

Jacobs Journal of Gastroenterology and Hepatology

Case Report

Henoch-Schönlein Purpura and Ulcerative Colitis: Comorbidity or Coincidence?

Christoph K. Thoeninger^{1*}, Katja Specht², Roland M. Schmid¹, Wolfgang Huber²

¹*II. Med. Klinik und Poliklinik, Klinikum rechts der Isar, Technical University of Munich, Germany*

²*Department of Pathology, Klinikum rechts der Isar, Technical University of Munich, Germany*

**Corresponding author: Dr. Christoph K. Thoeninger, Klinikum rechts der Isar, Technical University of Munich Ismaninger Str. 22, 81675 Munich, Germany, Tel.: ++49-89-4140-2251; Email: christoph.thoeninger@lrz.tum.de*

Received: 10-15-2014

Accepted: 11-26-2014

Published: 12-19-2014

Copyright: © 2014 Christoph

Abstract

The burden of Crohn's disease and ulcerative colitis is substantially increased by extraintestinal manifestations (EIMs). In addition to EIMs, there is very rare occurrence of autoimmune pathologies like Henoch-Schönlein purpura (HSP) in inflammatory bowel disease. HSP is an inflammatory disease damaging small vessels by immune complex depositions, and affects the skin, joint, kidneys and gastrointestinal tract, especially in children.

Here, we report a rare case of HSP occurring in a female adult patient suffering from ulcerative colitis. Our patient presented with acute abdominal pain, bloody diarrhoea, arthralgia, palpable purpura and petechiae on lower limbs, and had a history of ulcerative colitis (UC). A recurrence of past episodes with *Clostridium difficile*-induced colitis was ruled out. Clinical, endoscopic and laboratory examinations provided evidence for a co-occurrence of HSP and an acute episode of UC. She was treated with steroids (prednisolone 80mg/d with progressive dose reduction) and mesalazine (4g/day) that induced rapid remission of the gastrointestinal symptoms, leg rash and arthralgia.

We describe a rare manifestation of HSP in a female patient that emerged during active UC. We discuss overlapping pathophysiological mechanisms underlying both HSP and ulcerative colitis in detail, which may stimulate the discussion about comorbidity or coincidence of both disorders.

Keywords: Ulcerative Colitis; Extraintestinal Manifestation; Henoch-Schönlein Purpura

Introduction

Extraintestinal manifestations (EIMs) are common in inflammatory bowel disease. 20-40% of patients with Crohn's disease (CD) present with extraintestinal conditions like joint disorders, ocular or hepatic manifestations such as primary sclerosing cholangitis, and erythema nodosum or pyoderma gangrenosum [1]. Concerning ulcerative colitis (UC) the prevalence of EIMs is lower, ranging up to 15-20% [1].

Unlike clinically well-known skin and joint manifestations of UC, patients with UC may present with other autoimmu-

nopathies, however the association is rare. Interestingly, the occurrence of Henoch-Schönlein purpura (HSP) has been reported in UC [2,3]. HSP is an inflammatory vascular disease involving small vessels with the deposition of immune complexes containing IgA and affecting the skin, joints, kidneys and the gastrointestinal tract. It is commonly seen in children with symptoms of palpable purpura, abdominal pain or gastrointestinal bleeding, arthralgia, and haematuria, but usually with a benign and self-limiting course [4]. In adults, the clinical presentation of HSP is more severe due to an elevated risk for severe renal failure and skin necrosis [5]. The diagnosis of HSP is made according to criteria re-

cently proposed by the European League Against Rheumatism (EULAR) revising the ACR criteria of 1990 [6]. According to them, a patient is classified as HSP in the presence of purpura or petechiae with lower limb predominance plus of one of the four criteria: abdominal pain (including intussusception and gastrointestinal bleeding), vasculitis with predominant IgA deposit, arthritis or arthralgias, and renal involvement (i.e., proteinuria or hematuria).

Gastrointestinal features of HSP typically include colicky abdominal pain, nausea and vomiting, that worsens after meals. Less common, there is also occult rather than overt gastrointestinal bleeding [7]. The small intestine is the most affected site because of its sensitivity towards ischemia. Vasculitis-induced, inflammatory intestinal tissue injury presents with petechiae, hyperaemia, fistulas and ulcers mimicking CD [7-9]. The occurrence of HSP cutaneous vasculitis in CU has rarely been described with reports mainly from children [2]. Here, we report a rare case of HSP as coincidence and/or extraintestinal manifestation of CU in a female adult patient.

