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Case Report

Pediatric Hematohidrosis – Case Report of a Rare Disease

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Abstract

Hematohidrosis is a very rare condition of sweating blood. A 2-year 9-month-old boy presented to our hospital with a history of repeated episodes of oozing blood from navel, eyes, ear lobules, forehead, leg, toe even from neck and it disappeared as soon as it was mopped leaving behind no sign of trauma but reappear again. The patient was diagnosed with hematohidrosis clinically by exclusion, confirmed by biochemical and microscopic examination of fluid. His oozed blood had a high number of RBC and WBC and it had Chloride levels below normal than serum but corresponded to sweat. With B-blocker (propranolol) his condition had improved significantly and resolved on follow-up.

Keywords: *Bleeding, hematohidrosis, hematidrosis, pediatric, sweat blood, propranolol.*

Introduction

Hematohidrosis is a rare condition in which a human being sweats blood.[1] It has been very rarely reported in literature. Also named hematidrosis.[2] Here patient presents with the excretion of bloody fluid/sweat from intact skin or mucosa.[3,4] Cases have been reported in ancient history, most notably in the Bible when Jesus was in the Garden of Gethsemane (Luke 22:44) and by Leonardo da Vinci when describing the sweating of blood by a soldier in battle.[5] The literature suggests anxiety or other emotional stress as the most common precipitating events. Hypertension, vasculitis, sympathetic overactivation, physical exertion, stromal weakness of the dermis, head injury, primary headache disorders, systemic disease, vicarious menstruation, factitious behaviors, and psychosomatic disorders have also been proposed as possible etiologies of hematohidrosis.[4,5,6] As there is no confirmatory test for this disorder, the diagnosis of hematohidrosis is clinical in nature.[6] The diagnosis requires the exclusion of bleeding diathesis, vasculitis, scurvy, or connective tissue disorders where vascular fragility may result in bleeding.[6] The absence of self-inflicted or secondary injuries is also an important feature.[7] The term “hematofolliculohidrosis” was proposed by Manonukul et. al. because it appeared along with sweat-like fluid and the blood exuded via the follicular canals.[7,8] The presence of erythrocytes and other cellular components in the bloody discharge of hematohidrosis is necessary to distinguish from chromhidrosis [presented with the secretion of colored

sweat] and pseudochromhidrosis [discoloration of normal colorless sweat by an exogenous agent on the skin surface].[7,9] Recently, a possible genetic predisposition was also proposed by Salas-Alanis JC et. al.[10] Though rare but even during the 18th and 19th centuries several reports have been published,[11] the first published medical report accessible in PubMed dates from 1918 in the British Medical Journal.[12] It is a rare disease, and its mechanism is still unknown, while the use of some medications like propranolol has reported a clinical benefit in some case reports.[13]

Case Presentation

A 2 year 9-month-old boy 1st issue of a non-consanguineous parent was reported in our pediatric department on April 2023 with the complaint of spontaneous bleeding from different sites of the body for 7 months. He is a diagnosed case of Frequent relapse nephrotic syndrome (FRNS) [Histopathology- Minimal Change] since his 24 months of age. The mother noticed that for the last 7 months while he was on prednisolone treatment her son started bleeding from different sites of his body. Bleeding usually occurs from nose, umbilicus, great toe, forehead, and sometimes along with urine. The bleeding persists for a few seconds and then disappeared after mopping leaving behind no sign. Initially, for a couple of months the episodes were irregular, stop spontaneously but again reappeared. For the last 2 months, he used to bleed every day, frequency and severity both gradually increased. The most common sites of oozing were forehead, calf muscle, navel, neck, and cheek. Occasionally he developed hematuria with proteinuria but no epistaxis, hematemesis, or hematochezia was seen (figure 1,2,3,4,5). The child was active and no abnormality was detected on general examination other than proteinuria due to presence of systemic disease. Systemic examination was normal. He has no history of excessive or uncontrol bleeding following cut injury or trauma. No history of gum bleeding, skin bleeding in the form of purpura, or ecchymoses. No family history of bleeding disorder. His physical growth is age-appropriate, and the developmental milestone was also age appropriate except for occasional slurring speech.

