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Case Report

Endoscopy and the management of IgA vasculitis: a clinical analysis of 261 pediatric immunoglobulin A (IgA) vasculitis cases with gastrointestinal involvement and endoscopic examinations of 69 patients

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Abstract: Objective: To analyze the gastrointestinal manifestation of IgA vasculitis in pediatric patients, including clinical and endoscopic features. Methods: We retrospectively reviewed 261 pediatric IgA vasculitis patients with gastrointestinal involvement who were admitted to our hospital between January 2010 and December 2011 and analyzed their medical records, including their clinical presentations, laboratory data, endoscopic findings and treatment strategies. Results: The study group consisted of 261 children with a boy to girl ratio of 1.6:1, and with a mean age of 6.8±2.6 years. Gastrointestinal symptoms were the initial manifestations in 101 cases (38.7%), while the others complained of these symptoms either during or after the purpuric phase. All IgA vasculitis children (100%) had abdominal pain, and 139 (53.3%) had vomiting, 73 (28.0%) had melena, 42 (16.1%) had hematemesis, and 7 cases (2.7%) had diarrhea. More than half (155 cases, 59.4%) had arthritis/arthralgia and 103 patients (39.5%) had renal involvement. The main endoscopic findings from 69 patients included mucosal congestion, redness, petechia, multiple ulcers and nodular change. The average steroid dosage used during their hospitalization for the patients who underwent endoscopic examination was significantly higher than those who did not undergo an endoscopy ($P < 0.05$). Conclusions: IgA vasculitis may present with acute abdomen symptoms with or even without typical skin manifestations, and endoscopy could enable an earlier diagnosis and better management of IgA vasculitis cases.

Keywords: Immunoglobulin A (IgA) vasculitis, clinical manifestation, endoscopy, corticosteroids

Introduction

Immunoglobulin A (IgA) vasculitis (IgAV), formerly Henoch-Schonlein Purpura, is the most common systemic vasculitis in childhood. IgAV is mediated by immune deposits (typically with IgA1), resulting in inflammation and necrosis of the wall of small and medium-sized blood vessels with the extravasation of erythrocytes, infiltration of tissue with neutrophils, and deposition of nuclear fragments from degenerating neutrophils. The estimated annual incidence of IgAV in China is 14.06 cases per 100,000 children [1] with variations possibly due to changes in social, economic, health, and environmental conditions [2].

The diagnostic criteria for IgAV include palpable purpura without thrombocytopenia with at least one other manifestation: abdominal pain, IgA deposition, arthritis or arthralgia, or renal involvement. Abdominal pain, associated with nausea, vomiting, or bleeding, occurs in 51-74% of patients [3-6], with 42% having severe pain [7]. In 12-19% of cases, abdominal pain was the presenting symptom [4, 6]. The pain is characteristically colicky and localized to the periumbilical and epigastric regions. It worsens after meals similar to bowel angina or ischemia [3].

So, atypical IgAV cases are liable to be misdiagnosed and mistreated. With the incidence increasing, the investigation of every potential case in these patients and expanding our knowledge about IgAV with gastrointestinal involvement are important for the successful management of IgAV. With this aim, we retro-

spectively reviewed the clinical characteristics, endoscopic features and treatment in IgAV patients with gastrointestinal involvement.

Materials and methods

A total of 416 IgAV patients were admitted to our hospital between January 2010 and December 2011. Among these patients, only those with IgAV with abdominal pain were considered for inclusion in this study, and there were 261 cases. The criteria for IgAV diagnosis was made according to guidelines established by the European League Against Rheumatism (ULAR), Pediatric Rheumatology International Trials Organization (PRINTO), and the Pediatric Rheumatology European Society (PRES) [8]. All the cases developed skin purpura and abdominal pain, and some also had acute arthritis, acute arthralgia, or renal involvement. There were 101 cases whose abdominal pain occurred prior to the appearance of the skin purpura. Their medical records, including information about their ages, sex, average hospital stays, clinical presentations, laboratory data, gastroscopy findings, and treatment protocols, were reviewed retrospectively. All patients underwent laboratory tests such as antinuclear, anti-DNA, anti-ENA antibodies, routine blood, C-reactive protein, urine tests, fecal occult blood, coagulation profile, IgA, IgG, IgM, IgE, D-dimer, and so on. A gastroscopy was done on 69 (26.4%) of the patients with signs of gastrointestinal bleeding and, among these, 10 cases were further examined with a colonoscopy as considered necessary by the attending physicians. The study was approved by the Ethics Committee at the First affiliated hospital of Wenzhou Medical University.

