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ORIGINAL PAPER

The clinical course of varicella and herpes zoster in children with inflammatory bowel disease – a prospective study

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ABSTRACT

Introduction: Children with inflammatory bowel disease (IBD), particularly those treated with immunosuppressive drugs, are a risk group for severe, complicated and even fatal course of varicella-zoster virus (VZV) infection. The study aimed to analyse the clinical course, therapeutic approach and outcome of varicella and herpes zoster (HZ) in paediatric patients with IBD.

Material and methods: A prospective multicentre study including children with IBD and diagnosis of varicella or HZ was conducted September 2015 – June 2019. In all patients, a diagnosis of VZV infection was made on the basis of the characteristic rash.

Results: We identified 26 patients, including 14 with Crohn's disease and 12 with ulcerative colitis. Twelve patients were diagnosed with varicella and 14 with HZ. No patient was immunized with varicella vaccine; no patient with varicella after known direct exposure received varicella zoster immunoglobulin. The median interval between diagnosis of IBD and diagnosis of VZV infection was 2 years and 10 months. Twenty patients were treated with immunosuppressive drugs, including thiopurine, an anti-tumour necrosis factor agent, mycophenolate mofetil, methotrexate and prednisone. Eight children were hospitalized in the course of VZV infection. Anti-viral treatment with acyclovir was used in 8/12 patients with varicella and 12/14 patients with HZ. Complications were diagnosed in 2 patients with varicella who were also receiving immunosuppressive therapy (both developed superficial bacterial infection). No complications were observed in patients with HZ. Neither dissemination to other organs nor fatal outcome was reported. Exacerbation of IBD was observed in 4 patients.

Conclusions: The clinical course of VZV infection in children with IBD is variable. Severe clinical course and complications seem to be rare. On the other hand, both varicella and HZ can be a risk of exacerbation of IBD.

KEY WORDS:

Crohn's disease, chickenpox, shingles, immunosuppressive therapy, ulcerative colitis.

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INTRODUCTION

Varicella-zoster virus (VZV) is a member of the herpesvirus family. Primary VZV infection, called varicella (chickenpox), is a highly contagious illness characterized by diffuse vesicular rash and fever. Varicella occurs mainly in childhood. In healthy children, varicella is usually mild, but complications occur in up to 5% of cases (e.g., bacterial superinfection, pneumonia, encephalitis). In adults and immunocompromised patients at any age (due to disease or medication) it tends to be more severe or even fatal with prolonged viremia, pneumonia, hepatitis, involvement of the central nervous system, and thrombocytopenia, all due to VZV. After primary infection the virus establishes latency in the dorsal root ganglia. Reactivation of latent VZV causes herpes zoster (shingles) (HZ), typically manifested by vesicular rash affecting the skin of 1–2 dermatomes. The main risk factor for VZV reactivation is age. However, HZ can occur at any age, particularly in individuals with weakened immune systems, such as those undergoing immunosuppressive treatment. In adults and especially older adults, HZ tends to be more severe with an increased risk of postherpetic neuralgia. Immunocompromised patients are at a markedly higher risk of disseminated disease and severe complications (e.g., encephalitis, hepatitis) [1]. In countries (e.g. Poland), where varicella immunization is not routinely used, VZV infections are common.

Inflammatory bowel disease (IBD) is a group of chronic and relapsing inflammatory diseases affecting the gastrointestinal tract. One can distinguish 2 disorders: Crohn's disease (CD) and ulcerative colitis (UC). The disease can lead to malnutrition and thus to decreased cellular and humoral immunity. The use of immunomodulators, such as corticosteroids, thiopurines (azathioprine, 6-mercaptopurine), methotrexate, cyclosporine, tacrolimus, mycophenolate mofetil or newer biological agents such as tumour necrosis factor α inhibitors is beneficial for the disease control but also is associated with an increased risk of severe viral and bacterial infections, including VZV infections [2]. On the other hand, any infection may cause an exacerbation of the IBD course.

This study aimed to characterize VZV infections among children with IBD and their impact on the IBD clinical course.