He was thoroughly investigated for all types of blood dyscrasias, connective tissue disorder, immunological, vasculitis, or rheumatic disorder and all investigations were found to be normal. The effluent bloody samples showed all the components of the peripheral blood, with a high number of RBCs, and WBCs mingled with a few epithelial cells.

We send the oozing blood as a sample to test electrolytes and found the chloride level below normal in comparison to his same time send serum electrolytes which co-related with the chloride level in sweat. The other workup was within normal limits, including CBC, PBF, BMP, aPTT, PT/INR, LFTs, RFTs, TSH, iron, total iron-binding capacity (TIBC), iron saturation, coagulation factor like fibrinogen, Factor VIII, IX, XIII, XVII, Von Willebrand factor (VWF) antigens, D-dimer. Platelet function analysis and platelet antibody were not done due to non-availability. Skin biopsy was not done in our case. With clinical correlation, patient was diagnosed with hematohidrosis and prescribed propranolol 10 mg twice daily. Psychiatric evaluation & neurological assessment was also done, and interventions included guided relaxation techniques and cognitive-behavioral therapy (CBT), and tablet lorazepam 0.5 mg/day. Wang et al reported antihistamines played a role so we provide an H1 receptor inhibitor (Chlorpheniramine maleate 2 mg, tid) and an H2 receptor inhibitor (Famotidine) too.

The main focus of our treatment was controlling his proteinuria and hypertension. Parents have explained the antecedents of the bleeding episodes and how they should respond to such episodes including playing with children and giving him proper attention. After 2 months of treatment bleeding/oozing had stopped gradually, child's behavior also showed a positive change. Bleeding episodes took time to control as his hypertension persists due to use of prednisolone. At the first follow-up after 1 month of discharge, he was doing well with no bleeding.