Case Presentation

A 30-year old woman was admitted to our university hospital with bloody diarrhoea and severe abdominal pain. She also complained about ankle arthralgia, petechiae and palpable purpura on lower limbs (Fig.1). She had a history of CU formally diagnosed 7 months ago and was treated with mesalazine (2g/day) for maintenance of remission at the time of admission. She reported recurrent ankle arthralgias since several years, and a prior episode of skin rash on lower limbs. Especially, the arthralgias were frequently associated with episodes of diarrhoea and abdominal pain.

Laboratory tests performed at admission revealed anaemia (haemoglobin count of 11.0 g/dl), and a systemic inflammatory response (C-reactive protein [CRP] of 2.7 mg/dl) with normal white blood cell counts. Serum urea and creatinine were normal. Urine examinations revealed no proteinuria, but microscopic haematuria with 75 blood cells per high-power microscopic field in urinary sediments. We evaluated the immunological status and observed normal values for IgG, IgA, C3 and C4. Immunological assays were negative for the following serum antibodies: anti-double stranded DNA, anti-lactoferrin, anti-Sm, anti-RNP-70. Slightly elevated titers were observed for antineutrophil cytoplasmic antibodies (pANCA; 1:16) and for antinuclear antibodies (ANA; 1:120). In addition, three episodes of *Clostridium difficile*-induced colitis were reported, but a recurrence of infection was excluded by stool analysis and endoscopy at admission.

A colonoscopy revealed moderate pancolitis with erythema, erosions, friability and an absent vascular pattern (Fig. 1). In the histopathological examination of colonic biopsies, signs of

a highly active colitis with dense infiltrates of eosinophil granulocytes and plasmocytes, crypt distortions and abscesses were observed indicating the presence of UC (Fig. 1). Skin and kidney biopsies were not taken to avoid further harm for the patient. According to the EULAR criteria⁶ HSP diagnosis was established as our patient fulfilled all criteria by presenting typical cutaneous manifestations, abdominal pain, joint and renal pathology.

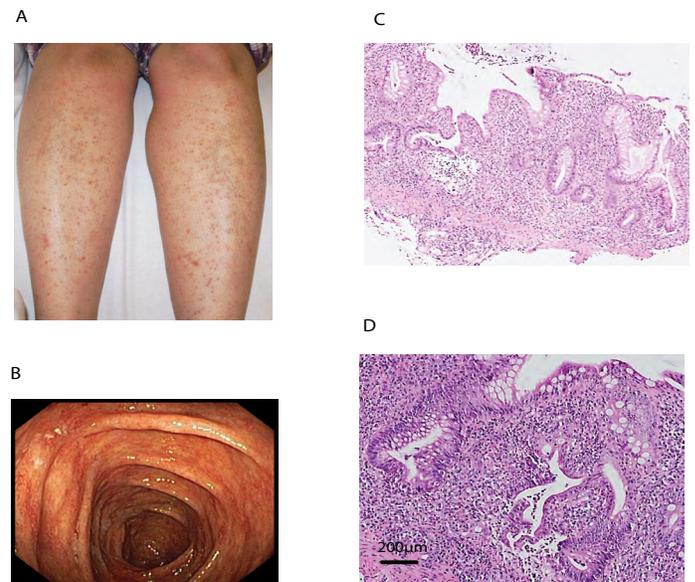


Figure 1. Petechiae and palpable purpura were found on the lower limbs (A). Endoscopy revealed erythema, erosions, friability and an absent vascular pattern in the colon (B). Histopathologically, severe active inflammation with crypt distortions and abscesses, eosinophil granulocytes and plasmocytes indicated active ulcerative colitis (C, D).

Accordingly, she was treated with prednisolone (80mg/day) with progressive dose reduction, and mesalazine (4g/day) was given as add-on therapy. Bloody diarrhoea disappeared within 4 days. Leg rash and ankle arthralgia also disappeared after 2 weeks. Due to the frequent recurrence of CU symptoms and severity of HSP one started a therapy with azathioprine (2mg/kg/day) after interdisciplinary discussions with rheumatologists and informed consent by the patient. Two month later the patient was well with a normal bowel habit, no rash or joint pain.