Statistical analysis

Continuous variables were expressed as the mean ± standard deviation (SD) or median (interquartile range). Categorical variables were expressed as percentages. Data on the average hormone dosage for patients who, during hospitalization, did or did not undergo endoscopy were compared using an independent *t*-test. All statistical analyses were performed using SPSS 16.0. A P value < 0.05 was considered statistically significant. We used an independent *t*-test.

Results

Demographic characteristics of patients

The study group consisted of 261 children, 161 boys (61.7%) and 100 girls (38.3%), and the ratio of boys to girls was 1.6:1. The minimum age was 2.75 years old, and the maximum age was 17 years and 9 months, with a mean age of 6.8±2.6 years. The shortest hospital stay was 2 days, the longest was 77 days, and the average hospital stay was 11.3±7.6 days (**Table 1**).

Clinical features

Although all children selected for this study had typical skin manifestations such as petechiae and ecchymosis during the whole course of IgAV, 101 cases (38.7%) complained of gastrointestinal discomfort as the initial manifestations while others had these symptoms either during or after the purpuric phase. As listed in **Table 1**, all the 261 cases had various gastrointestinal symptoms, including abdominal pain (100%), vomiting (53.3%), melena/hematochezia (28%), hematemesis (16.1%), diarrhea on a few occasions (2.7%), and headache and dizziness in one case (0.4%). Other major manifestations besides skin and gastrointestinal indications were arthritis (59.4%) and kidney damage (39.5%, 103 cases). Among the 79 cases with a potential trigger events before IgAV onset, the majority (69 cases) had respiratory tract infections while the rest had consumption of seafood (7 cases), drug withdrawal (2 cases), or vaccination (1 case).

Laboratory test findings

At the time of diagnosis, 172 cases (65.9%) of the patients had leukocytosis or leukopenia and 32 cases (12.3%) had anemia. D-dimer was found increased in 199 cases (76.2%). CRP levels increased in 72 cases (27.6%). IgA, IgG, IgE and IgM were increased in 131 (50.2%), 67 (25.7%), 59 (22.6%) and 31 case (11.9%), respectively. Among the 103 cases (39.5%) had normal renal function but abnormal urine, 68 (26.1%) had both mild proteinuria and hematuria, 22 (8.4%) had microscopic isolated hematuria, and 13 patients (5.0%) had isolated mild proteinuria. Occult blood was positive in the stools of 129 cases (49.4%) (**Table 2**). Among the 69 patients with upper respiratory tract infections, a throat swab culture yielded beta-

Table 1. Clinical manifestations of the patients

Clinical manifestation	No. of patients/Percentage (%)
Age distribution (min/max) mean ± SD	(2 years and three quarters/17 years and three quarters) 6.8±2.6 years
Gender male to Female (ratio)	161:100 (1.6:1)
Average length of hospital stay (min/max) mean ± SD	(2 days/77 days) (11.3±7.6) days
GI manifestation	
Abdominal pain	261 (100)
Vomiting	139 (53.3)
Melena/hematochezia	73 (28.0)
Hematemesis	42 (16.1)
Diarrhea	7 (2.7)
Arthritis	155 (59.4)
Kidney damage	103 (39.5)
Headache and dizziness	1 (0.4)
Head facial swelling	1 (0.4)
Scrotal edema	1 (0.4)
Complications	
Intussusception	3 (1.1)
Segmental bowel necrosis	1 (0.4)
Dynamic Intestinal obstruction	1 (0.4)