MATERIAL AND METHODS

STUDY DESIGN AND SETTING

This multicentre prospective study included children (0–18 years) with CD or UC who were diagnosed with varicella or HZ between 1 September 2015 – 1 June 2019. Five Polish inpatient centres dedicated to paediatric patients with IBD reported their cases using an electronic questionnaire addressing demographic, epidemiological, and clinical data. Any patient younger than 18 years with VZV infection was eligible for inclusion.

DATA COLLECTION

Demographic data included sex and age at occurrence of VZV infection. Epidemiologic data included known exposure to VZV (patients with varicella), previous history of varicella (patients with HZ), and varicella immunization status. Clinical data included: diagnosis of CD or UC with duration, activity (according to paediatric Crohn's disease activity index and paediatric ulcerative colitis activity index for CD and UC, respectively), treatment for IBD at the time of VZV infection and clinical course of varicella and HZ: severity, complications, hospitalization, treatment, outcome and impact on the IBD course. Both varicella and HZ were diagnosed based on the presence of a characteristic rash.

STATISTICAL ANALYSIS

Statistical analysis was performed using Statistica 13 (TIBCO Software Inc., USA). Categorical variables were compared using the Fisher exact test. Continuous variables are presented as medians with interquartile ranges (IQRs). A two-sided p-value < 0.05 was considered significant.

ETHICAL CONSIDERATION

The study was performed in accordance with the ethical standards in the 1964 Declaration of Helsinki and its later amendments. The ethics committee of the Medical University of Warsaw approved this study (KB/113/2016).

RESULTS

Between 1 September 2015 – 1 June 2019, 26 patients with VZV infection were reported: 12 with varicella and 14 with HZ among approximately 800 patients with IBD treated in the participating centres. The estimated incidence of varicella and HZ was 1.5% and 1.75%, respectively. The median age of patients was 13 (range 2–17 years) and eleven were male. None of the patients was vaccinated against VZV. Fourteen patients had a diagnosis of CD, and twelve of UC. The median duration of IBD before VZV infection was 2 years 10 months (range 1 month to 15 years). At the onset of VZV infection, 20 patients were treated with immunosuppressive drugs (IS), including monotherapy with thiopurine (8 patients), an anti-tumour necrosis factor (anti-TNF) agent (2 patients), mycophenolate mofetil (1 patient) and a combination of anti-TNF agent + thiopurine (6 patients), anti-TNF agent + methotrexate (2 patients) and prednisone + thiopurine + anti-TNF agent (1 patient). Characteristics of all patients are presented in Table 1.

TABLE 1. Characteristics of inflammatory bowel disease patients with varicella-zoster virus infection