Conclusion

In the present report we describe a manifestation of PSH in a female patient that emerged during an active episode of CU. Our patient had a history of active CU and the diagnosis was again confirmed by histopathological examination. Importantly, the criteria necessary to establish a diagnosis of HSP were

also fulfilled. In our serological analyses, she was also tested positive for pANCA autoantibodies which are highly prevalent in CU with, however, little sensitivity [10,11]. These antibodies are commonly found in other vasculitic disorders, but were also discovered in several HSP patients, especially with gastrointestinal symptoms [12-14]. A *Clostridium difficile*-related colitis known to trigger HSP [7] could be excluded.

The co-occurrence of PSH and inflammatory bowel disease has rarely been observed and reported. To the best of our knowledge, there are only three cases of HSP in CU, predominantly seen in children [2,3], and several reports describing Crohn's like disease in HSP [8,9,15]. Intriguingly, skin and joint manifestations of PSH were observed only during active gastrointestinal inflammation in these cases. It resembles, thus, certain EIMs such as erythema nodosum or peripheral arthritis which are related to UC or CD activity, whereas pyoderma gangrenosum or primary sclerosing cholangitis usually run an independent course. Acute episodes of HSP have also been reported following treatment with the anti-tumour necrosis factor- α (anti-TNF α) agents infliximab and adalimumab in CD and UC [16,17].

In general, the pathophysiological causes of HSP and CU are only little understood. HSP is considered a specific immune-mediated entity triggered by infections, medications, vaccines and tumors [7]. Microscopically, it is characterized by polymorphonuclear neutrophils (PMNs) infiltration around vessels and IgA and complement deposits [18]. Although not entirely resolved, IgA seems to play a pivotal role in HSP. It has been suggested that a diminished glycosylation of IgA1 in the hinge region of this IgA subclass, observed in HSP, may facilitate aggregation into macromolecular complexes, which then activates the alternative pathway of complement [19]. IgA-related derangements, however, do not play a role in the pathogenesis of inflammatory bowel disease. In contrast, current concepts suggest a dysregulation in the homeostatic balance between regulatory and effector T-cells (i.e., Th1 vs. Th2) with exaggerated Th2 responses mediated by non-classical natural killer T-cells [20]. A disequilibrium of cellular immunity may also be involved in the pathophysiology of HSP. A flow cytometric analysis of blood samples from children suffering from acute HSP revealed that the proportions of Th2 cells were significantly higher, levels of T-regulatory cells were lower and the ratio of Th1/Th2 was decreased compared to healthy controls [13]. In addition, CU and HSP share another characteristic feature of exaggerated immune responses as it was shown that TNF α levels are elevated in serum or affected skin of HSP patients and also in serum or mucosa of individuals suffering from CU [18,20]. Interestingly, it was suggested that increased TNF α and defective and/or decreased T-regulatory cells may prime neutrophils and, thus, stimulate ANCA formation with deleterious effects on tissue integrity [13].

According to, at least partially, overlapping pathophysiological mechanisms in CU and HSP and the significance of ANCA in CU and PSH patients with predominant gastrointestinal symptoms one can speculate that PSH may be more than a coincidence in CU as we and others have described in case reports. It, however, warrants further epidemiological and immunobiological studies in humans to definitively resolve whether PSH represents a comorbid condition or even extraintestinal manifestation of inflammatory bowel disease. Such studies may be worth considering as one could gain novel insights into pathophysiological mechanisms underlying (auto-inflammatory disorders, and reveal new therapeutic targets).

Competing interests

The authors declare no competing interests.

Contributorship

CKT, KS, WH: conception and drafting the article; RMS: critical revision regarding the intellectual content.

Acknowledgements

This work was supported by the Technische Universität München within the funding programme Open Access Publishing.

