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BRIDGING IGA VASCULITIS GAPS – ATYPICAL GASTROINTESTINAL MANIFESTATIONS AS A PREDICTOR OF RELAPSE

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ABSTRACT

IgA vasculitis (IgAV), also known as Henoch–Schönlein purpura (HSP), is the most common systemic vasculitis in children. The diagnosis is made based on the presence of characteristic purpuric lesions in combination with either one of the joint, gastrointestinal, or renal manifestations. Despite having a generally excellent prognosis, 30-40% of the patients experience relapse. During relapse, purpuric lesions typically precede the other systemic symptoms that tend to manifest with a milder severity compared to the initial presentation. We report a case with atypical presentation of lgAV relapse. A 7-year-old boy diagnosed with IgAV, had multiple episodes of relapse in the past three years. He developed atypical gastrointestinal symptoms (rectal bleeding, colicky abdominal pain and vomiting) and was treated initially as gastritis. The diagnosis of lgAV relapse had only become evident 12 days later, after the appearance of purpuric rashes. His symptoms were unusually more severe during the relapses. The presence of severe gastrointestinal manifestations without the characteristic purpuric rashes makes lgAV relapse more challenging to diagnose. This case report serves as an addition to literature where early recognition of these symptoms can act as a good indicator to diagnose IgAV relapse. High index of suspicion among the clinicians is important as delay in establishing the diagnosis may subsequently compromise further clinical outcome.

1.0 INTRODUCTION

IgA vasculitis (IgAV), also known as Henoch–Schönlein purpura (HSP), is the most common systemic vasculitis in children, with an incidence of 26 per 100,000 in Malaysia [1]. The main pathogenesis is leukocytoclastic vasculitis (LCV) and deposition of immunoglobulin A (IgA) immune complexes in small blood vessels [2]. Common presentations include purpuric rash with joint, gastrointestinal and renal involvement. According to Saulsbury (2001), approximately 30% – 40% of IgAV patients experience at least one relapse during a two-year period after the first diagnosis [3]. Albeit IgAV being a self-limiting disease with excellent prognosis, the use of atypical gastrointestinal manifestations as an indication for IgAV relapse remains controversial. A national multicentric retrospective study mentions that severe gastrointestinal manifestations with recurrent rash frequently caused relapses [4]. This case report highlights the atypical gastrointestinal manifestations observed in this child with multiple IgAV relapses.

2.0 CASE PRESENTATION

A 7-year-old boy with a history of lgA vasculitis diagnosed at the age of five, presented with two episodes of rectal bleeding. He was apparently well until twelve days prior to his admission, when he started experiencing abdominal pain associated with non-bilious vomiting and several episodes of diarrhoea. There was no blood seen in the vomitus or stool initially. Over the next two days, he was seen by two different general practitioners due to persistent symptoms. A presumptive diagnosis of gastritis was

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made, and he was prescribed antacids along with dietary advice to avoid chocolate, which was thought to be the main trigger. On day four of illness, he started to develop purpuric rashes which started at the feet and spread to his shins, thigh, buttock, forearms and arms. (Figure 1). Subsequently, he developed rectal bleeding and passed out blood clots. The diagnosis of relapse IgAV became apparent, and he was admitted for further management. Notably, he did not have haematuria, joint pain or joint swelling. He also denied any fever or symptoms of upper respiratory tract infection during this episode.

