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A case report of a child with attention deficit and hyperactivity disorder with persistent acral swelling and desquamation following methylphenidate

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Abstract

Background: Methylphenidate is a relatively safe medication used frequently in ADHD with only a few dermatological side effects reported up to date.

Case presentation: In this paper, we present a 9-year-old boy with ADHD who experienced digital desquamation after using methylphenidate-containing prescriptions. His mother gave the informed consent.

Conclusion: Our patient was the first one having persistent non-pruritic, non-painful acral swelling and desquamation without having benefit from discontinuation of medications containing ethylphenidate, and without any rheumatological condition, to the best of our knowledge.

Keywords

ADHD; methylphenidate; desquamation; case report; side effect.

Abbreviations

ADHD: Attention Deficit and Hyperactivity Disorder; MPH: Methylphenidate hydrochloride; IR: Immediate release; OROS: Osmotic-release oral system

Introduction

Methylphenidate hydrochloride (MPH) is a commonly prescribed medication for attention deficit and hyperactivity disorder (ADHD). The most commonly experienced side-effects of MPH are insomnia, loss of appetite and weight loss, irritability, gastrointestinal and cardiovascular symptoms. A few cases have been reported in the literature with dermatological reactions as well, namely alopecia, exfoliative dermatitis, urticaria and angioedema, fixed drug eruption, and exanthematous pustulosis [1,2]. While direct relation between the medication and the dermatologic side effects are discussed and supported by

the disappearance of reactions after medication withdrawal, other contributors and possible confounding factors should also be considered. Parental stress and coping mechanisms during the pandemic, two of the possible confounders, were indeed observed to have a direct impact on children's wellbeing [3]. The higher the maternal anxiety was related to the worse outcome in children with stress [3]. This fact could explain recently emerged or prolonged skin reactions during the pandemic, as it provokes health-related anxiety, especially in vulnerable people.

Here we present a 9-year-old boy having MPH-induced digital desquamation which was not resolved after medication withdrawal. The information is taken from the interview with his mother. Photographs were taken by his family. Written and verbal consent to publish this report and the photographs were taken from his mother.

Case Report

TK is a 9-year-old boy who has been followed with ADHD and dyslexia diagnosis for the last 2 years. He was given atomoxetine (Strattera) in March 2019 for 10 days, which caused abdominal pain, fatigue, and somnolence. After that, they stopped seeing his doctor and using Strattera despite having benefited partially.

In May 2020, he came with his mother to our Child and Adolescent Psychiatry Clinic and was given MPH-IR (Medikinet) 10 mg/day. For the first month of usage, they reported abdominal pain only, which was occurring approximately one hour after intake. After using MPH-IR 10 mg/day for two-month, they noticed erythema and painless peeling on his fingers and toes, starting from the tips. When the dosage increased to 20 mg/day, these digital symptoms increased. For two weeks, they stopped taking MPH-IR and saw lessening in peeling. His medication was changed to MPH-OROS (Concerta) 18 mg/day, which again triggered peeling as previously.

We decided to discontinue any prescription containing MPH and to start atomoxetine again. At the same time, he was referred to dermatology. He was asked to check to peel before (Figure 1) and 30 minutes after (Figure 2) taking a bath. They also checked immediately after the bath (Figure 3). It was noted by the family that swelling and peeling of fingers and toes had increased after exposure to water. With atomoxetine 20mg/day, there was still desquamation on fingers and toes but abdominal pain was not present except having any anxiety-provoking event. He started picking peeled skin after four months of atomoxetine.

After six months of atomoxetine 20 mg/day, they needed to decrease dosage to 10mg/day despite benefiting from attention because of decreased appetite, occasional abdominal pain, and continuing digital desquamation. As his participation in class significantly diminished without any medication, we decided to give him Guanfacine. He took 0.5 mg/day for one month, which was not beneficial in terms of attention and decreased his blood pressure severely. Hence, they stopped taking it as well. The last control with his doctors was due to abdominal pain last month. Her mother reported that his blood tests were noted to be all well in this visit. When we asked if there were any other symptoms during all these times, his mother mentioned fever once only with one of the medications but she could not remember which one exactly.

They visited dermatologists for skin peeling a few times, all recommended Madecassol cream (10 mg Centella asiatica extract) for peeled skin and expected the peeling to diminish after discontinuation

of medications. Unfortunately, his fingers and toes have continued to swell and desquamate despite not taking any medication for the last five months. They noticed a subtle decrease in the severity of peeling. His mother noted that the swelling in his fingers diminish 15 minutes after the bath but the swelling in his toes gets much more severe so that TK picks them later on. As the peeling presents even after cessation of MPH, we wondered whether there is an underlying autoimmune or autoinflammatory condition triggered by MPH. Thus, we asked for a couple of blood tests. Results showed only mild monocytosis [WBC: 6.03 10^3/uL (3.91-10.90), #MON: 1.71 10^3/mm^3 (0.29-0.95), Hgb: 13.1 g/dL (13.2-16.6)], normal acute phase reactants [ESR: 6 mm (6-12), CRP: 2.9 mg/L (0-5), LDH: 168 U/L (135-225), Ferritin: 43.2 ug/L (30-400)], normal liver and thyroid functions [ALT: 9 U/L (0-41), AST: 22 U/L (0-40), TSH: 3.020 mIU/L (0.60-4.84)], and normal Rheumatoid factor (< 10 IU/mL).

