Case Report

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Successful Treatment of Unremitting Gastro-Intestinal Hemorrhage and Rashes of Henoch-Schönlein Purpura with Colchicine & Cryoprecipitate: A Case Report and Literature Review

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Abstract

Severe gastrointestinal manifestations and rashes of Henoch Schonlein Purpura (HSP) may not always respond to prednisolone or another immunosuppressive agent. Though reduced factor XIII may play a role in gastrointestinal manifestations but its role in management of skin rashes is uncertain. Here, we reported a case treated with different immunosuppressive agents but didn`t respond. Thereafter, despite having the normal factor XIII assay, the unremitting GI symptoms and skin rashes, has improved after prescribing colchicines & infusion of Cryoprecipitate containing factor XIII.

Keywords: HSP; Gastrointestinal Bleeding; Rash; Cryoprecipitate; Colchicine.

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Introduction

Henoch Schönlein Purpura (HSP), a non-granulomatous, small-vessel vasculitis, is clinically characterized by the presence of non-thrombocytopenic palpable purpura, arthritis, abdominal symptoms and renal disorders. It is typically a self-limiting and benign childhood disease, affecting 8 to 20/100,000 children per year (1-3). The pathogenesis of HSP is that of leukocytoclastic vasculitis characterized by the presence of polymeric IgA1 containing immune complexes predominantly in the dermal, gastrointestinal, and renal capillaries. The severity of clinical features and outcomes varies greatly. Skin is the most commonly involved site, especially the gravity/pressure dependent areas, which usually improves within 6-8 weeks as the last symptom. Gastrointestinal (GI) manifestations occur in approximately two-thirds of cases, which may vary from colicky abdominal pain (44%) to GI bleeding (22%) or intussusception (≤3%) (3). The manifestations of HSP usually remit spontaneously but recurrence may occur in 33% of the cases. Several studies have reported an association between factor XIII deficiency and severe gastrointestinal symptoms in pediatric HSP patients (2-6). There is paucity of literature regarding the management of drug resistant gastrointestinal hemorrhage and rash without renal involvement in a patient. Here we report a case of HSP with unremitting GI symptoms and skin rashes who

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improved after administration of colchicine and infusion of cryoprecipitate containing factor XIII.

Case report

A 9-year-old previously healthy boy was admitted with the complaints of purpuric rashes over different parts of the body with occassional abdominal pain for 6 weeks. The skin rashes started at the extensor surface of lower extremities and then progressed gradually to the buttocks, upper extremities, and the trunk. They faded gradually over days along with reappearance of newer clusters of rashes. The abdominal pain was periumbilical, intermittent, colicky, and severe and interfered with his daily activity. For such complaints, he was treated with prednisolone 2mg/kg daily for two weeks in a local hospital without any significant improvement. Then, he was referred to a tertiary level hospital for further management.

His physical examination upon arrival revealed a well-looking, normotensive, afebrile, anthropometrically well thriving boy with multiple nontender, palpable purpuric rashes of different sizes scattered bilaterally over the legs, thighs, buttocks, and upper limbs. Some of them blanched on pressure. There was no H/O hematuria, protinuria, feature of arthritis, or CNS involvement. His investigations revealed: neutrophilic leucocytosis TC $12x10^9$/L with 89% neutrophils; hemoglobin 13.5g/dl; platelet count $350x10^9$/L; and normal ESR and CRP, renal function, electrolytes, 24H UTP, S amylase, prothrombin time (PT), partial thromboplastin time (PTT), international normalized ratio (INR), and vasculitis assay (C3, C4, ANA, Anti ds DNA, pANCA, cANCA). USG and plain radiography were not performed as clinical features were not suggestive of inussesception. However, upper GI endoscopy revealed congested gastric and enteral mucosa.

After admission, the patient was initially treated with methylprednisolone injection (10mg/kg/dose) for three consequetive days followed by oral prednisolone. Subsequently, prednisolone was tapered gradually and mycophenolate mofetil (MMF) was added. Despite adding new drugs, new crops of rashes reappeared along with abdominal pain and passage of black tarry stool (melena) several times. It was thought that the patient was not responding to MMF and new GI symptoms might be due to this drug, so it was discontinued after 10 days and colchicine (0.6 mg twice daily) was added to prednisolone. As there were persistent relapses of abdominal cramps and melena despite discontinuing MMF, blood was send abroad for qualitative assay of factor XIII activity. In the meantime, as the patient's condition was not imroving, five units of cryoprecipitate (each unit equal to 20ml) were transfused, which resulted in a significant improvement shortly characterized by disappearance of abdominal pain and discontinuation of melaena (confirmed by stool OBT). After five days, the report of qualitative assay of factor XIII activity was normal. However, there was a dramatic clinical response to cryoprecipitate transfusion. It should be noted that the qualitative assay of factor XIII activity can only detect very severe FXIII deficiency and is not sensitive. Quantitative assays could be an alternative tool to determine the exact plasma level of the FXIII but this test could not be performed due to unavailability. The rest of the drugs were tapered slowly over 7 months. The patient was free of symptoms until his last visit.