References

1. Lakatos PL, Lakatos L, Kiss LS, Peyrin-Biroulet L, Schoepfer A, et al. Treatment of extraintestinal manifestations in inflammatory bowel disease. *Digestion*. 2012, 86(suppl1): 28-35.
2. de Oliveira GT, Martins SS, Deboni M, Picciarelli P, Campos LMA et al. Cutaneous vasculitis in ulcerative colitis mimicking Henoch-Schönlein purpura. *J Crohns Colitis*. 2013, 7(2): 69-73.
3. Tursi A, Inchingolo CD. Ulcerative colitis in Henoch-Schönlein purpura: which came first, the chicken or the egg? *Colorectal Dis*. 2013, 15(6): 762-763.
4. Blanco R, Martinez-Taboada VM, Rodriguez-Valverde V, Garcia-Fuentes M, Gonzalez-Gay MA. Henoch-Schönlein purpura in adulthood and childhood. *Arthritis Rheum*. 1997, 40(5): 859-864.
5. Pillebout E, Thervet E, Hill G, Alberti C, Vanhille P, Nochy D. Henoch-Schönlein purpura in adults: outcome and prognostic factors. *J Am Soc Nephrol*. 2002, 13(5): 1271-1278.
6. Ozen S, Pistoro A, Iusan SM, Bakkaloglu A, Herlin T et al. EULAR/PRINTO/PRES criteria for Henoch-Schönlein purpura, childhood polyarteritis nodosa, childhood Wegener granuloma

- matosis and childhood Takayso arteritis: Ankara 2008. Part II: Final classification criteria. *Ann Rheum Dis.* 2010, 69(5): 798-806.
7. Ebert EC. Gastrointestinal manifestations of Henoch-Schönlein purpura. *Dig Dis Sci.* 2008, 53(8): 2011-2019.
8. Samuel S, Loftus EV, Sandborn WJ. Henoch-Schönlein purpura in an adult mimicking Crohn's disease and pyoderma gangrenosum. *Dig Dis Sci.* 2011, 56(7): 2205-2206.
9. Yavuz A, Yildiz M, Aydin A. Henoch Schonlein purpura mimicking Crohn's ileitis. *J Crohns Colitis.* 2011, 5(3): 271-272.
10. Reese GE, Constantinides VA, Simillis C, Darzi AW, Orchard TR et al. Diagnostic precision of anti-Saccharomyces cerevisiae antibodies and perinuclear antineutrophil cytoplasmic antibodies in inflammatory bowel disease. *Am J Gastroenterol.* 2006, 101(10): 2410-2422.
11. Plevy S, Silverberg MS, Lockton S, Stockfish T, Croner L et al. Combined serological, genetic, and inflammatory markers differentiate Non-IBD, Crohn's disease, and ulcerative colitis patients. *Inflamm Bowel Dis.* 2013, 19(6): 1139-1148.
12. Hong SM, Chen YC, Hsueh S, Jeng CC, Fang JT et al. Adult-onset perinuclear antineutrophil cytoplasmic antibody-positive Henoch-Schönlein purpura in diabetic nephropathy. *J Nephrol.* 2009, 22(1): 164-170.
13. Kim JE, Shin JI. Positive c-ANCA in Henoch-Schönlein purpura: what is the mechanism? *Rheumatol Int.* 2013, 34(7): 1017.
14. Zhang Y, Wu YK, Ciorba MA, Ouyang Q. Significance of antineutrophil cytoplasmic antibody in adult patients with Henoch-Schönlein purpura presenting mainly with gastrointestinal symptoms. *World J Gastroenterol.* 2008, 14(4): 622-626.
15. Saulsbury FT, Hart MH. Crohn's disease presenting with Henoch-Schönlein purpura. *J Pediatr Gastroenterol Nutr.* 2000, 31:173-175.
16. Marques I, Lagos A, Reis J, Pinto A, Neves B. Reversible Henoch-Schönlein purpura complicating adalimumab therapy. *J Crohns Colitis.* 2012, 6(7): 796-799.
17. Nobile S, Catassi C, Felici L. Herpes zoster infection followed by Henoch-Schönlein purpura in a girl receiving infliximab for ulcerative colitis. *J Clin Rheumatol.* 2009, 15(2): 101.
18. Yang YH, Chuang YH, Wang LC, Huang HY, Gershwin ME et al. The immunobiology of Henoch-Schönlein purpura. *Autoimmun Rev.* 2008, 7(3): 179-184.
19. Saulsbury FT. Clinical update: Henoch-Schönlein purpura. *Lancet.* 2007, 369(9566): 976-978.
20. Ordaas I, Eckmann L, Talamini M, Baumgart DC, Sandborn WJ. Ulcerative colitis. *Lancet.* 2012, 380(9853): 1606-1619.