Prenatal and natal history was normal with uncomplicated pregnancy and birth. His only known medical condition was being atopic and allergic from an early age. He has used allergy medications since he was 3. There is no similar history in his family including his elder sister or any similar reaction seen in him with another medication. His mother and his father are not related.

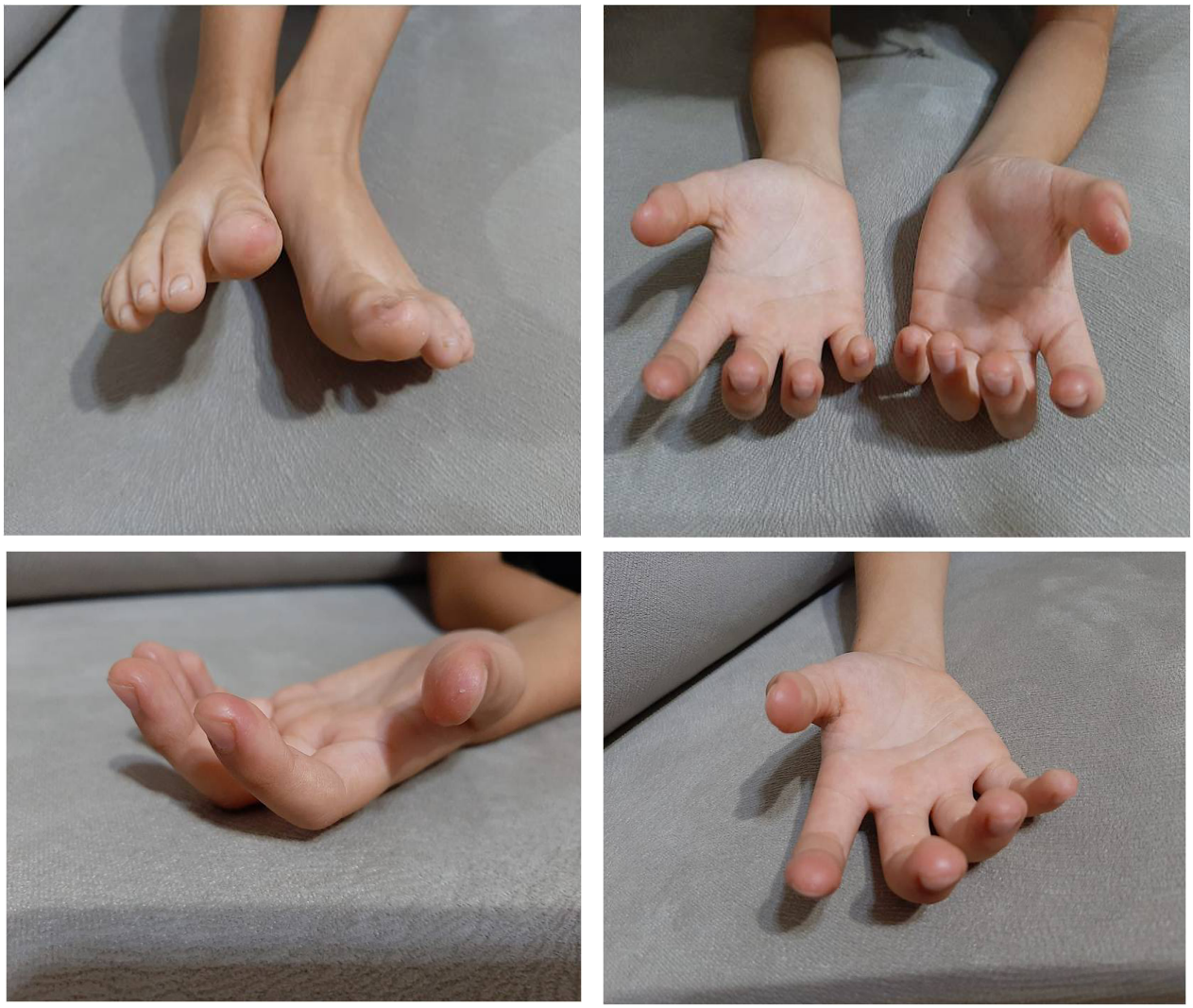

Figure 1: Before taking a bath. Taken by his mother at home.