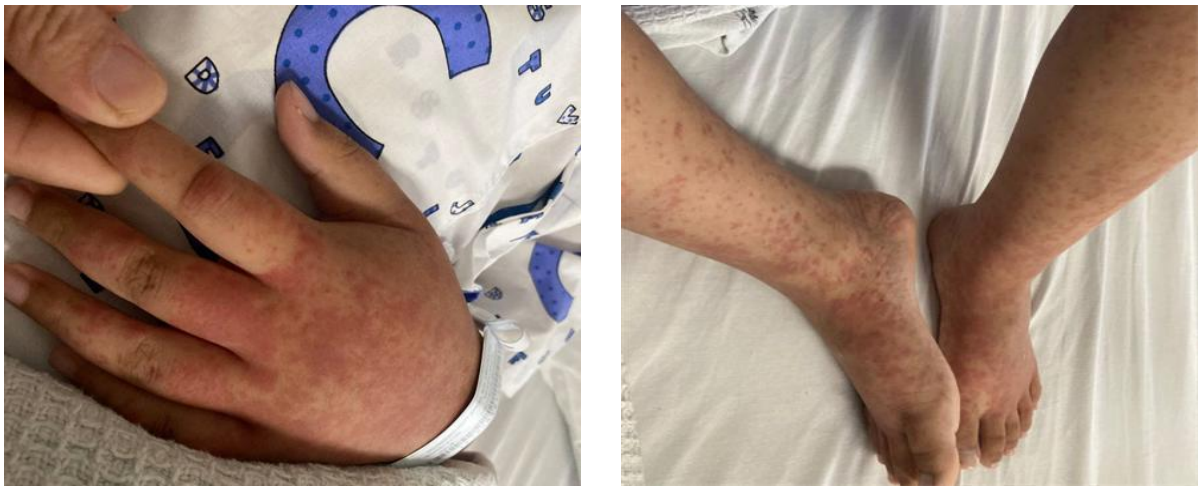

Figure 1. Purpuric rashes over right hands and bilateral lower limbs

Two years ago, the patient was first diagnosed with IgAV. He presented with purpuric skin rashes over the lower limbs and abdominal pain without rectal bleeding, renal or joint manifestations. He achieved remission following a three-month course of oral prednisolone. At age six, he experienced the same symptoms as before, but it was accompanied by one episode of loose stool containing blood streaks, which resolved spontaneously within two days without medication. He remained asymptomatic thereafter until the current episode. Upon admission, the child appeared irritable and in visible discomfort. Palpable purpuric rashes were distributed on the back of his ears, bilateral upper and lower limbs, trunk and buttocks, sparing the face. There were no signs of active arthritis, joint swelling or tenderness. Abdominal examination revealed periumbilical tenderness without palpable masses or organomegaly. Murphy's sign was negative and other systemic examinations were unremarkable.

Blood investigations revealed elevated ESR, (22 mm/hr), leucocytosis, (18.49 X 10^9/L), and thrombocytosis, (536 X 10^9/L). Urinalysis showed pH 5.5, with protein 1+, ketone 1+ and blood 2+. Further investigations were conducted to rule out differential diagnoses, including systemic lupus erythematosus, pancreatitis and intussusception. Results for antinuclear antibody (ANA), complement levels (C3, C4), immunoglobulins (IgG, IgA and IgM), anti-dsDNA and serum amylase were negative. Liver function tests, electrolytes, blood gases and iron studies were within normal limits. Imaging done, including chest and abdominal X-ray revealed no abnormalities while abdominal ultrasound excluded intussusception and appendicitis. Initial treatment with intravenous hydrocortisone 100mg QID was started but failed to improve the rash after 48 hours. A skin biopsy was performed, and the treatment was escalated to pulsed intravenous methylprednisolone 500 mg OD, which led to marked improvement of the rash within two days. The skin biopsy confirmed the diagnosis of IgAV, revealing leukocytoclastic vasculitis with thickened dermal blood vessels without fibrinoid necrosis. Immunofluorescence staining demonstrated IgA deposition along the capillary walls of the superficial dermis.

Subsequently, his treatment was tapered down to oral prednisolone 20mg OM and 10mg ON, which was gradually tapered over two weeks. At follow-up, he was in remission and had resumed his normal daily activities.

3.0 DISCUSSION

The lack of standardised definitions for relapsing and persistent lgA vasculitis poses as a significant diagnostic and therapeutic challenge for clinicians, as there remains a lack of consensus on classification and management of these cases [7]. Recent UK guidelines define recurrent IgAV as the reappearance of typical non-blanchable, purpuric rash after a symptom-free period of greater than one month [8].

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Recurrent episodes often mirror the initial presentation in terms of organ involvement, although late relapses occurring months or years after the first episode, while uncommon, have been reported [9-10]. Calvo-Rio et al. (2016) identified gastrointestinal (GI) symptoms, such as postprandial abdominal pain, GI bleeding, nausea and vomiting, as key predictors of relapse, whereas a history of prior infection appeared protective [11]. In contrast, Rigante et al. (2024) highlighted an association between lower joint arthritis and GI involvement during relapses, a finding not supported by Paek et al. (2020) suggesting a variability in clinical presentation [12-13].

