# Isolated intestinal manifestation of an invasive varicella zoster virus reactivation in an immunocompromised patient: a case report

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## Abstract

**Invasive varicella zoster infection is a rare but severe infectious disease, potentially affecting almost every organ system and presenting with a variety of symptoms. It is usually seen in immunocompromised patients, but also occurs in immunocompetent patients. Isolated intestinal manifestations without skin lesions are even more scarce. We present a case of a 78-year old immunocompromised man with an isolated intestinal Varicella Zoster reactivation. If not early diagnosed and treated, an invasive infection can lead to life-threatening complications. Therefore, awareness in both immunocompromised as immunocompetent patients is very important in the daily clinical practice.** (Acta gastroenterol. belg., **2024,** 87, **421-423**).

**Keywords:** varicella zoster, herpes zoster, abdominal pain, immunity, immunosuppression, corticosteroids.

## Introduction

Varicella Zoster is a DNA virus, belonging to the herpes viridae family. The primary infection is a self-limiting disease that mainly occurs in young children. The virus is transmitted through respiratory secretions, leading to the well-known disease of varicella or chicken pox. Afterwards, the virus will replicate in the lymphatic tissue and becomes dormant in the nerve roots. Reactivation of the dormant virus in the presence of any immunosuppressive condition causes a secondary infection, known as herpes zoster or shingles. It mainly appears in the elderly and in immunocompromised patients, who typically report pain and paresthesia in one or two adjacent dermatomes. Invasive varicella zoster disease however will lead to a disseminated disease, defined as a diffuse skin rash (in at least 3 dermatomes) or life-threatening visceral complications including hemorrhage, encephalitis, aseptic meningitis, pneumonitis, pancreatitis and hepatitis. (1-4)

We present a case of an atypical invasive varicella zoster virus (VZV) reactivation in an immunocompromised adult patient.

## Case history

A 78 year-old man presented to the outpatient department in November 2021 with upper abdominal pain, anorexia with post-prandial vomiting, constipation and confusion since 5 days. In July 2020 he was diagnosed with a gliobastoma multiforme, for which he was treated with neurosurgery, adjuvant chemotherapy (temozolomide), radiotherapy (up to 60 Gy/2 Gy) and long-term low dose systemic corticoids (currently methylprednisolone 8 mg, orally every other day). The last brain MRI a few months earlier showed stable disease.

Clinical examination revealed a soft but slightly distended abdomen with focal epigastric pain at palpation. The patient was hemodynamically stable, without any clinical signs of shock.

Lab results showed a moderate inflammation with a CRP-value of 56mg/L without leucocytosis (6.780/mcL). White blood cell differentiation showed leucopenia (290/mcL in acute phase, as compared to 640/mcL in 04/2021 after adjuvant chemotherapy), no neutrophilia (5.250/mcL) and no eosinophilia. Other biochemical tests such as kidney and liver function, lipase and electrolyte values were within reference levels. A computed tomography (CT) scan of the abdomen was performed and showed a thickened wall of the proximal jejunum, explaining the sub-obstructive complaints (Figure 1). Endoscopy of the upper gastrointestinal tract was planned the day after admission and revealed numerous round purplish slightly elevated target lesions, covered with mucus and localized in the duodenum and the proximal jejunum (Figure 2). The mucosa in between these lesions appeared normal. Multiple biopsies were taken in the duodenum. Immunohistochemistry (IHC) was positive for varicella zoster virus (VZV). Additional serology with positive IgG and IgM as well as a strongly positive serum polymerase chain reaction (PCR) test confirmed the diagnosis of a varicella zoster reactivation.

In consultation with the microbiology department, the patient was started on acyclovir (10 mg/kg bodyweight, every 8 hours) on the third day of admission. Also, a short course stress dose of corticosteroids was administered in-hospital, in prevention of Addison's crisis. After five days of intravenous antiviral treatment, a relook endoscopy of the upper gastrointestinal tract showed a full resolution of the mucosal lesions. Simultaneously, a quick clinical and biochemical improvement was noted. The patient was

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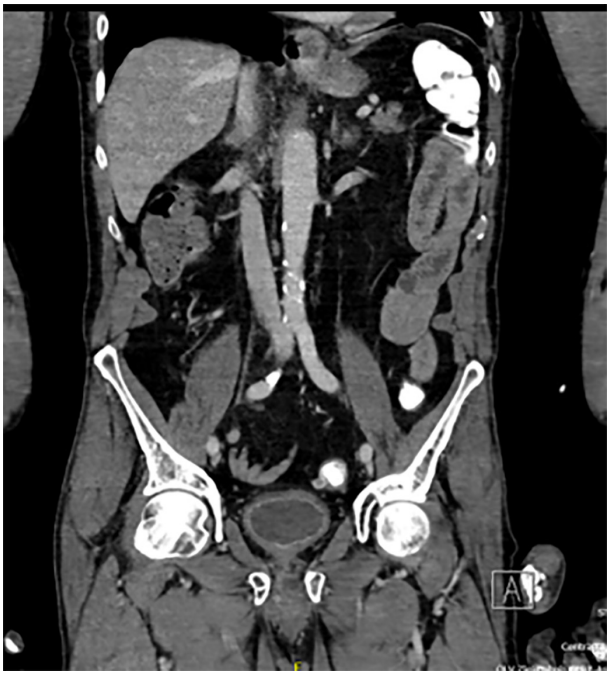

Figure 1. — Computed tomography (CT) scan of the abdomen at admission showed focal wall thickening of the proximal jejunum.

