Hematohidrosis induced by separation anxiety disorder during COVID-19 quarantine: a case report and brief literature review

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Abstract

Here, we report a case involving a 10-year-old Vietnamese girl who developed hematohidrosis during the coronavirus disease quarantine. She was hospitalized with a 3-week recurrent bleeding on the abdominal skin. Physical examination revealed no signs of injuries on the skin. Hematological and biochemical test results and coagulation profiles were all within normal ranges. No abnormal findings were observed on abdominal ultrasonography and computed tomography. Numerous erythrocytes were observed during the microscopic examination of fluid samples from the abdominal skin. It was speculated that hematohidrosis was precipitated by separation anxiety disorder, because the onset and remission of symptoms correlated with the beginning and end of the local quarantine, respectively. Our case report and brief literature review highlight the transient and benign nature of hematohidrosis. Although specific guidelines are not well established, hematohidrosis is a transient phenomenon that is treatable with pharmaceutical and non-pharmaceutical interventions, and its overall prognosis is favorable.

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Introduction

Hematohidrosis, also known as hematidrosis or hemidrosis, is a condition wherein a patient sweat blood from any part of the intact skin, including the scalp,[1] palms,[2] soles,[3] and mucous membranes.[4,5] This clinical entity was also anecdotally referred to in the bible when Saint Luke noticed Jesus Christ's sweat was similar to drops of blood as he prayed in the Garden of Gethsemane on the night before the crucifixion. This condition was first mentioned in the medical literature in 1952 by Goria,[6] who believed that the condition originated from psychogenic causes. Since the 2000s, the number of case reports or case series about hematohidrosis have been increasing, and most reports strengthened the association of hematohidrosis with stressful events or psychological disorders.[7,8]

The pathogenesis of this phenomenon remains unclear, and the current proposed pathologic mechanism is only hypothetical. So far, all reported cases showed normal hemostasis and unremarkable abnormalities on skin biopsy, except for platelet factor 3 dysfunction,[8] and pallets deficiency.[9] Although hematohidrosis seems horrifying and mystical, the disease is generally benign and transient.[7]

Case Report

This report received approval from the Research Ethics Committee of Ho Chi Minh City Hospital of Dermato-Venereology. Informed consent for the publication of this case report was obtained from the patient's father.

A 10-year-old Vietnamese girl was admitted to our hospital with a 3-week history of recurrent bleeding on the abdominal skin. One week before skin bleeding, her father noticed that she had complained of abdominal discomfort without loss of appetite, nausea, vomiting, diarrhea, or constipation. However, this vague abdominal pain did not affect the patient's daily activities. The

first episode of bleeding occurred spontaneously after washing her hands wherein she noticed bloodstains on her shirt. The bleeding stopped immediately after wiping and left no scar, injury, or wound, which helped to rule out factitious disorders (Figure 1). Afterwards, her abdominal skin discharged bloody fluid once to twice per day with increasing frequency and blood loss over time (Figure 2). Each episode lasted for 5-10 seconds with approximately 0.2-0.5 mL of bloody secretion loss. These bleeding episodes did not seem to be related to physical exertion, emotional stress, temperature change, or any obvious predisposing factors. Since the patient's parents had always stayed with her during the quarantine, they witnessed almost all bleeding episodes. Additionally, the abdominal discomfort intensified which made the patient cry in the absence of other digestive symptoms.

Her medical history was unremarkable, with no history of hematologic disease or abnormal bleeding from other sites. There was no history of trauma or medication intake, and the patient had not yet attained menarche. Dermatologic examination revealed no signs of self-inflicted injuries on the abdomen and other skin areas, which facilitated the elimination of factitious disorders. No tenderness nor abnormal findings were observed upon abdominal palpation. Laboratory results including complete cell blood count, liver enzymes, pancreatic enzymes, renal function, C-reactive protein level, and urinalysis, were all within normal ranges. No abnormal findings on abdominal ultrasonography and computed tomography were observed. Furthermore, the patient's coagulation profiles (prothrombin time, international normalised ratio, activated partial thromboplastin clotting time, and fibrinogen) were all normal. The patient declined a skin biopsy procedure due to fear of pain and blood. Numerous erythrocytes were observed during the microscopic examination of fluid samples from the abdominal skin.

