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CLINICAL FEATURES OF CUTANEOUS, ARTICULAR, AND VISCERAL FORMS OF HEMORRHAGIC VASCULITIS (HENOCH-SCHÖNLEIN PURPURA / IGA VASCULITIS)

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RELEVANCE
Hemorrhagic vasculitis (IgA vasculitis) is the most common systemic vasculitis among children and adolescents, characterized by a diversity of clinical manifestations. The involvement of the skin, joints, gastrointestinal tract, and kidneys can significantly impact patients' quality of life and lead to long-term complications, particularly renal failure. Therefore, an in-depth study of the clinical features of various organ involvements, timely diagnosis, and optimization of treatment strategies are urgent tasks in pediatrics and rheumatology.

Keywords: hemorrhagic vasculitis, IgA vasculitis, Henoch-Schönlein purpura, cutaneous purpura, arthritis, abdominal pain, glomerulonephritis, systemic vasculitis.

АКТУАЛЬНОСТЬ
Геморрагический васкулит (IgA-васкулит) является наиболее распространенным системным васкулитом среди детей и подростков, характеризующимся разнообразием клинических проявлений. Поражение кожи, суставов, желудочно-кишечного тракта и почек может серьезно влиять на качество жизни пациентов и приводить к долгосрочным осложнениям, в частности, к почечной недостаточности. В связи с этим, углубленное изучение клинических особенностей поражения различных органов, своевременная диагностика и оптимизация стратегий лечения являются актуальными задачами педиатрии и ревматологии.

Ключевые слова: геморрагический васкулит, IgA-васкулит, пурпура Шенлейна-Геноха, кожная пурпура, артрит, абдоминальная боль, гломерулонефрит, системный васкулит.

INTRODUCTION

IgA vasculitis (IgAV), historically known as Henoch-Schönlein purpura (HSP), is a systemic, immune-mediated, small-vessel vasculitis. First described in the 19th century by physicians Johann Schönlein (who noted the association of purpura and arthritis) and his student Eduard Henoch (who added the gastrointestinal and renal components), it is defined by the deposition of immunoglobulin A1 (IgA1)-containing immune complexes within the walls of small blood vessels. This process predominantly affects the capillaries, venules, and arterioles of the skin, joints, gastrointestinal tract, and kidneys. IgAV is the most common form of systemic vasculitis in children, with a peak incidence between 4 and 6 years of age and an annual incidence estimated at 10–20 cases per 100,000 children (Hetland et al., 2017). Although less common in adults, its presentation in this population is often more severe, with a higher prevalence of persistent renal disease and a greater risk of long-term complications (Audemard-Verger et al., 2015).

The clinical presentation of IgAV is classically defined by a tetrad of manifestations: palpable purpura, arthritis or arthralgia, colicky abdominal pain, and renal disease. However, these features do not always appear simultaneously, which can create diagnostic challenges. The prognosis is generally excellent, with most pediatric cases being self-limiting. Nevertheless, the severity of visceral involvement, particularly the development of IgAV nephritis, is the primary determinant of long-term morbidity and mortality (Ozen et al., 2017). This article aims to provide an expanded, comprehensive overview of the distinct clinical features associated with cutaneous, articular, and visceral manifestations of IgAV, highlighting differences in presentation and prognosis.

LITERATURE REVIEW

The etiology of IgAV is multifactorial, involving a complex interplay of genetic predisposition, environmental triggers, and an aberrant immune response. The central pathogenic event is the formation and deposition of immune complexes containing aberrantly glycosylated IgA1.

Immunopathogenesis: The key molecule in IgAV pathogenesis is galactose-deficient IgA1 (Gd-IgA1). In susceptible individuals, B-cells produce IgA1 molecules that lack galactose residues in the hinge region of the heavy chain. These Gd-IgA1 molecules are recognized as foreign by the immune system, leading to the production of anti-glycan IgG and IgA autoantibodies. The binding of these autoantibodies to Gd-IgA1 results in the formation of large, pathogenic immune complexes. These complexes circulate and deposit in the walls of small vessels in various organs. Once deposited, they activate the complement system, primarily through the alternative and lectin pathways, leading to the recruitment of neutrophils and other inflammatory cells. The subsequent release of proteolytic enzymes, reactive oxygen species, and pro-inflammatory cytokines causes endothelial damage, increased vascular permeability, and leukocytoclastic vasculitis, which is the histopathological hallmark of the disease (Ono & Ono, 2019).

