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ORIGINAL ARTICLE

Ureteral or vesical involvement in Henoch–Schönlein syndrome: a systematic review of the literature

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Abstract
Background Little information is available on ureteral or vesical involvement in Henoch–Schönlein syndrome. To determine the features of this condition we performed a formal analysis of peer-reviewed scientific literature on this topic.
Methods The US National Library of Medicine database was used as the data source. All articles published as full-length articles or letters were collected. Reports published in languages other than English, French, German, Italian or Spanish were not considered.
Results We analyzed 32 reports describing 35 cases (24 male and 11 female subjects aged between 3.5 and 63, median 7.0 years) with ureteral (n =30), vesical (n =4), or both ureteral and vesical involvement (n =1). The presentation included colicky abdominal pain, macroscopic hematuria (sometimes containing blood clots), urinary tract infection or urinary retention. The diagnosis of ureteral involvement was often fortuitous. Patients with vesical involvement were managed conservatively. However, the majority of those with ureteral involvement were managed surgically.
Conclusions Ureteral or vesical involvement is unusual and likely underappreciated in Henoch–Schönlein syndrome. Improved recognition and wider appreciation of this involvement can help to avoid associated morbidity. Management must be individualized for each patient. A multidisciplinary approach may be of value in planning medical treatment, surgical intervention, and follow-up.

Keywords Anaphylactoid purpura · Henoch–Schönlein purpura · Systematic review · Ureteritis

Introduction

Henoch–Schönlein syndrome is the most common form of childhood vasculitis with an estimated overall annual incidence of 10–20 cases per 100,000 children under 17 years of age [1]. Palpable non-thrombocytopenic purpura concentrated on dependent or pressure-bearing areas, arthralgia or arthritis, and abdominal pain are the distinctive presentations of this condition [1].

The most recognized genitourinary manifestation of Henoch–Schönlein syndrome is a kidney disease that affects 20–60 % of cases and principally determines the long-term prognosis of affected patients [1]. In addition, many boys develop scrotal signs or symptoms secondary to edema and hematoma of the scrotal wall or spermatic cord, testicular hemorrhage, subcapsular testicular hematoma, epididymitis or orchitis [1].

Ureteral or vesical involvement is uncommon. Since textbooks and recent reviews do not, or only marginally, mention this rare complication of Henoch–Schönlein syndrome, we systematically reviewed and analyzed all the available literature.

Materials and methods

Between November 2012 and April 2013 we performed a thorough computer-based search of the terms Henoch, Schönlein, Henoch–Schönlein, Schönlein–Henoch, anaphylactoid purpura, rheumatoid purpura, angiitis, vasculitis,

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hydronephrosis, ureter, ureteritis, and bladder in the US National Library of Medicine database. We used the principles established by the UK Economic and Social Research Council guidance on the conduct of narrative synthesis and on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (Fig. 1). For the final analysis we selected 32 reports available as a full-length article or as a letter, which included cases of ureteral or vesical involvement in Henoch–Schönlein syndrome published after 1960.

Henoch–Schönlein cases were classified as severe in the presence of a kidney disease characterized by nephrotic range proteinuria or in the presence of at least one of the following infrequent complications: muscle involvement; protein-losing enteropathy; pancreatitis; cholecystitis; intestinal infarction, perforation or stricture; altered mental status; seizures; paresis; blindness; peripheral neuropathy; pulmonary hemorrhage; carditis; uveitis. The remaining cases were classified as mild.

The two-sided Mann–Whitney–Wilcoxon test for two independent samples and the two-sided Fisher's exact test were performed for analysis. Significance was assumed when $P<0.05$.