Retrospectively, her family later discerned that their child seemed moody, depressed, and anxious after an extended period of heightened social distancing. The patient was not allowed to leave her house or meet her friends for several weeks; hence, she missed her friends and hoped to return to school. In addition, she suddenly wanted to co-sleep with her parents despite sleeping separately since the age of 5. She would cry and become more upset if her request was not satisfied. Therefore, we referred the patient to the Department of Psychiatry for a detailed psychological evaluation, which yielded a diagnosis of separation anxiety disorder.

Sertraline and alprazolam were prescribed twice daily at bedtime, along with nonpharmacological interventions. The patient's parents were well-informed about her disease, which helped solve their extreme concerns. The parents were advised to provisionally co-sleep with their child, spend more time listening and talking with her, and encourage her to communicate with

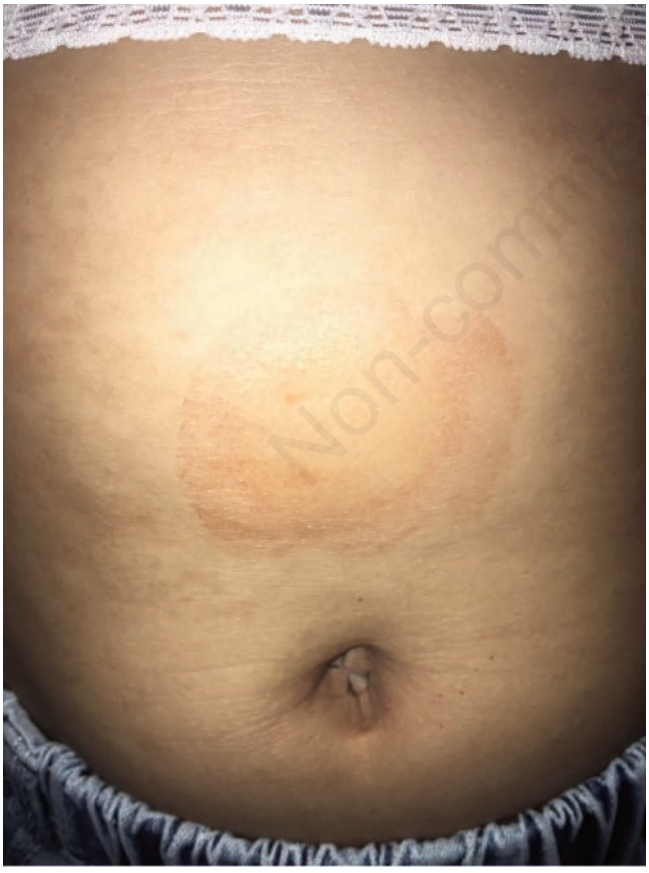

Figure 1. The first bleeding episode in a 10-year-old Vietnamese girl with hematohidrosis induced by separation anxiety disorder during COVID-19 quarantine. Bloody fluid is oozing from the abdominal skin.