Discussion

HSP is the most common childhood vasculitis that is usually self-limiting with an excellent prognosis. Therefore, the use of immunosuppressive agents in HSP is not supported. In most of the cases, treatment consists of symptomatic and supportive therapy. Previous case studies have shown a correlation between reduced plasma factor XIII activity and the severity of multiple organ disorders, especially abdominal symptoms, in pediatric HSP (6). Previous case reports suggest that factor XIII activity correlates well with the severity of abdominal symptoms but not with skin rashes. Nonetheless, there is paucity of data regarding the persistence of abdominal pain and rashes in a patient without renal involvement.

We reported a child that presented with typical HSP rashes along with severe GI manifestations including episodic cramping abdominal pain and melena with normal renal function. High-dose oral prednisolone, IV pusles, and other immunosuppressants – immunomodulators did not improve the symptoms.

Subsequently, abdominal complain improved clinically following cryoprecipitate transfusion containing factor XIII.

Factor XIII (FXIII) is the last enzyme in the clotting cascade. Its main function is to convert the loose

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fibrin polymer into a firm, highly organized, cross-linked structure with increased tensile strength that firmly anchors to the site of the wound and offers an in-built resistance to fibrinolysis. In factor XIII deficiency, standard clotting tests are normal, as the clotting end point is not affected by the absence of factor XIII (8). In our patient, the basic coagulation profile was normal, including PT, APTT, and INR, despite significant hemorrhagic gastrointestinal symptoms. In acquired factor XIII deficiency like HSP, routine screening tests for coagulopathies usually do not yield any abnormalities.

Low plasma levels of factor XIII activity have been reported in some conditions like inflammatory bowel disease, systemic lupus erythematosus, and rheumatoid arthritis, characterized by the presence of autoantibodies (9-11). Whether low levels of factor XIII contribute to hemorrhagic complications in these diseases remains to be proven. Massive intracerebral hemorrhage and compartment syndrome of the forearm due to hemorrhage were reported in two children with HSP and severe factor XIII deficiency (12,13).

Treatment of patients with small bowel bleeding in the context of HSP and large bowel hemorrhage in the context of ulcerative colitis with factor XIII concentrate has been reported to be effective in controlling bleeding (14).

Our patient had normal factor XIII activity with characteristic purpuric rash and gastrointestinal manifestations like abdominal cramps and melena. He showed a remarkable improvement from his gastrointestinal symptoms shortly after the transfusion of cryoprecipitate. Cryoprecipitate contains fibrinogen, factor VIII, von Willbrand factor, factor XIII, and fibonectin. In one study, factor XIII substitution therapy using a fibrinogen preparation containing abundant factor XIII with an antiplasmin agent resulted in improvement of severe gastrointestinal hemorrhage in 13 out of 17 children with HSP (15). In that study, all of the 17 patients had low factor XIII levelw. However, our case had normal factor XIII activity. This can be explained by the fact that the clot solubility test (in our case) has a poor sensitivity and may fail to detect the exact level of factor XIII activity.

Some other studies have found that administration of factor XIII in patients with moderate HSP causes a remarkable improvement of joint symptoms and renal dysfunction in addition to gastrointestinal symptoms (16). Prenzel et al found that factor XIII activity correlated well with the severity of abdominal symptoms (2). Few studies have reported a correlation between the severity of HSP and factor XIII deficiency. Hogendorf et al showed improvement of factor XIII and symptoms resolution in two affected children without any interventions (17). A case series of three children with HSP and isolated gastrointestinal symptoms showed a reduction in factor XIII activity prior to the development of skin rashes without the need for substitution treatment (18). Skin rashes of HSP are an immune vasculitis. When remission is not achieved with steroids, it has been shown that colchicine may be effective. Therefore, colchicine was started for our patient to inhibit polymorphonuclear cells chemotaxis to the site of inflammation.

In conclusion, severe HSP manifestations, particularly those related to life-threatening GI bleeding and steroid resistant rashes, might benefit from colchicine and transfusion of cryoprecipitate containing factor XIII despite normal factor XIII activity. There is no report of successful administration of these two different types of medications in two different difficult-to-treat entities of HSP in the literature.

We recommend considering factor XIII administration in any HSP patient with life-threatening GI bleeding since the replacement treatment of such temporarily deficient factor is curative. Cryoprecipitate could be an excellent alternative if factor XIII concentrate is not available.

Conclusion

We recommend considering factor XIII administration in any HSP patient with life-threatening GI bleeding since the replacement treatment of such temporarily deficient factor is curative. Cryoprecipitate could be an excellent alternative if factor XIII concentrate is not available.

Conflict of Interest

The authors declare no conflicts of interest.

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