Case	Sex	Age (years)	IBD diagnosis (activity according to PCDAI for CD and PUCAI for UC)	Time interval between IBD diagnosis and VZV infection onset (years)	IBD immunosuppressive treatment	Varicella: number of skin lesions; Herpes zoster: location (number of dermatomes)	Complications	Hospitalization	Treatment with acyclovir	Impact on IBD course (if yes, points in PUCAI/PCDAI)
Varicella										
1.	F	17	CD (0)	15	None	< 50	None	No	Orally 7 days	No
2.	F	10.5	CD (0)	8	MTX + IFX	< 50	BACT	3 days	Intravenously 3 days Orally 6 days	No
3.	M	5.5	CD (5)	2	None	> 50	None	No	No	No
4.	F	12	CD (25)	4	PUR	> 50	None	No	Orally 7 days	Yes (45)
5.	F	9	UC (10)	2	None	> 50	None	No	No	No
6.	M	11.5	CD (5)	3	PUR	> 50	None	No	Orally 7 days	No
7.	M	16.5	CD (0)	8	MTX + IFX	> 50	URTI	No	Orally 7 days	No
8.	F	17	UC (25)	1	None	< 50	None	No	No	No
9.	F	9	CD (5)	4	PUR	> 50	BACT	4 days	Intravenously 4 days Orally 3 days	No
10.	M	5.5	UC (60)	< 0.5	PUR	> 50	None	1 day	No	No
11.	M	13.5	CD (15)	13	PUR + IFX	> 50	None	11 days	Intravenously 3 days Orally 2 days	No
12.	F	2	CD (0)	1	PUR	> 50	None	No	Orally 5 days	No
Herpes zoster										
13.	F	17	CD (5)	1	PUR	Chest (1)	Pain	No	Orally 14 days	No
14.	M	13	CD (5)	1	PUR	Chest (2)	Pain	No	Orally 7 days	No
15.	F	16	UC (0)	3	None	Chest (1)	Pain	No	Orally 7 days	No
16.	F	13.5	UC (0)	2.5	IFX	Chest (3)	Pain	9 days	Intravenously 8 days Orally 6 days	Yes (35)
17.	M	9	UC (0)	3	PUR	Chest (2)	Pain	No	Orally days	Yes (50)
18.	F	15.5	UC (5)	3.5	PUR + IFX	Leg	Pain	No	Orally days	No
19.	F	10	CD (17.5)	< 0.5	PUR	Chest (1)	Pain	No	Orally 5 days	No
20.	F	10	CD (0)	5	PUR + IFX	Chest (1)	None	6 days	Orally 10 days	No
21.	F	13	UC (0)	< 0.5	PUR	Head	None	No	Orally 10 days	No
22.	M	14.5	CD (2.5)	< 0.5	PUR + IFX	Arm	None	15 days	Intravenously 10 days	No
23.	M	14	CD (0)	4.5	None	Chest (1)	None	No	Orally 10 days	
24.	F	15	UC (5)	11	ADA	Neck	None	No	Orally 10 days	No
25.	M	14	UC (0)	2.5	PR + PUR + IFX	Chest (1)	None	No	Orally 10 days	No
26.	F	17	UC (0)	12	MM	Leg	Pain	4 days	Intravenously 3 days Orally 7 days	Yes (25)

ADA – adalimumab, BACT – bacterial superinfection of skin lesions, CD – Crohn's disease, IBD – inflammatory bowel disease, IFX – infliximab, MM – mycophenolate mofetil, MTX – methotrexate, PCDAI – paediatric Crohn's disease activity index, PR – prednisone, PUCAI – paediatric ulcerative colitis activity index, PUR – thiopurine, UC – ulcerative colitis, URTI – upper respiratory tract infection, VZV – varicella zoster virus

VARICELLA

The median age of the patients was 11 years (IQR: 7.25,15.1; range 2–17 years). In 4 out of 12 patients (33.3%), varicella presentation was mild (with < 50 vesicles), while the others showed > 50 vesicles; the classification of varicella severity (< 50 vs. > 50 vesicles) was an author-defined threshold. Four patients (33.3%) were hospitalized (median days: 3.5; IQR: 2, 7.5; range 1–11 days). Eight out of 12 patients (66.7%) were treated with acyclovir for 5–9 days, in three of them it was initially given intravenously. Two patients (16.7%) were diagnosed with bacterial superinfection of the skin lesions and required antibiotic therapy. In one (8.3%), a concurrent upper respiratory tract infection occurred. There were no serious complications such as sepsis, neurological involvement, or pneumonia. There was no fatal outcome. Exacerbation of the IBD course was observed only in one patient (8.3%).

HERPES ZOSTER

Of 14 patients with HZ, 6 were male and the median age was 14 years (IQR: 13,15.5; range 9–17). In one (7.1%) patient the reported HZ was the second episode in life. In three patients (21.4%) HZ occurred in the first 6 months after diagnosis of IBD. Ten patients (71.4%) developed typical involvement of thoracic dermatomes (1–3). Four of the 14 patients (28.6%) were hospitalized (median days: 7.5; IQR: 5, 12; range 4–15 days). All patients were treated with acyclovir (for 5–14 days), in 3 patients (21.4%) antiviral therapies were administered intravenously. Seven out of 14 patients (50%) complained of pain in the affected skin area (in one case lasting 28 days) but postherpetic neuralgia defined as pain occurring after the resolution of skin lesions and lasting ≥ 3 months was not observed. Any other complications of HZ were not reported. In 3 of 14 (21.4%) patients with HZ, exacerbation of the IBD course was observed. The risk of exacerbation was not significantly higher than in the case of varicella (OR = 0.24; 95% CI: 0.02–2.78; $p = 0.317$).

