keratosis

Introduction

Pityriasis Rubra Pilaris (PRP) is a chronic inflammatory papulosquamous disease for which the exact cause is not yet clear, but many reports have associated it with autoimmune disorders, HIV infection, internal malignancies, streptococcal infections, hypothyroidism, and genetic mutation in a familial form [1-6].

PRP can be subdivided into five classes, with the classic adult type being the most common with the other forms being atypical adult, classic juvenile, circumscribed juvenile, atypical juvenile [4], and recently HIV-associated (or Type VI) has been added [7]. The pathogenicity of the PRP is not clear, but tissue necrosis factor-alpha (TNF-alpha) has been suggested to play a major role [7]. Moreover, alteration of vitamin A metabolism, post-infectious auto-immunogenicity drugs (Sorafenib) [9], and genetic predisposition (CADR14 gene) [1], have all been proposed as predisposing factors of PRP. 'Nonetheless, the pathogenic roles of these factors have not been proven with scientific evidence.

PRP can be treated with a wide range of options; this includes topical vitamin D derivatives, tazarotene, or emollients. Oral treatments include vitamin A, methotrexate, and TNF-alpha inhibitors. The response rate to these options varies [10].

Case presentation

A 24-year-old female attended our clinic with symptoms of hyperthyroidism (weight loss, tremor, excessive sweating, hair falling out, and nervousness). Along with these symptoms, she started having severe hand and feet dryness and excoriation of the skin. She was otherwise asymptomatic. At that point, she was not taking any medications except local emollient creams (over the counter), and she was not known to be allergic; she also had a negative family history of thyroid illness, atopy, or similar skin manifestations.

Upon examination, she was apparently thyrotoxic, having tremors, and tachycardia of 104 beats/minute with generalized hyper-reflexia. Goitre was palpable, with a soft surface and bruits were clearly appreciated upon auscultation. There was no exophthalmos, and the rest of systemic examination was unremarkable.

There was extensive skin dryness, hyperkeratosis, and skin breaks at the hands and feet. Moreover, there were widespread squamous plaques over the extensor surfaces of the joints (elbows and knees), which were not responding to emollients. Her workup confirmed the diagnosis of Grave's disease (Table 1).

Tests	Patient's data	Units	Reference ranges
ATG	14	IU/ml	<100
ATPO	7.9	U/ml	<50
Thyrotropin Receptor Antibodies	7.89	IU/L	<1.75
Na+	140	mmol/L	136 to 145
K+	4.2	mmol/L	3.3 to 4.8
Cla	107	mmol/L	98 to 108
Urea	26	mg/dL	12 to 40
Creatinine	0.9	mg/dL	0.7 to 1.2
Ca2+	9.2	mg/dL	8.9 to 10.2
25 OH VitD	31.5	ng/ml	30-100
Iron	133	Ug/L	37-145
TIBC	405	Ug/dl	
Albumin	4.5	g/dl	3.4-4.8
Alkaline phosphatase	106	U/L	35-104
ALT	21	U/L	0-31
Globulin	3.3	g/dl	2.8-3.4
WBCs	6.9	103/µL	3.6 to 11.0
HGB	12.3	g/dL	11 to 15
MCV	81.5	fL	77 to 92
MCH	26.7	pg	26 to 34
MCHC	35.8	g/dl	32 to 36
RDW	13.7	%	11 to 14
PLT	260	103/µL	150 to 400
ESR	24	mm/1hr	0-12

aACTH: Adrenocorticotropic hormone; **TSH:** Thyroid-stimulating hormone; **GH:** Growth hormone; **IGF-1:** Insulin like growth factor-1; **FAI:** Free Androgen Index; **SHBG:** Sex Hormone Binding Globulin; **FSH:** Follicular Stimulating Hormone; **LH:** Luteinizing Hormone, 25 OH; **VitD:** 25 Hydroxy Vitamin D total range; **ATG:** Anti-Thyroglobulin Antibodies, **ATPO:** Anti-Thyroid Peroxidase Antibodies, **T3:** Thyronine, **T4:** Thyroxine, **ALT:** Alanin aminotransferase. **HGB:** Hemoglobin; **MCH:** Mean corpuscular hemoglobin; **MCHC:** Mean corpuscular hemoglobin concentration; **MCV:** Mean corpuscular volume; **PLT:** Platelets; **RDW:** Red cell distribution width; **WBCs:** White blood cells; **ESR:** Eosinophil's sedimentation rate.

Table 1: Initial investigations results

The rest of workup included an ultrasound of the thyroid, which showed hypervascularity (thyroid inferno), nothing was abnormal. Thyroid scintigraphy showed a systemic enlarged gland with high diffuse uptake through both lobes measuring 7.6% (normal 0.4 to 4%), suggestive of Graves's disease. Abdominal ultrasound showed a normal sized liver with normal echotexure, no evidence of focal lesions. Spleen was not enlarged. Both kidneys appeared normal. No lymphadenopathy or masses appreciated, and no free fluid seen in the abdominal cavity. Chest x-ray showed clear lung parenchyma and bronchial tree.

We started her on Carbimazole and propranolol, since she was not convinced to accept the radioactive iodine (RAI) as she wanted to get pregnant. She was seen by three different dermatologists who concurred with the diagnosis of Pityriasis Rubra Pilaris; they advised her to continue emollients and to start a retinoid derivative, but she did not use them since she was planning to conceive. Unfortunately no tissue biopsy was obtained, since they all agreed that the condition goes clinically with PRP.