Moreover, in recent studies, IgAV relapse diagnosis can be further strengthened by lab investigations. A retrospective study by Rigante et. al (2024) highlights elevated neutrophil-to-lymphocyte ratio ≥ 3.27, low lymphocyte count, 25-hydroxyvitamin D deficiency and a persistent rash that lasts longer than a month are associated with GI involvement in relapses [13]. Li et al. (2023) observed that rare onset age, vomiting, purpura above the waist, and hypalbuminaemia ≤ 38.25 g/L were linked to severe GI manifestations [14]. Fecal calprotectin, highlighted by Paek et. al (2020) has emerged as a positive indicator of active gastrointestinal involvement and disease activity [12]. Zhang et al (2021) discovered correlations between IgAV relapse and gut microbiota with organisms such as *Escherichia-Shigella*, *Streptococcus* and *Fusobacteria* being implicated in IgAV relapses with GI symptoms. [15] This statement is further strengthened by Cao (2021) which suggested that faecal occult stool test can aid with detecting the alteration in the gut environment from IgAV with gastrointestinal manifestations which may affect the management [16]. Children with GI manifestations during IgAV relapses are at increased risk for intussusception, particularly if glucocorticoid therapy is not initiated within 72 hours of symptom onset [17]. Positive faecal occult blood tests, elevated D-dimer levels, and high neutrophil-to-lymphocyte ratios also necessitate prompt investigation [18-19]. Fang et al. (2020) noted that some patients with GI relapses may lack skin manifestations, making endoscopic evaluation, such as video capsule endoscopy (VCE), a valuable diagnostic tool for detecting intestinal lesions earlier than conventional esophagogastroduodenoscopy [20].

While treatment protocols for severe IgAV with GI involvement remain undefined, corticosteroids and immunosuppressive agents, including dapsone, have shown promise in managing relapses [21-22]. The prognosis of IgAV in children is significantly influenced by its progression towards IgAV nephritis (IgAVN) with severe or recurrent GI manifestations identified as substantial risk factors for kidney involvement. Studies indicate that IgAV cases initially presenting with GI symptoms have a 2.45-fold increased risk of progressing to IgAVN within one month and a 6.6-fold higher risk over time compared to cases that present with joint involvement or rashes. Additionally, moderate to severe GI symptoms elevate the risk of IgAVN by 4.66 times. Other studied risk factors include recurrent rashes, one or more disease relapses, age between 4 and 8 years, and the use of glucocorticoid therapy for GI symptoms [23]. The risk of glucocorticoid resistance in severe refractory cases such as Miki et al (2024) highlights the need for alternative therapies, such as cyclophosphamide or mycophenolate mofetil to achieve remission [24]. This case of a 7-year-old boy who presented with mainly GI symptoms during IgAV relapses, serves as an addition to the medical literature that supports atypical GI manifestations as an indicator for IgAV relapse. Early recognition and timely intervention remain crucial in improving outcomes and preventing complications in paediatric IgAV relapses.

4.0 CONCLUSION

IgAV is a common childhood vasculitic disorder with an excellent prognosis. Although there is relatively limited literature on atypical gastrointestinal manifestations as a predictive factor in IgAV relapses, faecal calprotectin has emerged as a crucial indicator to predict IgAV relapse in children with gastrointestinal symptoms. This case report serves as an addition to literature, highlighting that early recognition of these symptoms can act as a reliable indicator for diagnosing IgAV relapse. A high index of suspicion among the clinicians is essential, as delay in establishing the diagnosis may subsequently compromise further clinical outcome. There is much potential for further exploration regarding gastrointestinal manifestations and their role in predicting IgAV relapses.

5.0 CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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6.0 AUTHORS CONTRIBUTION

Gupta, I. D. (Conceptualization; Literature review; Clinical data collection; Writing - original draft)
Lim, P. P. (Literature review; Writing - critical revision of the article for important intellectual content)

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