*Jarosław Kierkuś[1], Edyta Szymańska[2], Sylwia Szymańska[3], Lidia Ruszkowska[4]

A case of pediatric patient with ulcerative colitis and extraintestinal skin manifestation – pyoderma gangrenosum

Przypadek pacjenta pediatrycznego z wrzodziejącym zapaleniem jelita grubego i skórną manifestacją pozajelitową w postaci piodermii zgorzelinowej

[1]Department of Gastroenterology, Hepatology and Feeding Disorders, The Children's Memorial Health Institute, Warszawa
Head of Department: prof. Józef Ryżko, MD, PhD
[2]Department of Pediatrics, Nutrition and Metabolic Disorders, The Children's Memorial Health Institute, Warszawa
Head of Department: prof. Janusz Książyk, MD, PhD
[3]Department of Pathology, The Children's Memorial Health Institute, Warszawa
Head of Department: prof. Maciej Pronicki, MD, PhD
[4]Department of Pediatric Dermatology, Specialist Hospital in Międzylesie, Warszawa
Head of Department: Lidia Ruszkowska, MD

Key words
inflammatory bowel disease, ulcerative colitis, pyoderma gangrenosum, extraintestinal manifestations, Schönlein-Henoch Purpura, complications

Słowa kluczowe
nieswoiste choroby zapalne jelit, wrzodziejące zapalenie jelita grubego, piodermia zgorzelinowa, manifestacje pozajelitowe, plamica Schönleina-Henocha, powikłania

Summary

Ulcerative colitis (UC) is an inflammatory disease of the intestines (inflammatory bowel disease – IBD) which is typically characterized by abdominal pain, diarrhea, vomiting, or weight loss. Manifestations such as skin rashes, arthritis, iritis, primary sclerosing cholangitis, pyoderma gangrenosum or erythema nodosum may also occur. They are rare and develop in approximately one-quarter to one-third of patients with IBD. Skin involvement is a fairly common problem, and may affect up to 25 percent of patients. Extra-intestinal symptoms can either precede intestinal disorders or they can be connected with exacerbation of bowel disease. All of them can either precede intestinal disorders or be connected with exacerbation of already diagnosed UC. Extra-intestinal symptoms preceding intestinal disorders may delay proper diagnosis and treatment which cause a lot of dangerous complications. We report a case of 9-years old boy with severe UC and pyoderma gangrenosum who was diagnosed primary as Schonlein-Henoch Purpura. Misdiagnosis appeared to be life-threatening in this patient.

Streszczenie

Wrzodziejące zapalenie jelita grubego (ang. ulcerative colitis – UC) należy do nieswoistych chorób zapalnych jelit (ang. inflammatory bowel disease – IBD), które typowo objawiają się bólem brzucha, biegunką, wymiotami oraz ubytkiem masy ciała. Jednakże objawy pozajelitowe takie jak wysypka skórna, zapalenie stawów, zapalenie tęczówki, pierwotne stwardniające zapalenie dróg żółciowych, piodermia zgorzelinowa czy rumień guzowaty mogą również wystąpić. Są one rzadkie i dotykają ok 1/4-1/3 pacjentów z IBD. Manifestacje skórne są jednymi z częstszych problemów i mogą dotyczyć nawet do 25% ludzi chorych. Objawy pozajelitowe mogą zarówno poprzedzać zaburzenia ze strony przewodu pokarmowego, jak i wiązać się z zaostrzeniem choroby podstawowej. Wszystkie te manifestacje mogą zarówno poprzedzać objawy jelitowe jak i wiązać się z zaostrzeniem już zdiagnozowanej UC. W przypadku, gdy manifestacje pozajelitowe wyprzedzają objawy z przewodu pokarmowego może dojść do opóźnienia postawienia właściwej diagnozy oraz wprowadzenia odpowiedniego leczenia, co może powodować wiele niebezpiecznych powikłań. Przedstawiamy przypadek 9-letniego chłopca z ciężką postacią UC z towarzyszącą piodermią zgorzelinową, która została początkowo błędnie zdiagnozowana jako plamica Schonleina-Henocha. W tym przypadku błędna diagnoza okazała się zagrażająca życiu.

Address/adres:
*Jarosław Kierkuś
Department of Gastroenterology,
Hepatology and Feeding Disorders
The Children's Memorial Health Institute
Al. Dzieci Polskich, 04-730 Warszawa
tel./fax +48 (22) 815-73-92
j.kierkus@czd.pl

INTRODUCTION

Ulcerative colitis (UC) is a chronic, autoimmune inflammatory bowel disease (IBD) that causes inflammation of the large intestine (colon) and rectum. It primarily causes abdominal pain, diarrhea, vomiting, or weight loss but may also cause systemic complications such as skin disorders, arthritis, inflammation of the eye, and liver disorders (specially primary sclerosing cholangitis – PSC) (1). Twenty to thirty-five percent of patients with IBD have at least one of its extraintestinal symptoms. Skin involvement

is a fairly common problem, and may affect up to 25 percent of people who suffer from IBD. Extraintestinal symptoms can either precede intestinal disorders or they can be connected with exacerbation of bowel diseases (1, 2).