Results

The literature retained for the final analysis included (Fig. 2) 35 Henoch–Schönlein cases (25 male and 10 female subjects) with ureteral [2–30] ($n=30$), vesical [31–33] ($n=4$), or both ureteral and vesical involvement [11] ($n=1$). The diagnosis of Henoch–Schönlein syndrome was based on the classical palpable purpuric rash in the presence of at least one of the following: diffuse abdominal pain, arthritis or arthralgia, or a pathological urinalysis [1]. Biopsy findings further supported the diagnosis of Henoch–Schönlein syndrome in 13 cases: skin biopsy ($n=3$), kidney biopsy ($n=5$) or both skin and kidney biopsy ($n=5$). Ureteral or vesical involvement was recognized at between 1 week and 14 months, a median of 1 month after onset of purpura. Henoch–Schönlein syndrome was mild in the 4 cases with isolated vesical involvement (in these subjects imaging studies excluded upper tract involvement) and severe in the case with both ureteral and vesical involvement. In the 30 patients with isolated ureteral involvement the syndrome was severe in 11 and mild in the remaining 19 cases.

Ureteral involvement

The 31 Henoch–Schönlein patients with ureteral involvement consisted of 23 male and 8 female subjects aged between 3.5 and 63 years (Fig. 2). Diagnostic imaging studies disclosing the ureteral involvement were performed in 9 patients with both colicky abdominal pain and macroscopic hematuria, in 8 with colicky abdominal pain, in 4 with macroscopic hematuria (but without concurrent abdominal pain), and in 2 with a urinary tract infection. The diagnosis of ureteral involvement was fortuitous in the remaining patients (diagnostic imaging performed for other reasons, e.g., before kidney biopsy). Microscopic hematuria had been noted in the patients without macroscopic hematuria or urinary tract infection.

Forty-six of the 62 ureteral units were obstructed in the 31 patients: the obstruction was unilateral in 16 and bilateral in 15 patients (Table 1). The obstruction mostly affected the proximal ureter. A 21-year old patient [24] initially presented with a proximal obstruction of the left ureter that was followed by an ipsilateral distal obstruction 4 weeks later. Twenty-eight ureters were partially and the remaining 19 were completely obstructed (Table 2). The management was expectative, medical with corticosteroid, surgical, or both medical and surgical. Ninety-five percent of the cases with complete obstruction required a surgical approach (with or without corticosteroids).

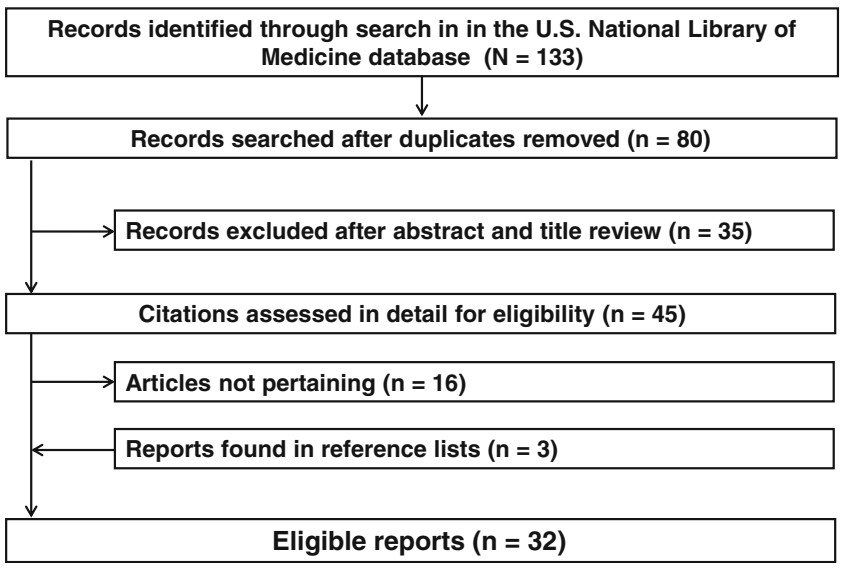

Fig. 1 Flowchart of the literature search process. The case of an Italian boy reported twice [3, 18] in the literature was considered only once

