

[ ORIGINAL ARTICLE ]

# The Usefulness of Video Capsule Endoscopy in Evaluating Gastrointestinal Manifestations of Immunoglobulin A Vasculitis

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## Abstract:

**Objective** Immunoglobulin (Ig) A vasculitis (IgAV) is a systemic vasculitis characterized by purpura and gastrointestinal involvement showing abdominal pain that usually occurs after the emergence of purpura. Criteria for evaluating gastrointestinal manifestations of IgAV are unavailable at present, so we conducted a study to investigate the usefulness of video capsule endoscopy (VCE) for detecting gastrointestinal manifestations of IgAV.

**Methods** The clinical data of 10 patients who underwent VCE for IgAV at our hospital from 2012 to 2017 were collected. Nine patients underwent esophagogastroduodenoscopy, and five underwent colonoscopy. We compared the endoscopic severity determined by VCE to the findings of esophagogastroduodenoscopy and colonoscopy.

**Results** The rates of positive findings of esophagogastroduodenoscopy, VCE, and colonoscopy were 56%, 100%, and 80%, respectively. In 70% of cases, the most severe gastrointestinal findings were detected by VCE. VCE was performed on average 16.8 days after the emergence of purpura, and in 8 of 10 patients, its result triggered the initiation of steroid therapy or the control of the steroid dose.

**Conclusion** VCE is very useful for confirming gastrointestinal involvement in IgAV and may be used to determine the timing of steroid therapy initiation. We recommend performing VCE when IgAV is suspected in patients with gastrointestinal symptoms.

**Key words:** immunoglobulin A vasculitis, endoscopic findings, video capsule endoscopy, gastrointestinal manifestations, steroid therapy

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## Introduction

Immunoglobulin (Ig) A vasculitis (IgAV) (formally known as Henoch-Schönlein purpura) is a small-vessel vasculitis mediated by type III hypersensitivity. IgA-mediated immune complexes are deposited on the walls of vessels of the skin, kidneys, gastrointestinal tract and joints, leading to skin rashes, renal disease, gastrointestinal involvement, and ar-

thritis. IgAV usually affects children between 3 and 15 years old, while it is less common in adults (1). Calvo-Río et al. reported that the most frequent precipitating events are a previous infection (38%), usually of the upper respiratory tract, and/or drug intake (18.5%) shortly before the onset of the vasculitis (2).

Gastrointestinal involvement in the form of abdominal pain, nausea, vomiting, or bleeding occurs in 10-85% of patients (2-13). In this case series, we describe our experience

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**Table 1. Clinical and Pathologic Features of Our Ten Cases.**

Case No.	Age/ Gender	Gastrointestinal symptoms	Days from skin rashes*	Pathological diagnosis : LCV		Treatment
				Skin	Gastrointestine	
1	81 /F	Abdominal pain, melena	Prior	LCV	ND	Prednisolone, factor XIII
2	17/M	Abdominal pain, nausea	At the same time	ND	NA	Prednisolone
3	47 /M	Abdominal pain	1 day	LCV	LCV	Prednisolone
4	14 /F	Abdominal pain, melena	2 days	LCV	ND	Prednisolone
5	40/M	Abdominal pain	3 days	LCV	ND	Prednisolone
6	46/M	Abdominal pain	7 days	LCV	ND	Prednisolone
7	51 /F	Abdominal pain, melena	27 days	LCV	LCV	Prednisolone
8	38/F	Abdominal pain	One month	LCV	NA	Prednisolone
9	61/F	No symptom	-	LCV	NA	Prednisolone
10	57/M	No symptom	-	ND	NA	Prednisolone

\*: Days to emergence of gastrointestinal symptoms from skin rashes.

M: male, F: female, LCV: leukocytoclastic vasculitis, ND: not detected, NA: not available

with the evaluation of gastrointestinal manifestations of IgAV, including the assessment of small intestinal lesions by video capsule endoscopy (VCE).

## Materials and Methods

The clinical data of 10 patients were collected. All patients underwent VCE for IgAV at the University of Fukui Hospital from May 2012 to May 2017. Five patients were examined using a second-generation capsule endoscope (PillCam<sup>®</sup> SB2; Medtronic, Dublin, Ireland), and the other 5 were examined using a third-generation capsule endoscope (PillCam<sup>®</sup> SB3; Medtronic). Images of capsule endoscopy were analyzed using the RAPID<sup>®</sup> software program, version 6.5 or 8.0 (Medtronic, Dublin, Ireland). Most patients underwent esophagogastroduodenoscopy and colonoscopy, and endoscopic findings were graded according to the following scale developed specifically for the purpose of this study: grade - (no apparent findings), grade + (some erosion), grade ++ (severe ulceration).