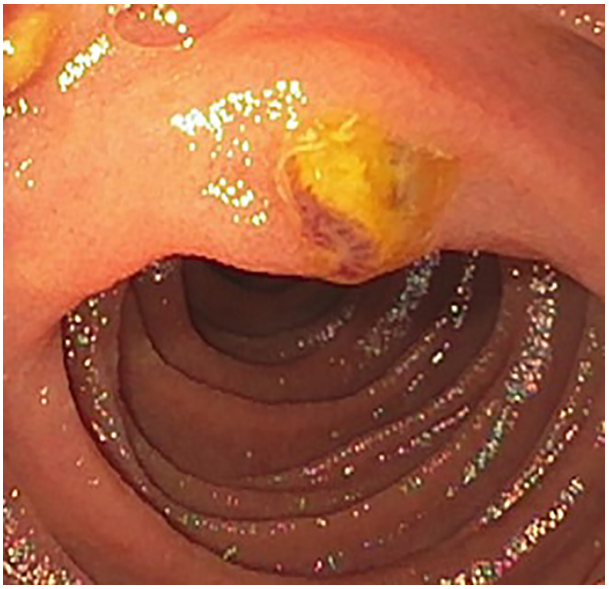

Figure 2. — Round purplish slightly elevated target lesions, covered with mucus in an intestinal Varicella Zoster infection, located in the duodenum D2.

discharged and oral treatment with acyclovir (800mg 5 times daily) was continued for a total duration of 14 days.

Because involvement of the central nervous system was feared, the neurologist was consulted and suggested close observation without lumbar puncture. Fortunately the patient's confusion rapidly improved after starting treatment. So we only can presume a possible concomitant varicella infection of the central nervous system, without any microbiological or cytological proof.

## Discussion

Disseminated varicella zoster virus (VZV) infection is a rare (2% in general population) but severe infectious disease that presents with a variety of symptoms (1-6). It can affect almost every organ system and lead to life-threatening complications including hemorrhage (e.g. intracranial hemorrhage, hemorrhagic gastritis, adrenal hemorrhage, splenic rupture, hemorrhagic pulmonary edema), encephalitis, aseptic meningitis, pneumonitis, pancreatitis and hepatitis (1-6). The typical vesicular rash is the leading symptom in up to 90% of patients and is sometimes complicated by hemorrhage of purulence (3). The absence of apparent skin lesions, like in this case report, is infrequently described and can lead to a delay of correct diagnosis and treatment (7). For confirmation of diagnosis, immunohistochemical staining of biopsy specimens for varicella zoster virus as well as a PCR assay are needed (1).

The disseminated VZV is mostly seen in immuno-compromised patients (lifetime prevalence 15-30%), but it also occurs in immunocompetent patients for example after recent steroid use either long- or short-term (1-4). The case report by Mohaghegh et al. described for example an atypical disseminated VZV in a female patient with critical COVID-19 infection, treated with dexamethasone (4). However the use of systemic steroids is a well-known risk factor for herpes reactivation, less is known about the steroid dose and duration at risk. In a cohort study of patients with several oncological and inflammatory conditions (asthma, autoimmune disease), the hazard ratio for herpes zoster was 2.37. A recent published guideline, discussing herpes reactivation in cancer patients, stated that dosages of at least 10 mg prednisolone equivalent (PEQ) for a minimum of 14 days increase the risk of VZV reactivation (8). Particular in our case, the patient was treated with a low and non-immunosuppressive steroid dose on the moment of the herpes reactivation. The patient was treated earlier with temozolomide, known to increase the risk for HSV encephalitis when concomitantly used with dexamethasone. Moreover the impact on lymphocyte function of temozolomide, steroids and radiation therapy, like in this case report, can last for several months (8).

There is no evidence for the routine use of antiviral prophylaxis in the specific setting of our patient, nor it is generally recommended for patients with solid tumors. However, the guidelines of Henze et al. suggest to consider prophylaxis in patients treated with high-dose and long term steroid regimens, particularly in combination with other immunosuppressive agents. Most evidence about prophylaxis is gathered in the setting of transplantation (either solid organ or stem cell transplant) where a dose of 400mg has been shown effective (8).

Isolated intestinal manifestations of an invasive VZV, as described in this case report, are scarce. Only

a handful of case reports have been published over the last decades. The mortality rate is very high (46-55%) (3). The case report by Anaya-Prado et al. described a rare case of paralytic ileus and Ogilvie's syndrome, secondary to segmental paresis of the small intestine due to visceral neuropathy by VZV. Conservative measures together with antiviral therapy are the mainstay of treatment and unnecessary surgery is to be avoided (5). Serris et al. described a case of hemorrhagic shock due to hemorrhagic gastritis, caused by a VZV reactivation in a female patient with an underlying low-grade lymphoid malignancy. The ulcero-necrotic mucous lesions can be apparent anywhere in the gastro-intestinal tract. They are mostly found in the stomach and more seldom in the esophagus, duodenum, small bowel and the colon. Those mucous lesions can complicate with bleeding. The bleeding ceased after intravenous antiviral therapy was started (6).

Both uncomplicated and complicated Varicella Zoster reactivations in the immunocompromised setting require intravenous treatment with acyclovir at a dose regimen of 10mg/kg bodyweight every 8 hours. Immunocompetent patients with a disseminated VZV should also be admitted for intravenous therapy.

Thus if not early diagnosed and adequately treated, an invasive varicella zoster infection can lead to life-threatening complications. Even if skin lesions are absent, the gastro-intestinal tract can be solitary affected. Therefore, awareness in both immunocompromised and immunocompetent patients is important in the daily clinical practice. (1-3)

**Conflict of interest**

The authors have no relevant conflicts of interest to disclose.

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