Table 2. The patients' laboratory tests

Laboratory tests	No. of patients Percentage (%)
Increased D-dimer	199 (76.2)
leukocytosis or leukopenia	172 (65.9)
Increased IgA	131 (50.2)
Occult blood	129 (49.4)
Abnormal urine routine	103 (39.5)
Increased CRP	72 (27.6)
Proteinuria and hematuria	68 (26.1)
Increased IgG	67 (25.7)
Increased IgE	59 (22.6)
Anemia	32 (12.3)
Increased IgM	31 (11.9)
Isolated hematuria	22 (8.4)
Isolated mild proteinuria	13 (5)

hemolytic streptococci and *staphylococcus aureus* in 7 (2.7%) and 3 (1.2%) cases, respectively. Renal biopsies were performed in 17 children (6.5%), with mesangial proliferation in 13 children and focal segmental in 4 children. The platelet counts and coagulation profiles were normal. The results of antinuclear antibody, anti-DNA antibodies, and anti-ENA antibody tests were negative.

Gastroscopic, colonoscopy features and other examinations

To investigate the causes of obvious bleeding (73 cases with melena/hematochezia and 42 cases with hematemesis, 93 cases that did not occur concomitantly in the same patient) from the gastrointestinal tract or other sources, 69 patients were further examined by endoscopy. The endoscopic findings included redness, swelling, petechiae, submucosal hemorrhage, purpura, erosions, multiple ulcers and nodular changes (**Table 3**). The second portion of the duodenum was the most frequently involved location in the upper GI tract (51 cases), and damage in this area was also the most serious (**Figure 1**). The frequency involved with IgAV in other locations included 39 in the duodenal bulb, 39 in the gastric antrum, 3 in the gastric fundus and 3 in the gastric body. Colonoscopic examination was abnormal in 9 of the 10 tested patients (**Table 3**). The lesions in the colonoscopies appeared similar to those in the upper GI tract, but the distribution was different. Erythema, edema, petechia, and multiple ulcers were common in the colon. Only one patient had petechia in the ileum.

For the purpose of differential diagnosis, 247 cases (94.6%) went through a routine ultrasound examination of the abdomen. Positive findings included renal enlargement, intraperitoneal fluid collections, bowel wall thickening, abdominal lymph node enlargement, broadening of the renal pelvis, intussusception, polycystic kidney and scrotal edema. 23 cases (8.8%) had bowel wall thickening, edema or

Table 3. 69 patients had an endoscopic examination, including 10 patients who had a colonoscopic examination. The performance for the different levels of gastrointestinal mucosa under gastroscopy and enteroscopy changed. One patient could have more than one lesion

Lesions and locations	Gastroscopy no. of 69 patients Percentage (%)	Colonoscopy no. of 10 patients Percentage (%)
Erythema\edema\petechia in Antral mucosa and/or gastric fundus and/or in gastric body	39 (56.5)	/
Erythema\edema\petechia and Nodular change in Duodenal bulb and duodenal descending part	39 (56.5)	/
Nodular change in duodenal descending part	16 (23.2)	/
Ulcers in duodenum	12 (17.4)	/
Erythema\edema\petechia in Rectum, sigmoid colon, descending colon	/	9 (90)
Ulcers in Rectum, sigmoid colon, descending colon	/	7 (70)
Erythema\edema\petechia in ileum	/	1 (10)