Written informed consent was obtained from all subjects or their guardians.

## Results

### Summary of the 10 cases

The clinical data are summarized in Table 1 (5 women, 5 men; mean age, 45.2 years). Gastrointestinal symptoms, such as abdominal pain, nausea, and melena, were present in 8 cases (80%). These symptoms were often preceded by the emergence of skin rashes, which on average lasted 8.6 days. In two cases, abdominal pain appeared a month after the start of skin rashes. However, the time interval between the emergence of rashes and gastrointestinal symptoms was not related to other clinical factors, such as disease severity or treatment outcome. The histological assessment of purpuric skin lesions showed leukocytoclastic vasculitis (LCV) in 8 cases (80%). Biopsies taken from the gastrointestinal tract

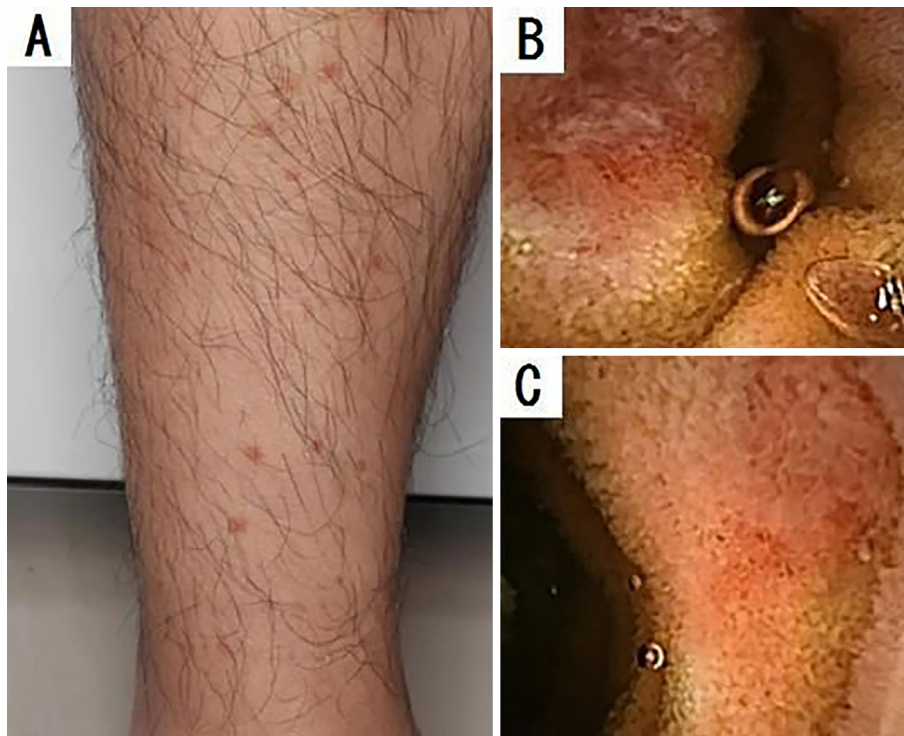
revealed LCV in 2 of 6 cases (33%). Prednisolone was administered in all 10 cases (100%), leading to clinical improvement in all cases except for case 1. In this patient, IgAV and renal failure occurred after treatment for hepatocellular carcinoma. Descriptions of three representative cases (2, 6, and 10) are presented below.