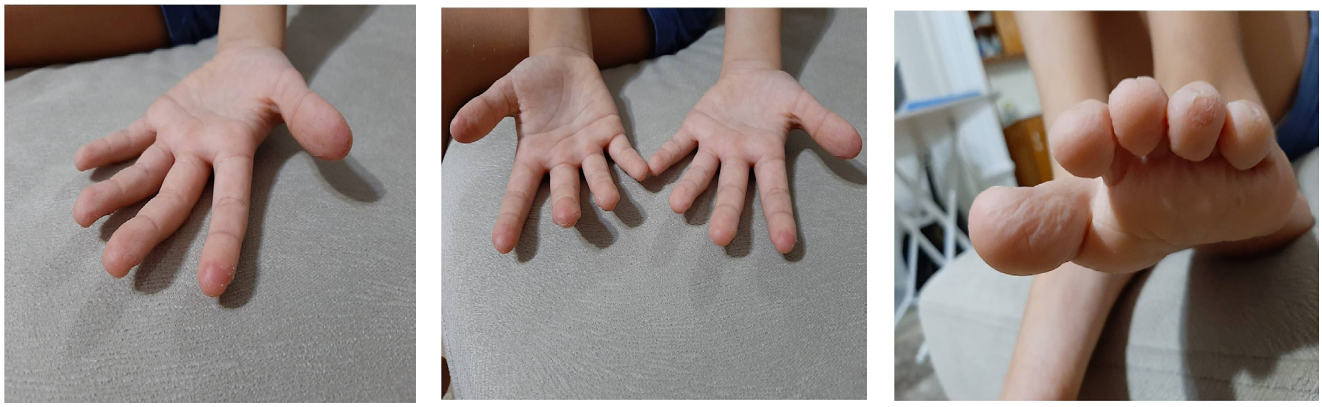

Figure 2: 30 mins after taking a bath. Taken by his mother at home.