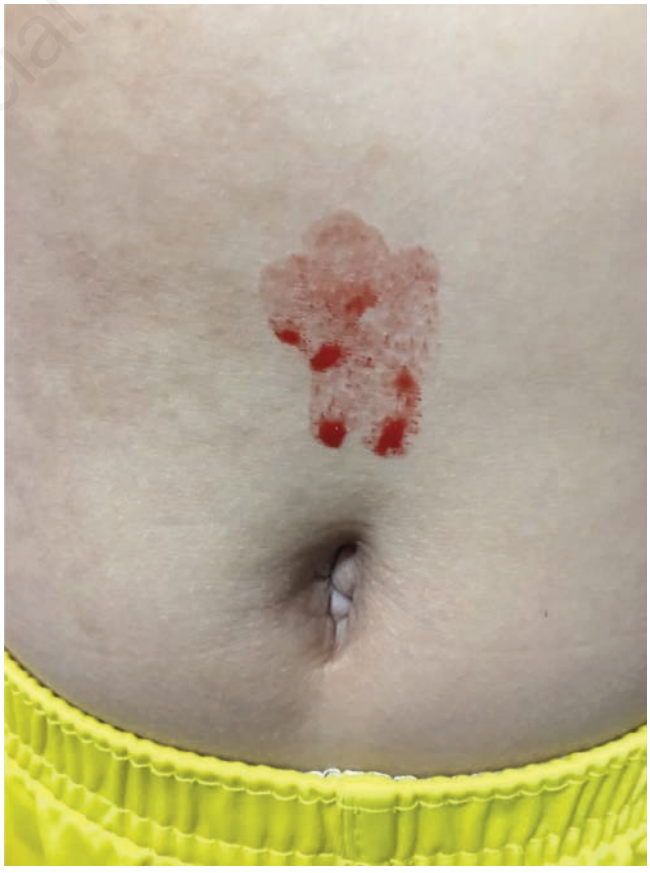

Figure 2. Blood loss after 3 weeks of onset in a 10-year-old Vietnamese girl with hematohidrosis induced by separation anxiety disorder during COVID-19 quarantine. The amount of blood loss has increased.

friends and relatives through phone calls. Within 2 weeks, the bleeding frequency and intensity of abdominal pain decreased. The child bled once daily but no longer experienced abdominal discomfort. Additionally, there was minimal blood loss in each episode, which rapidly dried out and left dried bloodstains (Figure 3). After the local authorities started easing the coronavirus disease-related restriction, the patient's parents noticed that her psychological problems were alleviated. Therefore, the patient intentionally stopped sertraline and alprazolam but continued the nonpharmacological therapies. During a 6-week follow-up period, she was free from abdominal pain and seemed to ignore her bloody sweat (Figure 4).

Discussion

Hematohidrosis is a fascinating and mystical phenomenon of the eccrine glands that necessitates further clinical investigations.[10] To date, only a few medical professionals believe in this clinical event despite numerous documented cases (76 cases) prior to the 21st century.[11] From 1996 to December 2016, 25 cases were reviewed by Kluger,[7] and most were presented with attesting pictures or a bleeding episode witnessed by a physician or nurse. Therefore, it is apparent that hematohidrosis is an actual medical condition that should be investigated further. Its etiopathology has not yet been elucidated and remains debatable. Coagulation tests were performed in almost all hematohidrosis cases,[7,8] but only two cases had hematological abnormalities, including platelet factor 3 dysfunction,[12] and platelet and vitamin K deficiencies.[9] In these two patients, the bleeding symptoms were more severe and involved extracutaneous sites. Despite recurrent episodes of blood oozing, hematohidrosis appears to be more psychogenic rather than hematologic in origin.[6-8] With this, emotional stressors and mental disorders were the leading trigger factors in previous hematohidrosis cases.[7,8] Various related psychological diagnoses of hematohidrosis were noted, such as depressive disorder,[13] oppositional defiant disorder,[14] dissociative and anxiety disorders,[15] and separation anxiety disorder. These psychological stresses were thought to activate sympathetic systems and disturb blood vessels. The abundant net-like vessels around the sweat glands continue to dilate until they rupture and allow the passage of bloody sweat.[11] Moreover, Matsuoka and Tanaka,[16] and some other authors supported this hypothesis by identifying microvessels adjacent to the sweat glands on skin biopsy.