Pyoderma gangrenosum (PG) is the most common type of skin disorder that may occur in IBD (3). Its etiology is unknown but it may be an autoimmune condition, as it is related to other autoimmune disorders, besides IBD, also to rheumatoid arthritis, myeloid blood dyscrasias, and hepatitis (4). The disease affects about 5 percent of people with UC and about 1 percent of patients with Crohn's disease (CD), another type of IBD (5). At times, the occurrence of pyoderma gangrenosum ulcers corresponds to an active flare-up of IBD, and may respond when the underlying IBD is treated. Other cases, however, do not appear to be directly related to disease activity, and PG may begin or even worsen when the IBD is quiescent (6). If skin involvement appears earlier than intestinal disorders, it may delay proper diagnosis and treatment which causes a lot of dangerous complications.

We report a case of 9-years old boy with severe UC and pyoderma gangrenosum who was diagnosed primary as Schönlein-Henoch Purpura. Misdiagnosis appeared to be life-threatening in this patient.

CASE REPORT

In March 2011, a 9 years old boy presented with abdominal pain, chronic bloody diarrhea, and anemia together with skin lesions on the left lateral ankle was administered to the Department of Pediatric Gastroenterology at Academic Hospital. At admission, he was in good general condition, presented with paleness, cushing's features, growth deficiency and healing ulcerative lesion within left lateral ankle. Laboratory tests revealed microcytic anemia and trombocytosis. Table 1 includes laboratory parameters and bacteriologic stool analysis at admission.

Table 1. Laboratory parameters and bacteriologic stool analysis at admission.

Parameter	Characteristic
Morphology:	
Hemoglobin (g/dl)	9.3
Blood palates (x 10^9/l)	800
Leucocytes (x 10^9/l)	11.1
Biochemistry:	
Glucose (mg/gl)	131.0
Urea (mg/dl)	29.3
Creatinine	0.24
Bilirubin (mg/dl)	0.23
Direct bilirubin (mg/dl)	0.12
ALT (U/L)	52.0
AST (U/L)	26.0
GGTP (U/L)	197.0
Stool bacteria culture:	
Salmonella	Negative
Shigella	Negative
Yesrinia	Negative
Campylobacter	Negative

ALT – Alanine Aminotransferase, AST – Aspartate Aminotransferase, GGTP – Gamma-glutamylo-transpepdydase

The diagnosis of Schönlein-Henoch Purpura (SHP) with skin and intestinal manifestations was established. Since that time, the boy has been hospitalized several times due to recurrence of abdominal pain, bloody diarrhea and skin lesions. Each time the same diagnosis of SHP was made. Antibiotics and systemic steroids were administered as the first line therapy. Following this treatment clinical symptoms receded but occult blood was still detected in stools. However, any attempt of steroids dose reduction ended up in intensification of both intestinal and skin symptoms. Finally, in March 2012, the boy was transferred to the Surgical Department. The biopsy of skin lesions was taken, and diagnosis of pyoderma gangrenosum was made on the base of histopatologic examination. Figures 1 and 2 present histopathological features of patient's skin lesions. Steroids were administered again and the healing of skin ulceration was observed. On April, patient was referred to the Clinic of Pediatric Dermatology. During this hospitalization, the nature of skin ulcerations on boy's left lower limb was confirmed to be pyoderma gangrenosum. Therapeutic approach has been changed. Doctors displaced Solu-Medrol with Encorton 40 mg/24 h (reduced to 30 mg/h at discharge) together with locally administered Protopic 0.1% ointment, Yellonet dressing, and Bactigras with good tolerance. Following this therapeutic strategy, healing of ulcerative lesions was observed. With suspicion of inflammatory bowel disease (IBD) patient was transferred to The Children Memorial Health Institute, the Department of Gastroenterology, Hepatology and Feeding Disorders in order to extend the diagnostics on gastrointestinal field. After proper preparation, both gastroscopy and colonoscopy were performed. Gastroscopy revealed no abnormalities, while endoscopic examination of the large intestine showed rigidity of its wall with reduced haustration, loss of normal vascular markings within whole colon, numerous pseudo-polyps, few active ulcerations, and many healed deep marks. Biopsy for histopatologic examination was taken. Finally, on the base of clinical course of disease and histopatologic examination, the diagnosis of severely active ulcerative colitis with extraintestinal skin manifestation was established. Our patient had following therapy administered: 5-ASA agents with Encorton 20 mg, Imuran 2 x 25 mg, Asamax 2 x 500 mg, and continuation of locally administered treatment. On May 2012, another relapse of disease was observed, and the dose of steroids was increased with no clinical improvement whatsoever. Finally, in May 2012, after completing all formalities, biological therapy with infliximab was administered with both clinical response and healing of skin ulceration. So far, the boy has received 3 doses of infliximab. He is in good general being, does not present with intestinal symptoms (PUCAI < 10), and his ulcerative lesion on the left ankle is healed.