DISCUSSION

Our prospective cohort of paediatric IBD patients with VZV infection included 26 children. Among them, the majority (20/26) received immunosuppressive treatment. In most patients, the course of varicella was mild i.e. with the presence of > 50 vesicles; complications were observed in 3/26 (11%). The course of HZ was mild. The relatively small number of patients is quite surprising because there is no routine vaccination against varicella in Poland. However, according to the Polish Immunization Programme since 2009 (also in the study period 2015–2019) it has been mandatory and reimbursed for immunocompromised children, including those before initiation of immunosuppressive therapy. Additionally, ECCO guidelines recommend vaccination against varicella in patients with IBD naive to the virus. Despite the recommendations, VZV vaccination is uncommonly used in clinical practice [3].

Cullen *et al*. in 2011 for the first time summarized case reports of the course of VZV infection in patients with IBD [4]. Several years have passed since then, so we decided to re-conduct and update the review of such case reports published so far. We hope that the summary in Table 2 will contribute to a better understanding of the clinical course of VZV infection and its impact on the course of IBD.

Interestingly, the course of varicella and HZ according to the cases described in our extended review was still moderate and mild, respectively. Most children recovered, but there were a few cases of varicella that resulted in death.

There are no well-planned studies assessing the severity of VZV infection in children with IBD. In a retrospective study similar to ours, assessing the course of VZV infection in children with rheumatic diseases treated with IS, Leuvenink *et al*. found complications in 18% of children [45]. In a previous observational study of 85 children with rheumatic diseases treated with etanercept and methotrexate, no complications following varicella and HZ were observed [46].

Data from adults with IBD concerning the risk of HZ during treatment with anti-TNF agents are inconsistent [47–49]. Differences in the obtained results may be a result of different study populations and different treatments. Limitations of those studies include the retrospective nature of the research. Data from case reports also differ one from another. Most patients recovered from VZV infection without complications, however, fatal outcomes were also reported. According to Winthrop *et al*., and Uchiyama *et al*., patients taking JAK inhibitors (e.g. tofacitinib) have an increased risk of developing VZV infection. Moreover, any immunosuppressive drug can potentially lead to VZV reactivation [38, 44]. Interestingly, patients may develop HZ after receiving the varicella vaccine in the past or despite receiving the recombinant zoster vaccine but the risk of such events is much lower than reactivation of wild VZV [41, 43].

We found antiviral treatment with acyclovir used in 8/12 (66.7%) patients with varicella. Among those four not treated with antiviral drugs, one patient was on IS therapy, and neither complication of varicella nor exacerbation of IBD was observed. All patients with HZ received acyclovir.

All American and European recommendations, including Polish ones, are clear and recommend the use of acyclovir in patients with varicella and HZ treated with IS drugs [3, 50, 51]. In previously published studies, patients with IBD and varicella generally received acyclovir, while a large proportion (e.g. 50%) [4] of patients with HZ was not treated with antivirals. However, it mainly

TABLE 2. Reports of varicella and herpes zoster in inflammatory bowel disease patients