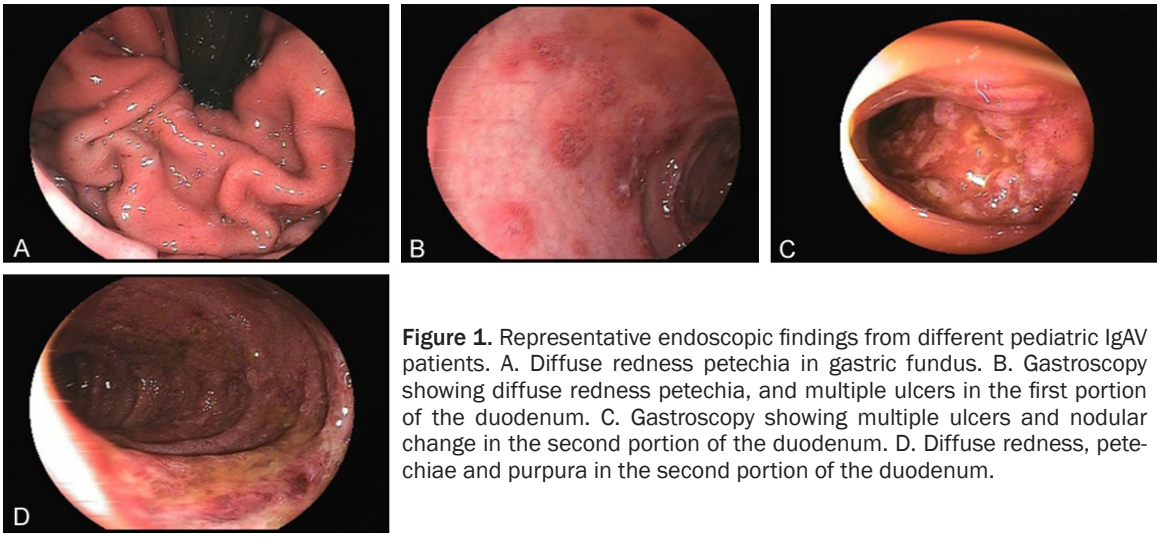

Figure 1. Representative endoscopic findings from different pediatric IgAV patients. A. Diffuse redness petechia in gastric fundus. B. Gastroscopy showing diffuse redness petechia, and multiple ulcers in the first portion of the duodenum. C. Gastroscopy showing multiple ulcers and nodular change in the second portion of the duodenum. D. Diffuse redness, petechiae and purpura in the second portion of the duodenum.

intraperitoneal fluid collections, and 25 cases (10.1%) had renal enlargement, and one patient had scrotal edema. Intussusception was detected in 3 cases (1.2%). Dilatation and hypomotility were observed by X-ray examination in one patient (0.4%). CT scans in 2 patients (0.8%) showed multifocal bowel wall thickening with skipped segments, mainly involving the jejunum and ileum. One patient had headache but a cranial CT examination and a lumbar puncture showed no abnormalities (**Table 4**).

Misdiagnosis

9 cases (3.6%) were misdiagnosed as gastroenteritis, and 3 (1.2%) cases as acute appendicitis.

Complications

3 cases (1.2%) with intussusception, and 1 case (0.4%) were found with segmental bowel necrosis or dynamic intestinal obstruction, respectively.

Treatment

All patients were treated with corticosteroids, such as methylprednisolone at 1-2 mg/kg per day as suggested by Joel et al. [9], but patients with severe gastrointestinal symptoms were given higher doses according to the clinical manifestation and endoscopic performance. The average hormone dosage (as high as 3.37 $mg.kg^{-1}.d^{-1}$) during hospitalization for those who underwent an endoscopy were statistically higher than those who did not undergo an endoscopy (as low as 1.47 $mg.kg^{-1}.d^{-1}$) (**Figure 2**). The patients who had complications were treated with operations and corticosteroids. The children misdiagnosed with IgAV were treated with antibiotics and cimetidine but with little symptom relief. One patient misdiagnosed with appendicitis underwent surgical treatment

Table 4. 247 ultrasound examinations of the abdomen, 5 CT scan, 1 X-ray

Findings	No. Of patient Percentage (%)
Ultrasound examination of the abdomen	247
Positive finding	52 (21.1)
Renal enlargement	25 (10.1)
Intraperitoneal fluid collections	17 (6.9)
Bowel wall thickening	10 (4.0)
Abdominal lymph node enlargement	5 (2.0)
Broadening of the renal pelvis	3 (1.2)
Intussusception	3 (1.2)
Polycystic kidney	1 (0.4)
Scrotal edema	1 (0.4)
Bowel wall edema	1 (0.4)
CT scan	5
Positive finding	5
Bowel wall thickening	2 (40)
Small intestinal wall edema	1 (20)
Edema of the scalp	2 (40)
X-ray	1
Positive finding	1
Dilatation and hypomotility	1 (100)