### Case 2

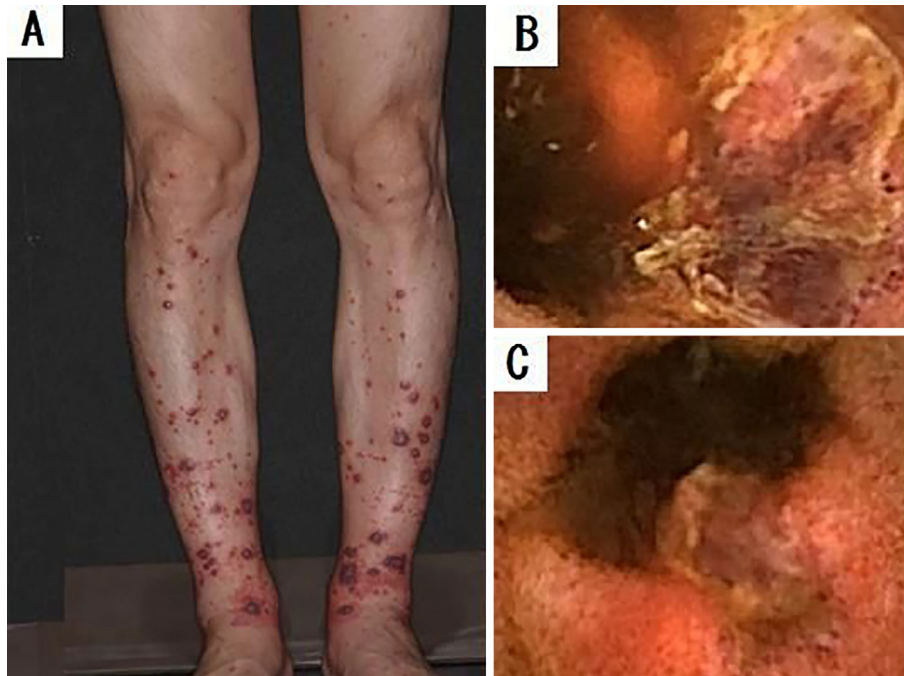
In January 2017, a 17-year-old man experienced purpura, abdominal pain, and nausea. Laboratory tests showed a normal white blood cell count, hemoglobin level, platelet count, coagulation time, serum IgA level, and coagulation factor XIII activity. A urinalysis revealed proteinuria. On VCE, ecchymotic lesions and edema were particularly common in the proximal jejunum. Circular ulcerations were also detected (Fig. 1). Skin biopsies did not reveal LCV. One week after VCE, oral prednisolone was prescribed at a dose of 0.8 mg/kg/day. The patient's abdominal pain abated promptly. VCE performed one month after the beginning of prednisolone administration demonstrated an improvement in the ecchymotic lesions and edema.

### Case 6

In July 2012, a 46-year-old man experienced abdominal pain. One week prior to abdominal pain occurrence, he developed purpura, which had been preceded by about four days by sore throat. Laboratory tests detected a normal white blood cell count, hemoglobin level, platelet count, serum IgA level, and coagulation factor XIII activity. The coagulation time was slightly prolonged. A urinalysis revealed proteinuria. Esophagogastroduodenoscopy showed geographical ulcers in the duodenum. Colonoscopy showed hyperemia in the entire large intestine. Erosion and ulcers were noted in the terminal ileum. VCE revealed erythema, erosion, and ulcers in the entire small intestine, which were particularly severe in the terminal ileum (Fig. 2). Skin biopsies revealed LCV. In contrast, an endoscopic duodenal biopsy did not show LCV. Oral prednisolone at a dose of 1.2 mg/kg/day was started, and VCE was performed 11 days af-



**Figure 1.** A photograph of the leg purpura (A) and video capsule endoscopy (VCE) images (B and C) of case 2. VCE was performed 8 days after the occurrence of purpura. The VCE images before treatment show circular ulcerations in the small bowel. These findings were the most severe after those in case 6. We graded these findings as grade++.



**Figure 2.** A photograph of the leg purpura (A) and video capsule endoscopy (VCE) images (B and C) of case 6. VCE was performed 19 days after the occurrence of purpura. VCE images show circular ulcerations in the small bowel. These findings were the most severe among all of the cases in this study. We graded these findings as grade++.



**Figure 3.** A photograph of the leg purpura (A) and video capsule endoscopy (VCE) images (B and C) of case 10. VCE was performed two months after the occurrence of purpura. VCE images show areas of circumferential redness and edema in the jejunum. We graded these findings as grade+.

**Table 2.** The Lesion Location and Severity of Each Endoscopic Findings.

Case No.	Esophagogastroduodenoscopy		Capsule Endoscopy		Colonoscopy
	Stomach	Duodenum	Jejunum	Ileum	Large intestine
1	+	+	+	+	++
2	N.A.	N.A.	++	+	N.A.
3	-	++	+	+	+
4	-	-	+	++	-
5	+	+	++	+	N.A.
6	+	+	+	++	+
7	+	+	+	+	++
8	-	-	+	+	N.A.
9	-	-	+	+	N.A.
10	-	-	+	+	N.A.
Rates of positive findings	5/9 (56%)		10/10 (100%)		4/5 (80%)
Rates of most severe findings*	1/9 (11%)		7/10 (70%)		2/5 (40%)

\*: For example, most severe endoscopic findings in each patient were detected by VCE in seven patients of all ten cases (70%).