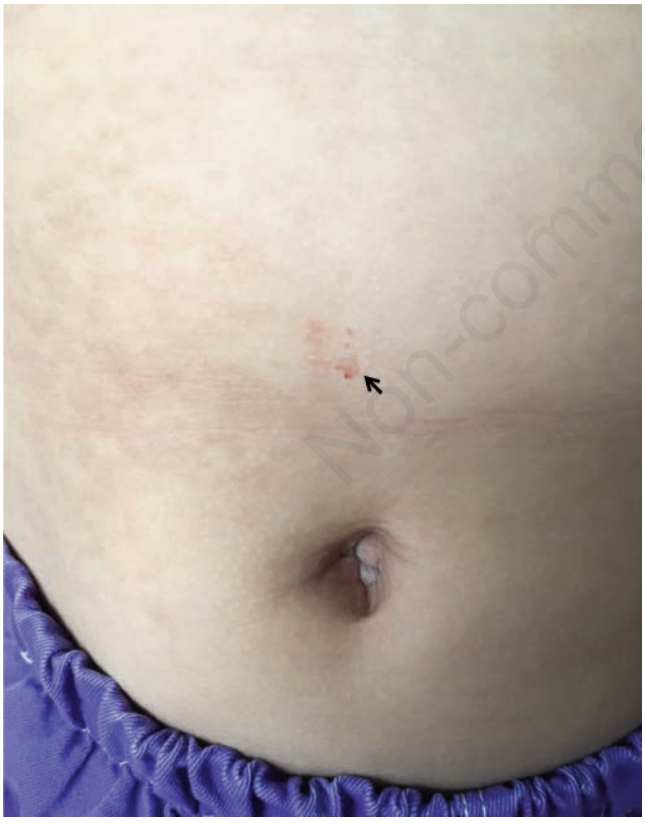

Figure 3. An image obtained after 2 weeks of treatment in a 10-year-old Vietnamese girl with hematohidrosis induced by separation anxiety disorder during COVID-19 quarantine. The bleeding frequency and abdominal pain intensity have reduced after 2 weeks of treatment. There is minimal blood loss per episode, with rapid drying of the blood (arrow).

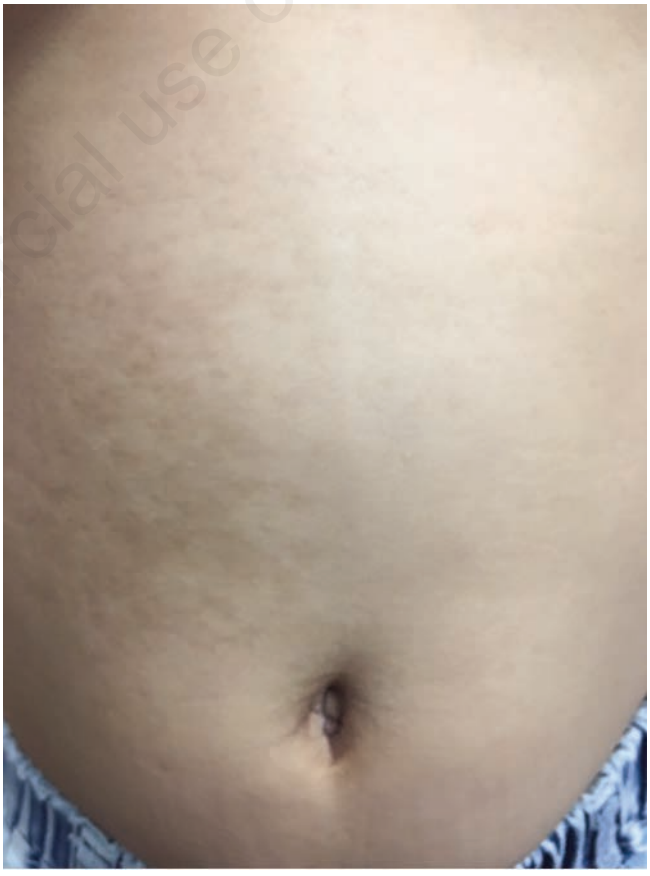

Figure 4. Follow-up image of a 10-year-old Vietnamese girl with hematohidrosis induced by separation anxiety disorder during COVID-19 quarantine. The image shows entirely clear abdominal skin with no residue. After the local authorities started easing the COVID-19-related restriction, the patient's parents noticed that her psychological problems were alleviated. The only continued nonpharmacological therapies. During a 6-week follow-up period, she was free from abdominal pain and seemed to ignore her bloody sweat. In the following 6 weeks, the patient seemed to ignore her bloody sweat.