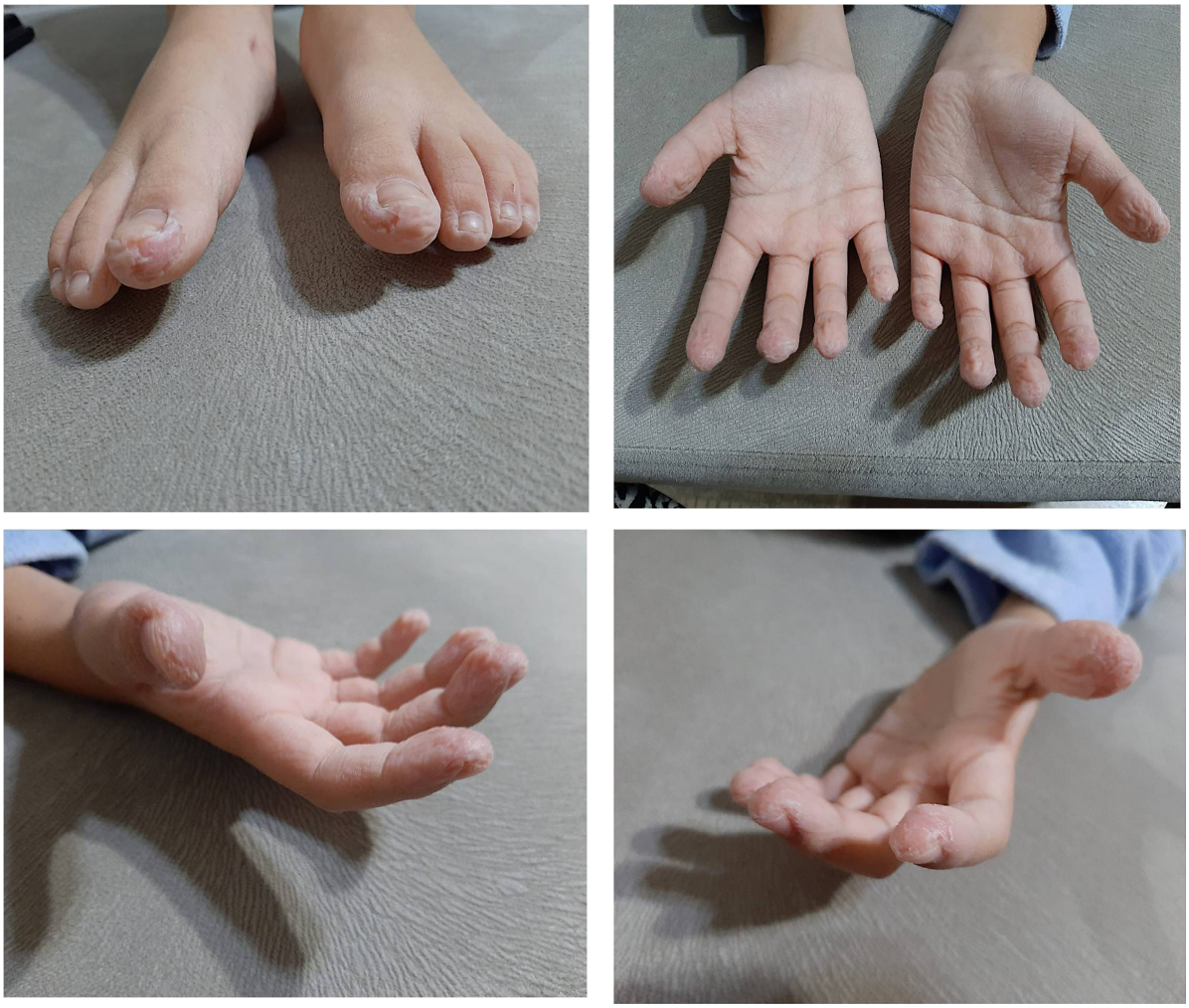

Figure 3: Immediately after taking a bath. Taken by his mother at home.

Discussion

ADHD is one of the most common neurodevelopmental disorders among the pediatric population. Approximately 3-8% of children had been diagnosed with ADHD, and more than half have persistent disorder into adulthood [4]. Psychopharmacology and therapy are two major interventions used as treatment. Among the pharmacological agents, stimulants have a significant response ratio, reaching 80% [4].

MPH is an increasingly used stimulant in ADHD, yet not without side effects. Nausea, sleep and weight changes, headache, irritability, cardiovascular effects, and abdominal pain are commonly noted with

the oral formulation of MPH [2]. There have been a few unusual adverse reactions reported as well, namely hallucinations, painful muscle cramps, increased sweating, inappropriate sexual behaviors, alopecia, urticaria, angioedema, immediate type intolerance, acne, acute skin picking symptoms, peripheral vasculopathy, Raynaud's phenomenon, Systemic Sclerosis, and skin eruptions [1,2,5-8]. Manifestations of these skin findings differ widely, from general to local, pruritic to non-pruritic, and exfoliative to non-exfoliative. Our case had local non-pruritic exfoliation started 2 months after initiation of MPH-IR, however, the symptom did not disappear after the withdrawal of prescriptions.

In the literature, two patients were observed to have the skin eruptions only with OROS formulation of MPH but remained symptom-free after switching to MPH-IR [4,5,9]. Ingredients of these different formulas were thought to be the underlying cause, however, there is no clear understanding for this fact yet. In our case, changing the drug formulation had no benefit. Eventually, even after withdrawal of MPH prescriptions and continuation with either atomoxetine or guanfacine alone, our patient has had persistent skin eruption while stopping MPH was helpful for all previously reported cases with skin exfoliation. Previously, desensitization was tried in a few cases and thought to be useful especially when there was no other alternative to MPH [10,11]. It could be promising for our patient as well if his desquamation disappears.

Persistent peeling after discontinuation of any MPH prescription was a unique situation. Thus, we investigated whether MPH has triggered and/or masked any rheumatologic condition especially juvenile rheumatoid arthritis and juvenile scleroderma. He was examined by a pediatrician with no anomaly found. He did not have any rheumatological signs or symptoms as oral aphthous, arthralgia, arthritis, Raynaud's phenomenon, and his blood results were normal. Considering the normal physical exam, history, and lab results, rheumatological etiologies were eliminated.

Another reason for such prolonged skin reaction could be personal and parental stress. This could also explain why he has abdominal pain triggered only by going to school, as it may be related to parental expectations in addition to his ADHD and dyslexia comorbidity. Thus, we considered the possible influence of high maternal anxiety that we observed in our case as a confounding factor of that continuing adverse effect. The literature findings support the idea that high maternal anxiety elicits worse health outcomes in children with a neurodevelopmental disorder such as Autism Spectrum Disorder [3]. Unfortunately, we could not have a chance to assess the anxiety level and coping mechanisms of the mother of our case, other than observing her stress-related behaviors as frequent doctor visits, to have a more concrete debate.

Currently, our patient could not use any psychostimulant for ADHD due to persistent side effects. He has been followed up closely by his parents and by us for any improvement regarding dermatologic findings. To the best of our knowledge, our patient was the only one in the literature reported with non-pruritic, non-painful acral swelling and desquamation following MPH usage with lack of response to the withdrawal of the medication with or without shifting to another formulation or active substance. Although our patient and most of the other reported cases have not had life-threatening dermatological reactions, any skin finding after MPH prescription must be monitored closely to have early preventive measures, better adherence to treatment, and quality of life for both patients and their parents. Also, both children and their parents could be controlled for stress and coping mechanisms to diminish their negative effects on dermatological or any other health-related outcome.

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