Endoscopic findings were graded according to the following scale: grade - (no apparent findings), grade+(some erosion), grade++(severe ulceration). N.A.: not available

ter that. The patient's abdominal pain abated promptly.

### Case 10

In February 2017, a 57-year-old man was admitted to the hospital because of palpable purpura, which had been observed for 2 months. Laboratory testing revealed a normal white blood cell count, hemoglobin level, platelet count, and serum IgA level. Coagulation factor XIII activity was not determined. The urinalysis results were normal.

Esophagogastroduodenoscopy detected no signs of IgAV. Although the patient did not report any abdominal pain, VCE was performed to assess the gastrointestinal involvement. Hyperemia and erosion of the entire small intestine were detected (Fig. 3). Skin biopsies did not reveal LCV. Oral prednisolone at a dose of 0.3 mg/kg/day was started 5 days after VCE. The purpura abated within a few days.

Table 2 lists the lesion locations and severity of gastrointestinal involvement, graded as described in the Methods.

The rates of positive findings by esophagogastroduodenoscopy, VCE, and colonoscopy were 56% (5/9 cases), 100% (10/10 cases), and 80% (4/5 cases), respectively. Importantly, in 70% (7/10) of the cases, VCE revealed the most severe findings. VCE was performed on average 16.8 days after the emergence of purpura, and in 80% of cases (8/10), those results triggered the initiation of steroid therapy or control of the steroid dose.

## Discussion

Gastrointestinal involvement in IgAV is common, occurring in 10-85% of cases (2-13). Stancanelli et al. reported that gastrointestinal symptoms consist of abdominal pain (86%), occult blood loss (66%), vomiting (40%), massive colorectal bleeding (20%), and diarrhea (20%) (9). IgAV is more frequent in children than in adults (1, 5, 13, 14). As purpura often precedes gastrointestinal symptoms (in 70-97% of cases) (6, 8, 10, 12, 13), pediatricians and dermatologists usually diagnose IgAV early based on characteristic skin lesions. The timing of steroid therapy therefore needs to be determined while considering the risks and benefits in each case. However, no clear-cut criteria have yet been established, so the subsequent emergence of gastrointestinal symptoms may serve as an indicator for starting steroid therapy.

According to Esaki et al. (5), multiple irregular ulcers in the second part of the duodenum are likely characteristic of duodenal involvement in IgAV, suggesting that gastrointestinal symptoms of IgAV can be generally detected by esophagogastroduodenoscopy. Typical computed tomography (CT) findings include multifocal bowel thickening with mucosal hyperenhancement, the presence of skip areas, and mesenteric vascular engorgement with the involvement of unusual sites, like the stomach, duodenum, and rectum (8, 13). CT and magnetic resonance imaging (MRI) may be able to detect severe gastrointestinal involvement, such as marked thickening of intestinal wall or findings of intestinal perforation. Unfortunately, such intestinal lesions are very small and difficult to detect on CT and MRI in patients in the early phase of IgAV. However, the lesions can be easily and noninvasively detected using VCE. It is therefore better to perform VCE for the detection of mucosal lesions and then perform complementary CT or MRI to evaluate the severity of the gastrointestinal involvement of IgAV. Although the small intestine is considered to be the most frequently affected site, and some reports have detected small bowel lesions in IgAV (4-9, 11, 12, 14-17), few studies have evaluated the entire small bowel in patients with IgAV (11). In the present study, gastrointestinal manifestations of IgAV, including the results of the examination of the entire small intestine by VCE, were retrospectively analyzed in 10 cases.