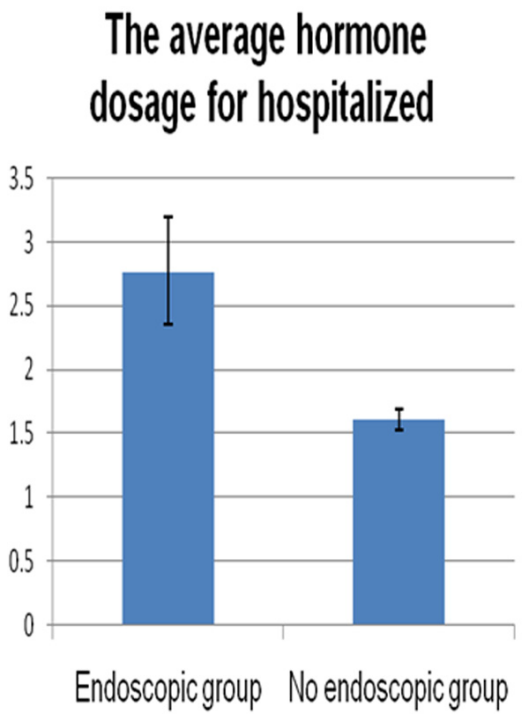

Figure 2. The average hormone dosage for hospitalized patients with (69 cases) and without endoscopy (192 cases) was significantly different ($P < 0.05$).

in another hospital and later transferred here. Another patient had an exploratory laparotomy done due to the concern for severe abdominal complications.

Discussion

Depending on the location and severity of the target vessels from IgA1 deposits and the subsequent consequences, the clinical presentations of IgAV can be various, with symptoms ranging from skin and extracutaneous involvement, such as the gastrointestinal system, joints, kidneys, and so on. This fickle feature of IgAV poses tremendous difficulty in its early definite diagnosis.

In the present study, 38.7% of our IgAV kids had GI symptoms prior to the cutaneous rash which is at the high end compared to 10-40% in the literature [10], and 53% had vomiting which is much higher when compared to 115 Chinese adult patients (13%) in one study [11]. The above findings raise the possibility that the gastrointestinal system of kids, still under the process of maturation, might be more vulnerable than adults to the attacks from the IgAV inflammation damage. GI bleeding (melena/hematochezia + hematemesis) rate (35.6%) or Occult blood rate (49.4%) (**Table 2**) was lower than that (75%) from another study focusing on the gastrointestinal involvement in pediatric IgAV patients with comparable case composition [12]. This may be associated with timely diagnosis and treatment, and it needs more research.

Renal involvement, including hematuria and/or proteinuria, occurred in 39.5% of our patients (**Tables 1** and **2**), a level comparable to another similar study carried out in Taiwan [12]. Joint involvement occurred in 59.4% of our patients, lower than that of other studies [12, 13].

Upon endoscopy, intestinal stricture was not seen in our case series, in contrast to findings in some case studies in children [12] and adults [11]. Other findings from our endoscopic examination of 69 patients included mucosal congestion, redness, petechia, multiple

ulcers, and nodular changes (**Table 3** and **Figure 1**), consistent with the literature [11]. Our study revealed that of the patients with duodenal lesions which did not occur concomitantly in the same patient, the most frequently involved location was in the upper GI tract. Although similar to other studies failing to pinpoint any unique endoscopic hallmark(s) for IgAV diagnosis, to the best of our knowledge, our report described the largest cohort of pediatric IgAV patients (69 cases) who had undergone endoscopy. Moreover, although over half of the sick kids had elevated serum IgA (**Table 2**), suggesting its possible involvement in the pathogenesis of our IgAV cases, we could not be certain of that due to the lack of tissue samples with IgA staining.

Treatment of IgAV is mostly supportive, and the use of corticosteroid has been controversial. In the present study, all of the patients were treated with steroids, and the average steroid dosages for those patients who underwent an endoscopy (69 cases) were statistically higher ($P < 0.05$) than those who did not undergo an endoscopy (**Figure 2**), and the underlying rationale remains to be investigated. The consensus in the literature is that steroids can significantly alleviate IgAV symptoms [14] but offer little help reducing the risk of renal involvement [15], which was also demonstrated in a retrospective study involving 1895 hospitalized patients in the US [16] and some other studies [17, 18].

Taken together, we summarized the demographic characteristics, clinical presentations, laboratory findings and treatment strategies for 261 pediatric IgAV cases in China. The cohort series of 69 cases that underwent an endoscopy is the largest, so far, in the English literature.

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Disclosure of conflict of interest

None.

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