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CASE REPORT

WILEY Pediatric Dermatology

Omeprazole-induced hypertrichosis in two children

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Abstract

Omeprazole significantly increases duodenal prostaglandin E_2 synthesis. Prostaglandins are involved in hair growth regulation: prostaglandin E_2 and prostaglandin F_2 alpha stimulate hair growth, and prostaglandin D_2 has an inhibitory effect. The use of omeprazole can cause acquired generalized hypertrichosis by increasing prostaglandin E_2 levels.

KEYWORDS
drug reaction, hair disorders

1 | INTRODUCTION

Proton pump inhibitors (PPIs) are widely used for peptic disease. Five percent of patients experience adverse effects of PPIs, which are usually mild and include headache, nausea, and diarrhea.[1] We report two children who developed reversible hypertrichosis related to treatment with omeprazole.

2 | CASE REPORT

2.1 | Case 1

A male infant started omeprazole therapy (1 mg/kg/d) at the age of 2 months for gastroesophageal reflux disease. He was referred because of excess hair since his third month of life. Physical examination revealed generalized hypertrichosis with thick, densely pigmented hair on his trunk, legs, arms, and face (Figure 1). There were no other skin, tooth, or mucosal findings. The rest of the clinical examination was unremarkable. A complete endocrinology examination excluded growth and sex hormone abnormalities, thyroid disease, and accelerated bone age. At the age of 4 months, omeprazole was withdrawn because of resolution of gastroesophageal reflux; after a few weeks, hypertrichosis started to fade, and 6 months later, it had completely disappeared (Figure 2). No recurrences had been observed 1 year later.

2.2 | Case 2

An 8-year-old boy was referred because of generalized excess hair that had begun 6 weeks before his visit. Personal history included maculo-papular cutaneous mastocytosis and recurrent abdominal pain, which had been treated for 2 years with oral sodium cromoglycate (100 mg/8 h), omeprazole (20 mg/d), and cetirizine (5 mg/d).

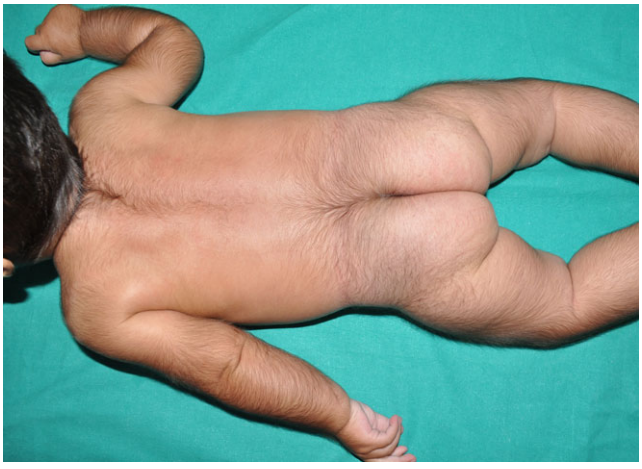

FIGURE 1 Physical examination revealed generalized hypertrichosis with thick, densely pigmented hair on trunk, legs, and arms

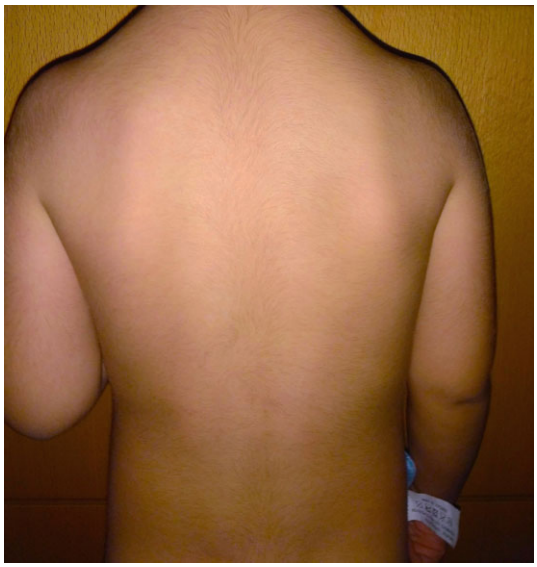

FIGURE 2 One year after omeprazole withdrawal

Three months before referral, he had been diagnosed with migraine and intestinal intussusception, for which flunarizine (5 mg/d) was administered, and the dose of omeprazole was increased to 40 mg/d. On examination, the patient was healthy and had an excess of dark hair on his face (cheeks and forehead), trunk, and extremities (Figure 3). Thyroid and sex hormones were also in normal ranges, and blood and urine porphyrin levels were normal. Magnetic resonance imaging excluded adrenal or pituitary tumors. Abdominal, hematologic, and testicular neoplasia were excluded according to ultrasound and normal serum tumor marker levels. Omeprazole was withdrawn and switched to a hyaluronate-containing mucosal barrier protector, and the other drugs were held; hypertrichosis started to fade and was completely resolved 2 months after omeprazole withdrawal. Three months later, no new excessive hair growth had been noted (Figure 4).