Low-invasive and fast examination procedures, such as VCE, are instrumental because IgAV primarily affects children, and manifestations become severe in some patients because of inadequate treatment. Abdominal pain typically ap-

pears within seven days after the occurrence of skin rashes unless steroid therapy is started. However, the timing of the appearance of gastrointestinal symptoms after skin rashes does not seem to have any relation to the endoscopic severity, response to therapy, or other clinical findings. Regarding the indication of VCE, we recommend VCE be performed for all IgAV patients initially, not merely in those showing negative findings on esophagogastroduodenoscopy and colonoscopy. This is because, in our series, the most severe findings were observed in the jejunum and ileum in 7 of all 10 cases (70%). Furthermore, VCE is thought to be less invasive and easier to perform than esophagogastroduodenoscopy and colonoscopy. In that sense, this approach is particularly useful for pediatric patients with IgAV. However, we would like to emphasize the fact that even non-symptomatic patients need to receive VCE in order to detect occult and tiny mucosal lesions. In our series, two patients were judged to require steroid therapy after the detection of intestinal involvement using VCE, even though they had no abdominal symptoms at all. Therefore, in patients with IgAV, it may be useful to perform VCE before the emergence of abdominal symptom for the early diagnosis or decision-making concerning steroid therapy.

In the present study, VCE proved to be very useful for confirming gastrointestinal involvement in IgAV, and its findings helped determine the timing of steroid therapy initiation. Appropriate steroid therapy should be conducted in patients with IgAV accompanied by gastrointestinal manifestations, renal involvement, and severe skin findings. The initial amount and method of administration (oral or intravenous) of prednisolone is usually determined based on the severity of those manifestations and their involvement in kidney and gastrointestinal tract. We regard VCE as an excellent device in evaluating gastrointestinal manifestations of IgAV objectively. The oral administration of 0.5 mg/kg prednisolone will be sufficiently effective in cases with only erosions and ulcers. However, intravenous steroid pulse therapy will be necessary for patients with deep, huge ulcers accompanied by bleeding and/or massive edema of the intestinal wall. In addition, VCE can also be used to evaluate the effect of steroid therapy.

As shown in Table 1, the rate of LCV in the biopsies taken from the gastrointestinal system was very low (33%) compared to that based on skin biopsies (80%). This may be attributable to sampling error, as typical histologic findings of vasculitis are not observed only at the site of the lesion, such as erosion or an ulcer base. Alternatively, the timing of sampling may be responsible. LCV tends to be easily detected in the acute stage of IgAV; however, the timing of the endoscopic examination varied from case to case, and some samples may have been taken at the granulation or healing scar stage.

Finally, we reviewed the previously published literature, which described a total of 35 patients with IgAV in whom VCE was performed to evaluate the gastrointestinal manifestations (Table 3). These corresponding studies were seven

**Table 3. Review of Previously Reported Cases.**

Published year	Number of cases	Gastrointestinal involvement	Endoscopic findings of small intestine	Treatment	Reference no.
2005	1	Abdominal pain	Redness, swelling, ulcers	N.A.	16
2006	1	Abdominal pain, nausea, vomiting, melena	Purpuric mucosal lesions, erosion, ulcers	Methylprednisolone, cyclophosphamide	9
2006	1	Abdominal pain, hematochezia	Ulcers	Prednisolone, cyclophosphamide, mycophenolate mofetil	14
2010	1	Abdominal pain, melena	Ulcers	Surgical resection, steroid pulse therapy	1
2011	5	N.A.	Patechiae, redness, erosions, ulcers	N.A.	17
2013	1	Abdominal pain, hematochezia	Ulcers	Conservative	7
2013	1	Abdominal pain, melena, diarrhea	Redness, erosions	Prednisolone	18
2014	2	Abdominal pain, melena	Erythema, ulcers	Prednisolone	15
2015	8	Abdominal pain	Ulcer, erosion, erythema	Steroid pulse therapy, prednisolone, cyclosporin	11
2015	13	N.A.	Erythema	N.A.	19
2015	1	Hematochezia, diarrhea	Ulcers	Prednisolone	20

N.A.: not available

case reports and four case series (1, 7, 9, 11, 14-20). Although these papers certainly suggest that VCE can detect small bowel lesions characteristic of IgAV, none compared the endoscopic severity as assessed by VCE to the findings of esophagogastroduodenoscopy and colonoscopy. Furthermore, the time interval between the appearance of skin rashes and gastrointestinal symptoms was not mentioned.

In conclusion, the present study was the first to demonstrate the usefulness of VCE for evaluating the gastrointestinal manifestations of IgAV. We strongly recommend performing VCE in patients with gastrointestinal symptoms when IgAV is suspected.

**The authors state that they have no Conflict of Interest (COI).**

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