Author	IBD	Age/sex	Immuno-suppression	Duration of immuno-suppression	Location	Antiviral treatment	Outcome
VZV primary infection							
Keene et al., 1978 [5]	UC	17 F	STER	12 days	Disseminated	None	Fatal
Deutsch et al., 1995 [6]	CD	15 M	6-MP	560 days	Pneumonia	Acy	Fatal
Mouzas et al., 1997 [7]	UC	19 F	STER	8 days	Disseminated	Acy	Resolved
	CD	19 F	STER, THIO	15 days	Skin	None	Resolved
	UC	23 M	STER	30 days	Skin	Acy	Resolved
	UC	6 M	STER	5 months	Skin	Acy	Resolved
Vergara et al., 2001 [8]	CD	27 M	STER, AZA	2 years	Disseminated	Acy	Fatal
Ricart et al., 2001 [9] Colombel et al., 2004 [10]	CD	25 F	AZA, IFX	56 days	Skin	Acy	Resolved
Triantafillidis et al., 2002 [11]	UC	31 M	STER	35 days	Skin	Acy	Resolved
Bernal et al., 2003 [12]	CD	40 F	THIO	2 years	Pneumonia	Acy	Resolved
Lemyze et al., 2003 [13]	CD	18 F	AZA	9 months	Pneumonia	Acy	Resolved
Leung et al., 2004 [14]	CD	26 M	STER, 6-MP, IFX	9 days	Disseminated: hepatitis	Acy	fatal
Tougeron et al., 2006 [15]	CD	33 M	STER, THIO, TNF	> 10 years 42 days	Disseminated: pneumonia, hepatitis	Acy	Resolved
Springfeld et al., 2008 [16]	CD	25 M	THIO	2 years	Disseminated: DIC, pneumonia, hepatitis	Acy + foscarnet	Fatal
Lawrance et al.,2010 [17]	CD	36 F	STER, MTX, IFX	3 months	Disseminated	N/A	N/A
	CD	21 F	STER, MTX, IFX	6 months	skin	N/A	N/A
	CD	23 M	STER, IFX	2,5 years	Disseminated	N/A	N/A
Salmon-Ceron et al., 2010 [18]	CD	Med 38 N/A	TNF*	N/A	Disseminated	Acy	Resolved
	CD	Med 38 N/A	TNF*	N/A	Disseminated	Acy	Resolved
Kunz et al., 2011 [19]	CD	12 F	STER, MTX, IFX	2 years	Skin	Valacy	Resolved
Slynko et al., 2013 [20]	UC	36 M	AZA, STER	2 years, 2 months	Disseminated: ARDS, MODS	Acy, VZIG	Resolved
Meriglier 2014 [21]	CD	29 F	ADA	14 days	Disseminated: hepatitis	Acy	Fatal
Nishimura et al., 2015 [22]	UC	16 M	STER	2 days	Skin	Acy	Resolved
Abreu et al., 2015 [23]	CD	N/A M	IFX, AZA	N/A	Disseminated: pneumonia (ARDS)	Acy	Resolved

TABLE 2. Cont.

Author	IBD	Age/sex	Immuno-suppression	Duration of immuno-suppression	Location	Antiviral treatment	Outcome
VZV reactivation							
Korelitz *et al*., 1999 [24]	CD	58	6-MP	19 days	Skin	None	N/A
	CD	70	6-MP	72 days	Skin	None	N/A
	UC	39	6-MP	60 days	Skin	None	N/A
	CD	43	6-MP	1584 days	Skin	None	N/A
	CD	28	6-MP	655 days	Skin	None	N/A
	CD	47	6-MP	186 days	Skin	None	N/A
	CD	73	6-MP	67 days	Zoster ophthalmicus	Acy	N/A
	UC	14	6-MP	120 days	Skin and CNS	None	N/A
	CD	61	6-MP	1375 days	Skin	None	N/A
	UC	70	6-MP	6794 days	Zoster ophthalmicus	Acy	N/A
	CD	66	6-MP	760 days	Skin	None	N/A
	CD	36	6-MP	19 days	Skin	Acy	N/A
Kader *et al*., 1999 [25]	UC	15 F	STER, THIO	N/A	Skin	None	N/A
Farrel *et al*., 2000 [26]	CD	N/A	IFX	N/A	Skin	None	N/A
Russel *et al*., 2001 [27]	CD	15 F	THIO, STER, TACRO	90 days	Skin	Acy	N/A
Ricart *et al*., 2001 [9]	CD	45 F	STER, THIO, IFX	28 days	Skin	Acy	N/A
Colombel *et al*., 2004 [10]	CD	17 F	STER, THIO, IFX	42 days	Skin	Acy	N/A
Baumgart *et al*., 2002 [28]	CD	45 M	STER, THIO, IFX	N/A, 510, 42	Skin	Acy	N/A
Bernal *et al*., 2003 [12]	CD	31 M	STER, THIO	4 years	Skin	Acy	N/A
	CD	32 M	THIO	730 days	Skin, oesophagus	Acy	N/A
Stephens *et al*., 2003 [29]	CD	Mean 15	IFX	N/A	Skin	Acy	N/A
	CD		IFX	N/A	Skin	Acy	N/A
	CD		IFX	N/A	Skin	Acy	N/A
Friesen *et al*., 2004 [30]	N/A	N/A	THIO, IFX	N/A	Skin	None	N/A
Shin *et al*., 2009 [31]	UC	21 M	STER	210 days	Multiple dermatomes	Acy	N/A