DISCUSSION

One of the extraintestinal skin manifestations often associated with IBD is pyoderma gangrenosum, but it still remains a very rare pathology. If skin involvement appears earlier than intestinal disorders, it may delay proper diagnosis and treatment. In our case, a 9 years

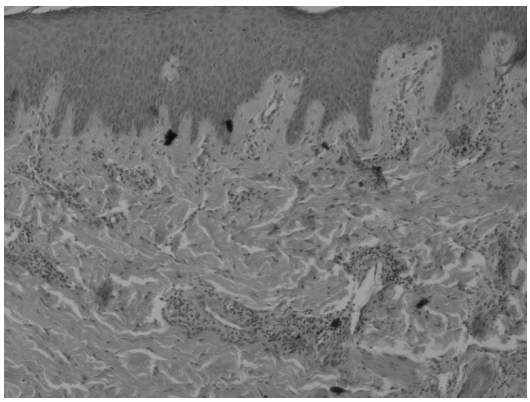

Fig. 1. Intensive polimorphic inflammation involving deep dermis and subcutis, lymphocyte mediated vasculitis. H-E staining, magnification x 20.

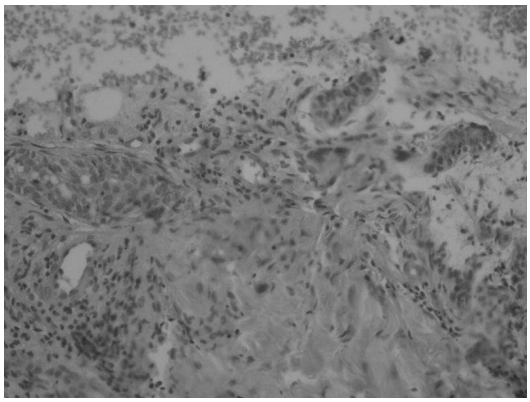

Fig. 2. Focal haemorrhage (upper side of the picture), intensive inflammation consisting of plasma cells and lymphocytes. Giant cells are present. H-E staining, magnification x 40.

old with severe UC and pyoderma gangrenosum was primary misdiagnosed as Schönlein-Henoch Purpura with both skin and intestinal manifestations. SHP is a self-limiting, autoimmune, small-vessel vasculitis, which usually affects children younger than 10 years (7). The disease is characterized by palpable purpuric rash, abdominal pain with or without evidence of gastrointestinal bleeding, and arthralgia or arthritis, fifty percent of patients have evidence of nephritis at the time of diagnosis (8). There are no specific diagnostic tests for SHP, and the treatment is symptomatic and does not alter the course of the disease. In our patient, the skin lesion was ulceration on left lateral ankle, which does not correspond with clinical features of SHP. Moreover, the course of disease was severe, recurrent, and refractory to steroid therapy, while Schönlein-Henoch vasculitis lasts from between a few days to several weeks, and usually resolves without specific therapy. Neither arthralgia/arthritis nor nephritis characteristic for SHP were observed in our patient. However only 15 percent of people develop renal disease at the time of diagnosis. Endoscopic examination was not performed at the beginning because of the poor general state of the patient, which delayed proper diagnosis and treatment. Only later, at the surgical department the biopsy of the skin lesions was taken and thus the diagnosis of PG was established. When patient was admitted to our clinic, endoscopic examination with biopsy taken was performed and final diagnosis of severe UC and PG was made. Due to his poor response to conventional treatment we decided to introduce infliximab as there are publications and case reports which have proved efficacy of biologic therapy in management of PG in IBD (9, 10).

We report this case because it is extremely important to remember of extraintestinal manifestations of inflammatory bowel disease, and therefore to include IBD in differential diagnosis in patients with abdominal pain, bloody diarrhoea and skin lesions. This case report proves how important is complex diagnostics consisted of referral and consultation in patients with complicated clinical course of their disease since misdiagnosis may delay proper treatment leading to dangerous complications, including life-threatening situations.

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