Meanwhile, the concept of stromal weakness in the dermis was introduced by Manonukul *et al*. in 2008, after a comprehensive histopathological and immunoperoxidase study of a 14-year-old girl with hematohidrosis.[1] These defects in the dermis will eventually dilate and enlarge, become blood-filled spaces, and then discharge blood onto the skin surface. Physical trauma might amplify this stromal weakness and lead to hematohidrosis. This hypothesis may contribute to the presentation of hematohidrosis after a head injury,[17] or traumatic pressure.[18] However, further research is required to determine its pathology.

Hematohidrosis can occur at any age (from 2 months to 72 years of age), but it rarely affects infants or the elderly.[9,13] Only two elderly and one infant cases have been published,[3,9,13] and there is a predilection for preadolescent children (median age, 13 years).[7] In addition, this condition is more common in women, accounting for >80% of cases. Its prevalence in Asian individuals (62%) was also recorded. Our patient matched these epidemiological features. All case reports/case series of hematohidrosis dealt with sporadic cases, except for a case series published in 2021.[9] This case series documented the first familial cases of hematohidrosis in two maternal half-siblings, suggesting a possible genetic predisposition.

Bloody sweat can occur on any part of the intact skin, including the scalp, palms, soles, and nails. However, the face is the most affected area, accounting for 96% of cases.[7] In addition, most patients with hematohidrosis sweat blood from more than one body area. There were only 3 cases where hematohidrosis occurred in a single isolated body region: abdomen,[13] perioral area,[19] and forehead.[17] Our case, in which blood oozed from an isolated area on the abdomen, was the second described case. Generally, bleeding episodes occur suddenly without warning signs and are usually self-limiting. However, more than one-fourth of patients experienced bleeding episodes preceded by local or general prodromal symptoms, such as tingling or soreness,[1,20] headache, abdominal pain,[5] mild preorbital tenderness,[21] and vomiting.[22] In our case, abdominal pain was accompanied by prodromal symptoms. However, we were uncertain if this was actual physical pain or simply a way for the child to get her parents' attention. Besides cutaneous manifestations, hematohidrosis might present with bleeding from other organ systems such as hemolacria (bloody tears),[22] epistaxis,[23] hemoptysis,[14] hematuria,[12] hematemesis,[3] and hematochezia.[9]

Due to its rarity, no clear diagnostic criteria nor specific treatments are available yet. Based on the hypothesis of sympathetic nerve activation, which raises blood pressure or increases vascular permeability, Wang suggested the use of propranolol, which acts on the sympathetic nervous system and proved this to be an excellent therapy [4,15].

Subsequently, propranolol and other beta-blockers have continued to prove their efficacy and safety in at least 10 more cases.[2,5,9,15,21,22,24-27]

However, it is not a cure-all drug, and several patients are unresponsive to it.[8,16] Hematohidrosis was also noted to occur in patients who were on propranolol for other reasons.[28] Similarly, there is a controversy about its effectiveness in hematohidrosis patients with underlying psychiatric disorders.[16] Other interventions to reduce sweating blood include psychotherapy,[13,19] and glucocorticosteroids.[3] Most recently, trial treatments with oxybutynin,[28] and tap water iontophoresis have been successful,[16] and this support the possible therapeutic role of hyperhidrosis therapy in this disease. Nonetheless, it is important to identify and remove the causative factors, specifically psychogenic disorders. In our case, the management strategy was concentrated on treating her separation anxiety disorder, which reduced the frequency of bleeding episodes. Sweating blood can be resolved spontaneously or with therapy.[19] A complete recovery may range from 1 week to 2 years without *sequelae*.[4,21] Withdrawal of b-blockers can occasionally be followed by relapse.[7]

Conclusions

In summary, although specific guidelines are not yet well-established, hematohidrosis is a transient phenomenon that is treatable with pharmaceutical and non-pharmaceutical interventions, and its overall prognosis is favorable. However, further investigations are required and recommended to fully understand the pathology of the disease.

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