TABLE 2. Cont.

Author	IBD	Age/sex	Immuno-suppression	Duration of immuno-suppression	Location	Antiviral treatment	Outcome
Govani *et al*., 2010 [32]	UC	21 M	STER, THIO	55 days	Skin	N/A	N/A
	UC	53 M	STER, THIO	475 days	Skin	N/A	N/A
Monaghan *et al*., 2010 [33]	CD	65 M	STER, THIO	7 days	Pneumonia	Acy	N/A
Salmon-Ceron *et al*., 2010 [18]	CD	Med 47	TNF*	N/A	CNS	None	N/A
Cullen *et al*., 2011 [34]	CD	49 M	6-MP	> 10 years	Skin, CNS	Acy	Resolved
Cruz *et al*., 2011 [35]	CD	20 M	IFX	266 days	Skin	Valacy	Resolved
Kunz *et al*., 2011 [19]	CD	14 M	STER, 6-MP, IFX	2 years	Skin	Valacy	Resolved (3 recurrent episodes)
Ma *et al*., 2013 [36]	CD	40 M	STER, ADA	19 months, 25 months	CNS	Acy	Post-meningitis Syndrome
Wang *et al*., 2014 [37]	CD	38 M	IFX	12 infusions + 3 days	Multiple dermatomes	Gancy, Acy topically	Resolved
	CD	43 F	IFX	3 days	Multiple dermatomes	Gancy	Resolved
Winthrop *et al*., 2018 [38]	UC	65 patients age N/A, 43% F	TOF	13–1185 days	Skin – 64, CNS – 1	Acy or Valacy	Resolved – 62, Neuralgia – 3
Garbo *et al*., 2020 [39]	CD	40 M	VDZ	3 months	Skin	Acy	Resolved
Santos *et al*., 2020 [40]	CD	52 M	IFX (+ HIV infection)	9 months	Myeloradiculitis (Elsberg syndrome)	Acy	Resolved
d'Arienzo *et al*., 2020 [41]	CD	16 M	ADA	2 years	Multiple dermatomes, CNS	Acy → Valacy	Resolved
Celada-Sendino *et al*., 2023 [42]	CD	64 M	UST à VDZ	6 months, 2 doses	Skin, CNS	Acy	Resolved
Lyman *et al*., 2023 [43]	UC	72 F	STER, IFX	N/A	Zoster ophthalmicus	Acy → Valacy	Cerebral VZV vasculopathy
Uchiyama *et al*., 2024 [44]	UC	67 M	TOF	1 year	Atypical vasculitis-like HZ	Valacy	Resolved

** Not known from data whether this was anti-TNF monotherapy. Approximately 80% of the patients in this study were on combination therapy.*