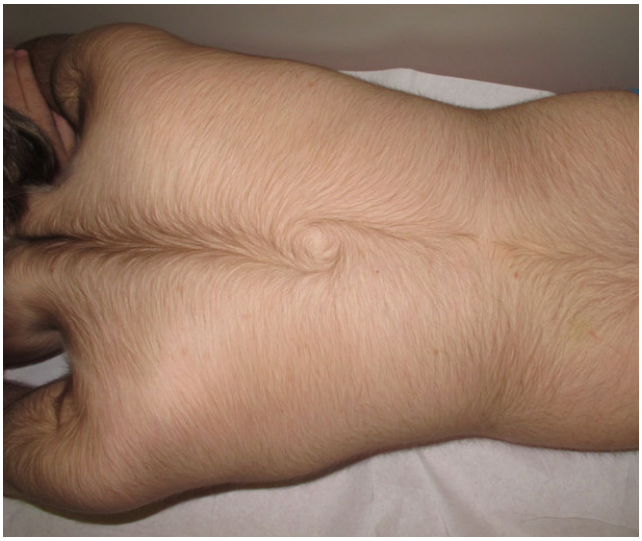

FIGURE 3 Excess dark hair on extremities and trunk

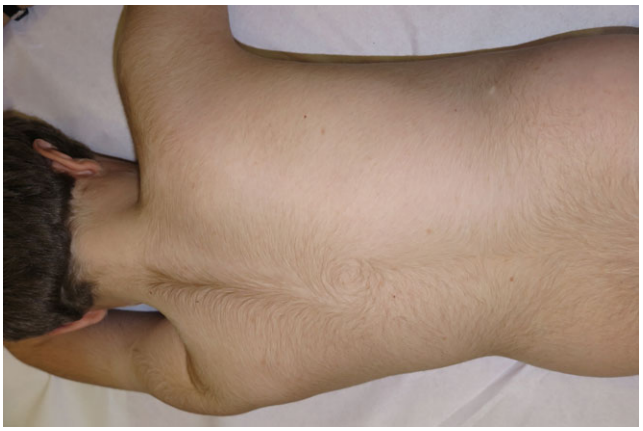

FIGURE 4 Marked reduction of hypertrichosis 5 months after omeprazole withdrawal

3 | DISCUSSION

Hypertrichosis is defined as excessive hair growth in any area of the body, in contrast to hirsutism, which is excessive hair growth affecting children or women with a male distribution pattern. Hypertrichosis can be classified as acquired or congenital and generalized or localized. The cause of acquired generalized hypertrichosis can be idiopathic, iatrogenic, or secondary to systemic diseases such as hypothyroidism, porphyria, celiac disease, dermatomyositis, tumors, or HIV infection.[2] Drugs such as cyclosporin A, corticosteroids, phenytoin, penicillin, spironolactone, acetazolamide, psoralen, diazoxide, and minoxidil can also cause acquired generalized hypertrichosis, with involvement mostly of the scalp, frontal region, trunk, and extremities.[3]

Omeprazole is a substitute benzimidazole that inhibits the proton pump, reducing gastric acid secretion helping to eradicate *Helicobacter pylori*. It blocks the final step of acid production by inhibiting the H^+/K^+ ATPase enzyme system at the secretory surface of the gastric parietal cells.[4] It is considered a safe drug, although adverse effects have been reported.[5] Administration of omeprazole for up to 6 years has caused cutaneous adverse events in fewer than 2% of recipients.[6] Reported skin reactions to omeprazole include toxic epidermal necrosis, Stevens-Johnson syndrome, bullous pemphigoid, lichen planus, angioedema and urticaria, pustular erythroderma, bullous localized drug disease, purpura, photosensitivity, and alopecia.[7,8] Although there is one case reported of alopecia areata healed after eradication of *Helicobacter pylori*,[9] cases of generalized hypertrichosis associated with omeprazole have not been reported in the medical literature. In our two patients, a relationship is likely because of the absence of other possible causes of hypertrichosis, onset shortly after starting or increasing the dose of omeprazole, and disappearance of excessive hair without recurrence after omeprazole withdrawal.

The pathomechanism for omeprazole-induced hypertrichosis is not known. Omeprazole significantly increases duodenal prostaglandin (PG)E_2 synthesis[10] and elevates the expression level of cyclooxygenase-2 protein and PGE_2 level.[11] Prostaglandin F_2 alpha analogues such as latanoprost can increase pigmentation, thickness, length, and

number of eyelashes.[12] Prostaglandins are involved in hair growth regulation; PGE_2 and PGF_2 alpha stimulate hair growth, whereas PGD_2 has an inhibitory effect.[13,14] Is has been suggested that a balance between PGE_2 and PGD_2 controls hair growth in mouse and human skin,[13] whereas drugs that stimulate hair growth may exert their effects by acting on prostaglandin pathways. It has been suggested that minoxidil increases production of PGE_2,[13] and topical cetirizine, which has been reported to be beneficial in androgenetic alopecia, decreases inflammatory cell infiltrate and PGD_2 production.[14] Prostaglandins may have an action on hair growth regulation through their vasomotor effects in the dermis, inducing blood flow in the perifollicular vessels, and by inducing DNA replication and stimulation of cell division and growth.[15]

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