Triggers and Susceptibility: The onset of IgAV is often preceded by an infection, most commonly an upper respiratory tract infection caused by Group A Streptococcus, but other bacterial and viral pathogens have also been implicated. It is hypothesized that microbial antigens may share structural similarities with the hinge-region glycans of IgA1, triggering the autoimmune response through molecular mimicry. Furthermore, certain medications and vaccinations have been anecdotally linked to the onset of IgAV. A genetic predisposition is suggested by the association of IgAV with specific human leukocyte antigen (HLA) alleles, such as HLA-DRB1 (Ma et al., 2021).

MATERIALS AND METHODS

This article constitutes a comprehensive narrative review aimed at synthesizing the current state of knowledge regarding the clinical manifestations of IgA vasculitis. The methodology was structured to ensure a broad and relevant capture of the existing literature.

Search Strategy: A systematic literature search was conducted across multiple electronic databases, including PubMed/MEDLINE, Scopus, Embase, and Google Scholar. The search was designed to identify all relevant articles published between January 2015 and September 2025 to focus on the most recent evidence. The search strategy combined keywords and Medical Subject Headings (MeSH) terms, structured around three core concepts: the disease, the affected populations, and the clinical features.

Inclusion and Exclusion Criteria: Articles were selected for inclusion based on a predefined set of criteria.

Inclusion Criteria: (1) Studies published in the English language; (2) Original research articles including systematic reviews, meta-analyses, large observational cohort studies (n > 50), and randomized controlled trials; (3) Major international clinical practice guidelines (e.g., from EULAR/PReS); (4) Studies focusing specifically on the clinical presentation, diagnosis, or prognosis of cutaneous, articular, and/or visceral (gastrointestinal and renal) manifestations of IgAV.

Exclusion Criteria: (1) Case reports and small case series (n < 20); (2) Editorials, letters to the editor, and conference abstracts; (3) Studies focused solely on pathophysiology, genetics, or treatment without detailing clinical features; (4) Non-English articles.

Data Selection and Synthesis: The article selection process involved two stages. Initially, titles and abstracts of all retrieved articles were independently screened by two reviewers to identify potentially relevant studies. In the second stage, the full texts of the selected articles were thoroughly reviewed to determine final eligibility. Any discrepancies between reviewers were resolved through discussion and consensus. Data from the included articles were extracted and synthesized thematically. Given the narrative nature of this review, a formal meta-analysis was not performed. Instead, the information was organized and presented according to the primary organ systems involved: cutaneous, articular, and visceral (subdivided into gastrointestinal and renal), to provide a clear and structured overview of the clinical spectrum of IgAV..

RESULTS AND DISCUSSION

The clinical manifestations of IgAV can be divided into cutaneous, articular, and visceral forms, with occasional involvement of other organ systems.

Cutaneous Manifestations Skin involvement is the presenting feature in over 75% of cases and is present in virtually all patients at some point during the disease course.

Appearance and Distribution: The hallmark is a symmetric, palpable purpuric rash. Lesions begin as erythematous macules or urticarial plaques that evolve into petechiae and non-blanching, palpable purpura within 24-48 hours. The distribution is typically gravity-dependent, appearing most prominently on the lower extremities and buttocks. In non-ambulatory infants, the rash may be more pronounced on the back, scalp, and face. In severe cases, purpuric lesions can become confluent, bullous, or even necrotic, leading to ulceration and scarring. Localized, non-pitting subcutaneous edema of the hands, feet, scalp, and periorbital area is also common, particularly in children under three years of age.

Histopathology: A skin biopsy, while not always necessary for diagnosis, reveals a classic leukocytoclastic vasculitis in the superficial dermal vessels, with neutrophilic infiltrates, fibrinoid necrosis, and extravasation of erythrocytes. Direct immunofluorescence is the gold standard for confirmation, showing granular IgA deposits within the vessel walls.

Articular Manifestations Joint involvement occurs in up to 80% of patients and is often a presenting symptom.

Characteristics: It manifests as an acute-onset, transient, and non-erosive arthritis or arthralgia. The inflammation is typically oligoarticular (affecting four or fewer joints). Pain is often the most prominent feature and can be disproportionate to the objective signs of swelling.

Affected Joints and Symptoms: The large joints of the lower extremities, particularly the ankles and knees, are most commonly affected. Patients experience pain, swelling, warmth, and limited range of motion. Significant periarticular swelling is a characteristic feature. The symptoms are self-limiting, usually resolving within two weeks without causing permanent joint damage, and typically respond well to supportive care and NSAIDs.