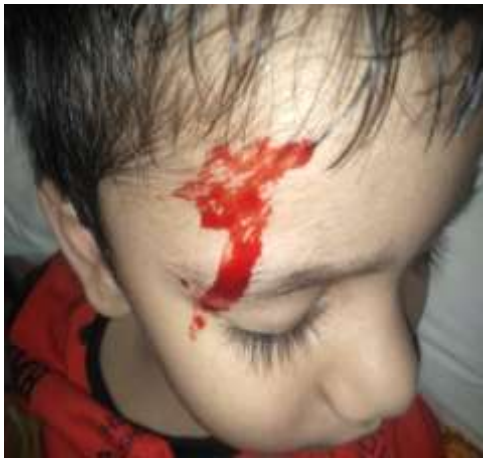

Figure 1a: Bleeding from forehead

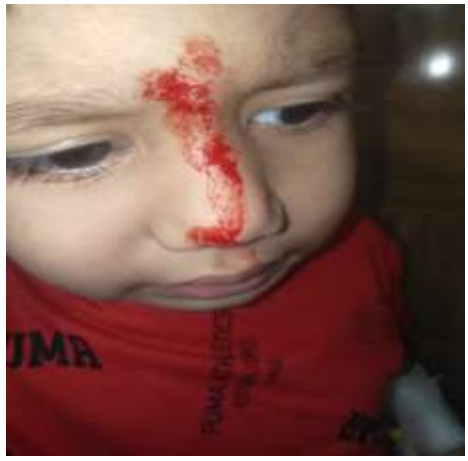

Figure 1b: Bleeding from forehead

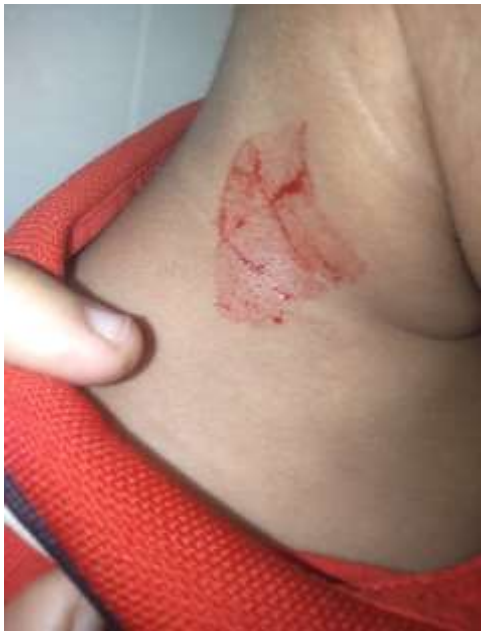

Figure 2: Bleeding from neck

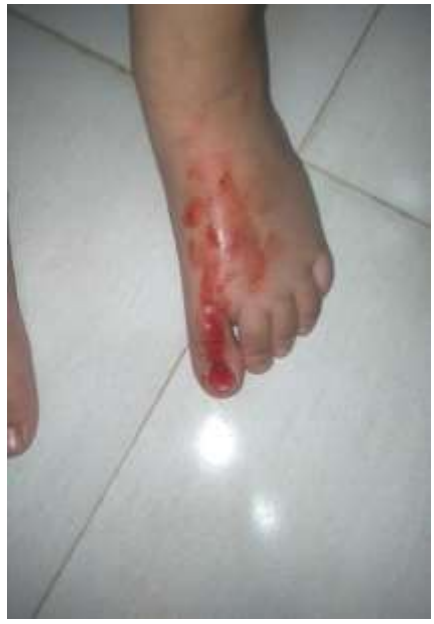

Figure 3: Bleeding from nail bed

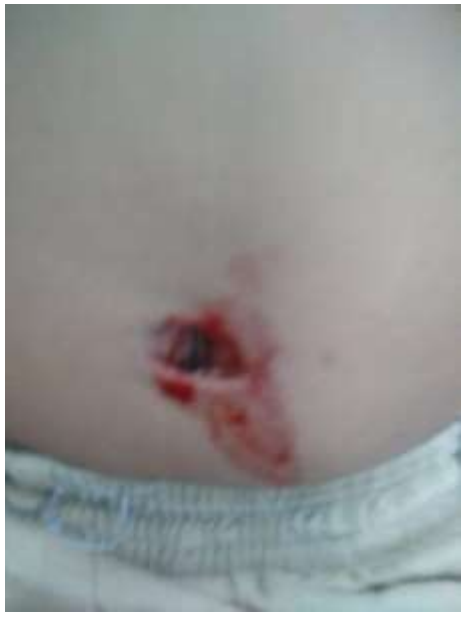

Figure 4: Bleeding from umbilicus

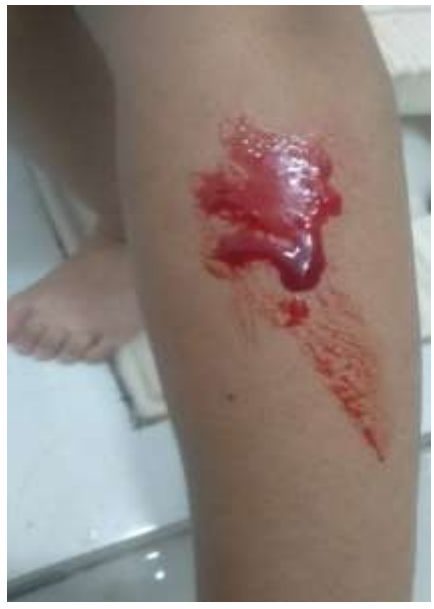

Figure 5: Bleeding from forearm

Discussion

Haematohidrosis is a very rare condition characterized by recurrent, spontaneous sweating of blood-stained fluid from intact skin.[3] Blood usually oozes from the forehead, nails, umbilicus, and other skin surfaces but can occur from anywhere on the body.[14,15,16] The episodes are usually self-limiting, last for minutes, and stops spontaneously. It may occur multiple times per day, with no diurnal variation even during sleep.[17] The amount of bleeding is typically small, more diluted than blood, and appears to be blood-tinged.[18] In some cases, described as pink and watery, clearer than blood. After wiping the blood-stained fluid from the skin, the underlying skin was found intact with no sign of bleeding, or color changes in skin.[14,17]