Tests	1st visit (before Carbimazole)	2nd visit (On Carbimazole)	3rd visit (After RAI)	4th visit (Follow-up after RAI, On T4)	5th visit (Follow-up after RAI, On T4)	Units	Reference ranges
T4	88.2	50.2	5.97	16.3	19.2	pmol/L	11.5 to 22.7
T3	30.5	24.9	2.2	4	4.6	pmol/L	3.5 to 6.5
TSH	<0.01	0.02	45.7	5.97	1.8	µIU/mL	0.55 to 4.78

Table 2: Follow-up biochemistry results

As there was no response to Carbimazole treatment over eight weeks (table 2), we advised her to go for RAI and to defer the conception for six months. She accepted the iodine treatment, which was done shortly afterwards. After three months, she went into hypothyroidism, which was treated by an appropriate dose of levothyroxine (follow-up thyroid hormones indices shown in table) [2].

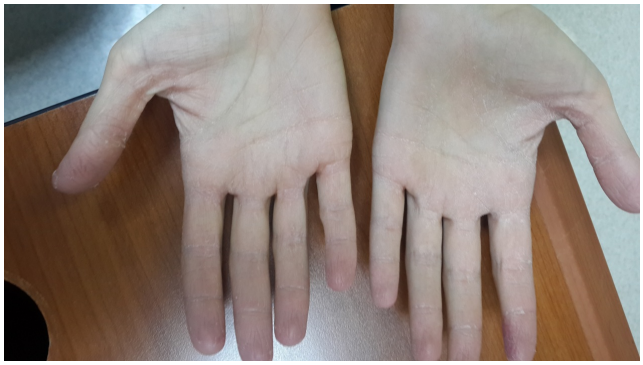

Figure 1: The picture shows residual keratosis and dryness of the hands after remarkable improvement from the initial status

Interestingly, the skin manifestations of the PRP improved remarkably after the normalization of the thyroid status, though nothing was taken other than the anti-thyroid agents and simple emollients [Figure 1 and 2].

Discussion

This is an interesting link that has not been explored before; our patient had PRP along with the early symptoms of Grave's disease. The diagnosis of PRP was made early by three dermatologists, but 'the patient was opposed to the use of retinoid supplements, though interestingly, the dermatological findings improved after the oral anti-thyroid medications, and almost resolved after the RAI therapy. It has been suggested that vitamin A deficiency predisposes to PRP, but in some cases of PRP, researchers found normal levels of vitamin A. This finding could indicate either a defect in vitamin A absorption or a carrier protein deficiency. These defects could be an explanation to why topical vitamin A is more effective than parenteral supplements [9,11].

Having a role in the absorption of vitamin A, thyroid deficiency was thought to be a predisposing factor for PRP in vulnerable individuals [12]. In the literature, PRP is thought to be associated with hypothyroidism [5,12,13], and it was suggested by Aline and his team to investigate for hypothyroidism in all cases with PRP [5]. Nevertheless, hyperthyroidism has not been reported in association with PRP to our best knowledge and literature search. Our patient was diagnosed with concurrent Grave's disease and PRP, and was treated initially with anti-thyroid medications followed by RAI treatment, after which her skin manifestations resolved almost completely.

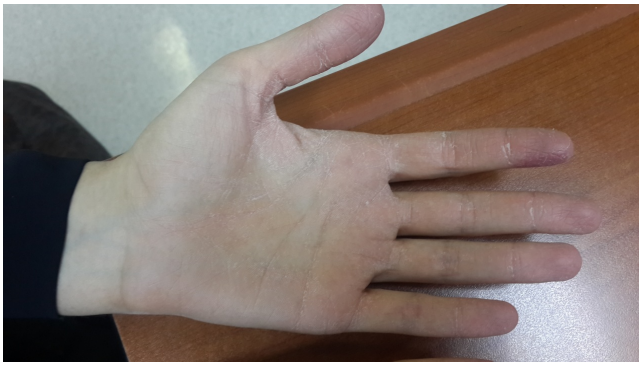

Figure 2: Closer image shows residual keratosis and dryness of the left hand

Unfortunately, we do not have pictures of the initial phase of the skin manifestation, but the picture [1] shows the hands after treatment, with minimal residual skin dryness and keratitis changes. A reasonable explanation for this phenomenon is still to be explored. Moreover, we were not able to ascertain whether the improvement was due to medical treatment, RAI, or just a weaning phase of the (Wax and Wean) nature of the disease; this could be elaborated with a meticulous follow-up of the patient, looking for PRP relapse.

PRP has been linked to many autoimmune diseases-myasthenia gravis, coeliac disease, and hypothyroidism [11-14]. Hypothyroidism can theoretically be linked to autoimmunity predispositions, as well as thyroid hormone deficiency, which is needed to convert the dietary carotenoids to an active vitamin A. Without the thyroid hormone, this conversion is almost abolished [12]. But deficiency of the thyroid hormone might outweigh the autoimmunity, since the reported cases of PRP and hypothyroidism did improve only with thyroxine replacement [11-14]. Based on our experience with this case, we favour an autoimmune hypothesis, since in thyrotoxicosis; there should be no impediment in the conversion of dietary carotenoids to active vitamin-A.

Conclusion

This is the first report of PRP in association with Grave's disease. This link needs to be consolidated with more case reports, and perhaps with large-scale studies. We stress on the previous suggestion of having

the thyroid function assessed in any case with PRP, for instance, the main pillar of treatment could be stabilization of the thyroid status plus emollients.

Abbreviations

PRP: Pityriasis Rubra Pilaris, RAI: radioactive iodine.

Acknowledgement

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