Visceral manifestations - Gastrointestinal (GI) Involvement GI involvement is present in 50-75% of patients and is a primary cause of hospitalization.

Common Symptoms: The most frequent symptom is colicky, diffuse abdominal pain, resulting from submucosal edema and hemorrhage due to mesenteric vasculitis. This is often accompanied by nausea, vomiting, and transient paralytic ileus. GI bleeding, manifesting as melena, hematochezia, or hematemesis, is also common.

Diagnostics and Severe Complications: Abdominal ultrasound is a useful initial imaging modality, which may show thickened bowel loops or signs of intussusception. While rare, severe, life-threatening complications can occur. Intussusception, typically ileo-ileal (as opposed to the more common ileocolic type in general pediatric populations), is the most frequent surgical emergency. Other serious complications include bowel ischemia, infarction, perforation, and massive hemorrhage. Endoscopy can be diagnostic in unclear cases, revealing characteristic findings of mucosal inflammation, petechiae, erosions, and "cobblestone" appearance.

Renal Involvement (IgAV Nephritis) Renal disease is the most significant determinant of long-term prognosis, affecting 20-50% of children and up to 70% of adults with IgAV.

Clinical Presentation and Monitoring: The spectrum of renal involvement ranges from asymptomatic urinary abnormalities to rapidly progressive glomerulonephritis. The most common presentation is isolated microscopic hematuria, with or without mild proteinuria. More severe manifestations include nephritic syndrome (hematuria, hypertension, renal insufficiency) or nephrotic syndrome (heavy proteinuria, hypoalbuminemia, edema). Renal symptoms typically appear within 4-12 weeks of disease onset. Routine urinalysis and blood pressure measurement are therefore mandatory for all patients for at least six months following diagnosis.

Indications for Biopsy and Prognosis: A renal biopsy is indicated in patients with persistent, severe proteinuria, nephrotic syndrome, or worsening renal function. Histological findings are identical to those of IgA nephropathy, featuring mesangial IgA deposition and variable degrees of mesangial proliferation, endocapillary hypercellularity, and crescent formation. The severity of histological findings, particularly the percentage of crescents, correlates with prognosis. The presence of nephrotic-range proteinuria and acute kidney injury at onset are the strongest clinical predictors of progression to chronic kidney disease (CKD) and end-stage renal disease (ESRD).

Other Manifestations (Rare) While less common, IgAV can affect other organ systems. Neurological involvement may include headaches, seizures, or focal deficits due to central nervous system vasculitis. Pulmonary involvement can manifest as diffuse alveolar hemorrhage, a life-threatening complication. Orchitis, causing testicular pain and swelling, is another recognized, albeit rare, manifestation.

CONCLUSION

IgA vasculitis is a complex multisystemic disorder characterized by a variable clinical course. While the classic tetrad of palpable purpura, arthritis, abdominal pain, and nephritis provides a useful diagnostic framework, the presentation can be heterogeneous, making timely recognition challenging. This review underscores that while cutaneous and articular manifestations are the most common and typically self-limiting, the prognosis is fundamentally dictated by the presence and severity of visceral involvement. Gastrointestinal complications can lead to significant acute morbidity, including surgical emergencies, whereas renal disease is the primary driver of long-term adverse outcomes, with a subset of patients progressing to chronic kidney disease or end-stage renal failure.

The clinical implication is clear: all patients diagnosed with IgAV require meticulous and sustained monitoring. This includes regular urinalysis and blood pressure checks for at least

six months post-diagnosis to detect the onset or worsening of nephritis. A high index of suspicion for severe GI complications is essential, particularly in patients with severe, persistent abdominal pain. A multidisciplinary approach involving pediatricians, rheumatologists, nephrologists, and gastroenterologists is often necessary for optimal management of severe or atypical cases.

Despite advancements in understanding its immunopathogenesis, significant gaps in knowledge remain. Future research must prioritize the identification of reliable prognostic biomarkers to predict which patients are at highest risk for developing severe renal or gastrointestinal disease. Furthermore, there is a pressing need for high-quality, randomized controlled trials to establish definitive, evidence-based treatment guidelines, particularly for managing severe IgAV nephritis and for the adult patient population, which remains understudied. Ultimately, a deeper, more nuanced understanding of the clinical spectrum and pathophysiology of IgAV will pave the way for more personalized risk stratification and targeted therapeutic interventions, improving outcomes for all affected individuals..

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