This disease has been described in various terms and has been often tied to religious belief as stigmatization.[7] Hematohidrosis is commonly described as an eccrine sweat disorder, but the evidence does not seem to support this classification.7 One proposed pathogenesis is defects in the dermis and changes in vascular tone, pressure, or endothelial integrity may allow a dilute, bloody fluid to reach the skin surface, but further study is required to definitively prove the pathogenesis.[7] Another proposed etiopathogenesis is that multiple blood vessels, which are present in a net-like form around the sweat gland constrict under the pressure of stress due to activation of sympathetic nervous system. As the anxiety increases, very small blood vessels (dermal capillaries) dilate to the point of rupture. The blood goes into the sweat glands, which push it along with sweat to the surface, presenting as droplets of blood mixed with sweat.[14,18] The exact cause of rupturing vessel is unknown. Some cases are associated with systemic disease, bleeding disorders, menstruation, excessive exertion, general symptoms such as headache, abdominal pain, nausea, or vomiting, high blood pressure, fear, and intense emotional stress.[19] Other conditions such as vascular disorders, hematologic dyscrasias, infections, influence of drugs, vicarious menstruation, and self-inflicted lesion should be excluded from the differential diagnosis.[4,14,16,20,21] However, in many cases no triggering factors have been identified.[17]

Carrion et al [15] did a systematic review and meta-analysis with 20 published cases of hematohidrosis and found the presence of bloody tears was associated with a systemic disease or clinical manifestations presented with systemic illness. He also reported cases can be from any age, median age was 24 months but cases of only 11 days, 4 months, and 11 months old were found. Shafique et. al.[7] reviewed reported the lowest age of 2 months.

Carrion et al [15] found the most common place of bleeding was the eyes, followed by face, ears, and uncommon places included the feet, eyelids, and axillae. Shafique et. al.[7] reviews found most common locations were face, eyes, ears, and hands. India has reported the most cases, followed by South Africa, Iran & other countries.

The extravasated blood has identical cell components as that of peripheral blood.[5] Many triggering factors have been identified such as substantial physical or emotional stress and fear, and the bleeding episodes are often accompanied by other symptoms like headache, abdominal pain, nausea, and vomiting,[16] but in our case, these were not present. On the other hand, histamine, although mainly released by mast cells, is also localized in many tissues including brain, sympathetic ganglion, and nerve fibers where it functions as a neurotransmitter involved in the regulation of peripheral sympathetic activity.[22,23] Moreover, histamine receptors H1R and H2R are co-expressed in most cell types, such as neurons and some ganglions, endothelial and epithelial cells, and they may function in a cross-regulation manner.[24] H1R and H2R inhibitors are mainly used for the treatment of allergic and gastric acid–related conditions. It is well known that histamine can also dilate vasculature and increase blood flow via activation of H1R and H2R located in blood vessels, disrupt endothelial barrier formation of venula indicated by changes in vascular endothelial cadherin localization at endothelial cell junction, and then increase vascular permeability, which could be abolished by histamine H1 receptor antagonists.[25]

Multiple reports have been published of successful treatment with beta-blockers,[8,16,20] by a significant reduction in the frequency of spontaneous blood oozing. Alasfoor et. al.[26] found Beta-blocker treatment was effective in 94% of cases in reducing or resolving symptoms.7 The most commonly used beta-blocker was propranolol dosed at 1-2mg/kg/day, with a maximum of 20 mg.[7,20] In our case, we also found propranolol (1-2mg/kg/day, bid) was effective in controlling the bleeding episodes. Though our case was very young but due to present systemic illness he was suffering from this condition. His bleeding episodes started improving after 2 weeks of treatment. Later on, he was advised of lorazepam. Psychotherapy primarily involved relaxation techniques, cognitive-behavioral therapy (CBT), and parental education in ways to reduce stress. Others also reported use of anxiolytics; most often clonazepam, lorazepam, tricyclic antidepressants (TCAs), along with beta-blockers. The key to successful treatment also includes counseling patient and his parent.

Conclusion

Hematohidrosis is a rare phenomenon whose etiology and pathophysiology are still unknown, and there is no specific therapeutic strategy available up to now. Parents and patients may be reassured that the condition is benign, and complete or partial resolution of symptoms can be expected with beta-blockers, psychotherapy, or observation alone.

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