6-MP – 6-mercaptopurine, Acy – acyclovir intravenously, if not said different, ADA – adalimumab, ARDS – acute respiratory distress syndrome, AZA – azathioprine, CD – Crohn's disease, CNS – central nervous system, DIC – disseminated, F – female, Gancy – ganciclovir intravenously, IBD – inflammatory bowel disease, IFX – infliximab, M – male, Med – median, MODS – multiple organ disfunction syndrome, MTX – methotrexate, N/A – information not available, STER – steroid, TACRO – tacrolimus, THIO – thiopurine (azathioprine/6-mercaptopurine), TNF – anti-tumor necrosis factor antibody, TOF – tofacitinib, UC – ulcerative colitis, UST – ustekinumab, Valacy – valacyclovir orally, VDZ – vedolizumab, VZV – varicella zoster virus

concerned patients described before 2000. In the study describing the course of VZV infection in children with rheumatic diseases receiving IS therapy, Leuvenink *et al*. found that only 12/22 children received acyclovir; the course of infection in those who did not receive acyclovir was uncomplicated [45]. The fact that not all IBD patients received acyclovir may be due to the public belief that varicella is a common and mild childhood disease and therefore can be treated at home without the need to visit a doctor. It is necessary to constantly remind, preferably in writing, about the need to treat all patients undergoing IS treatment with acyclovir in the event of a diagnosis of varicella or HZ.

Complications (superficial bacterial skin infection) were diagnosed in 2 patients with varicella and concomitant IS therapy (in 1 patient on the combo therapy and 1 patient on azathioprine) and none in patients with HZ. Neither dissemination to other organs nor fatal outcome was reported.

Previously published studies have described serious complications of VZV infection in both children and adults with IBD. Complications of varicella were much more frequently described, including pneumonia (including cases of ARDS), liver involvement, and central nervous system involvement; 5 fatal cases were also described, including two children (Table 2). Complications of HZ included involvement of the eye, central nervous system, lungs (pneumonia) and vessels (vasculitis); however, only 1 such case has been reported in children.

Also in studies describing the course of varicella in children with rheumatic diseases treated with IS, complications of varicella were more often described; no complications were observed in children with HZ [45]. According to other studies in both immunocompromised and immunocompetent children, there is a significant risk of complications. It concerns varicella [52, 53] and HZ, as well [54–56]. Hwang *et al*. reported a risk of disseminated HZ in immunocompromised children as high as 40% [57].

Exacerbation of IBD was observed in 4 patients; in 1 patient during varicella, and in 3 patients during HZ; all were on IS. Exacerbation occurred in patients on different IS regimens (thiopurine monotherapy, combo therapies, *etc*.), no specific regimen appeared to be overrepresented, though patient numbers were too small for inference.

There are very little data in the literature on the impact of VZV infection on the course of IBD. Three cases featured by Korelitz *et al.* remained in remission despite the need to discontinue the IS drug [24]. One patient reported by Nishimura *et al.* was observed to improve UC in symptoms, but in colonoscopic findings, the disease remained active [22]. When it comes to research on the impact of infection with other viruses on the course of IBD, most data come from research from the time of the last SARS-Cov-2 pandemic. Thus, Tsai *et al*., in an observational study of 90 Taiwanese patients with IBD and SARS-CoV-2, found that virus infection exacerbated gastrointestinal symptoms in almost 20% of them [58]. As we mentioned above, there are no good studies assessing the impact of viral infections on the course of IBD. So far, it has been found that noroviruses may exacerbate the course of CD and CMV – the course of UC [59].

Our study is the first to prospectively assess the course of varicella and HZ in children with IBD and their impact on IBD activity. We collected a small number of patients, but so far only a dozen cases of varicella and HZ in children with IBD have been described.

The study has several limitations. Although we had intended to include all cases VZV infections in paediatric patients with IBD from the participating centres, the sample size is small. There was a potential risk of underreporting and missed cases. The incidence of VZV/HZ among all IBD patients treated at participating centres during the study period could be only approximately estimated. The classification of skin involvement severity in varicella (< 50 vs. > 50 vesicles) was arbitrary.

CONCLUSIONS

The clinical course of VZV infection in children with IBD is variable. Severe clinical course and complications seem to be rare although a small number of reported cases does not allow for general conclusions. On the other hand, both varicella and HZ can be a risk of exacerbation of IBD. The existing recommendations of vaccination against varicella in children with IBD before initiation of immunosuppressive are not routinely used, both paediatricians and gastroenterologists should implement them into clinical practice.

DISCLOSURES

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