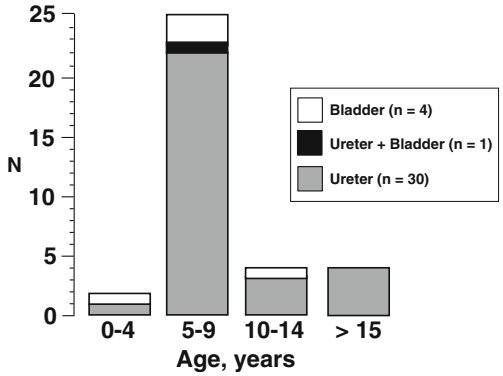

Fig. 2 Age distribution in 35 Henoch–Schönlein patients (24 male and 11 female subjects) with ureteral or vesical involvement

However, the majority of the cases (54 %) with partial obstruction were managed expectantly or medically.

The course was spontaneously favorable in 3 out of 6 partially obstructed ureters (50 %; including a boy with ureteral rupture [10]). Twenty-one ureters were treated with corticosteroids: the course was favorable in 10 and unfavorable in the remaining 11 ureters. Three initially expectantly managed ureters, 11 initially with corticosteroid managed ureters, and the remaining 17 ureters were approached surgically (with or without concurrent drug management with corticosteroids).

The surgical approach, which was mostly preceded by a pyelostomy, included: (1) Nephrectomy in 2 patients with unilateral proximal obstruction and very poor ipsilateral kidney function; (2) Insertion of a stent into the obstructed ureter in 2 cases; (3) Ileal ureteral replacement in 12 cases; (4) Pyeloplasty in the remaining ureters.

Stent insertion, ureteral replacement, and pyeloplasty were reported to be successful in all cases.

The course was similar in 19 patients with mild (surgery required in 19 ureters) and in 11 with severe (surgery required in 12 ureters) Henoch–Schönlein syndrome.

Ureteral specimens, examined histologically in 10 cases, disclosed fibrosis and chronic inflammation. Characteristic vasculitic findings were noted in 5 cases (a direct immunofluorescence study, performed in 2 children, disclosed depositions of immunoglobulin A).

Table 1 Ureteral obstruction in 31 patients (23 male and 8 female subjects) affected by Henoch–Schönlein syndrome. The ureteral obstruction was unilateral in 16 and bilateral in 15 patients. The difference between male and female subjects was not significant

	Right ureter (*n*)			Left ureter (*n*)		
	All	Female	Male	All	Female	Male
Proximal	14	4	10	19	4	15
Middle	2	1	1	3	1	2
Distal	5	2	3	4[a]	1	3

[a] Late obstruction of the left distal ureter developed in a 21-year-old man initially presenting with obstruction of the ipsilateral proximal ureter [24]

Table 2 Initial therapeutic intervention in Henoch–Schönlein patients with partial or complete ureteral obstruction

	Partial obstruction (*n* = 28)	Complete obstruction (*n* = 19)
Expectative	6	0
Corticosteroids alone	9	1
Surgery alone	7	10
Corticosteroids and surgery	6	8

Vesical involvement

The 5 patients with vesical involvement presented with gross hematuria. Acute urinary retention and a urinary tract infection were also noted in one case. Diagnostic imaging, sometimes associated with a cystoscopy, disclosed diffuse mucosal thickening of the bladder. In one case a blood clot obstructing the bladder outlet and a large intramural hematoma were also noted. The management was expectative (without corticosteroids). A bladder catheter was inserted in the patient with urinary retention secondary to a large blood clot [32]. A biopsy of the bladder mucosa to support the diagnosis was never performed.

Discussion

The long-term prognosis of Henoch–Schönlein syndrome is nearly totally attributable to kidney disease [1]. The present review complements the results of a preliminary review of the literature published 5 years ago [26]. It confirms that ureteral or vesical involvement, whose occurrence has never been analyzed quantitatively, is very rare, but, if present, is associated with substantial morbidity. Furthermore, the review substantiates the belief that ureteral or vesical involvement is the consequence of vasculitic lesions. Finally, the analysis suggests that Henoch–Schönlein syndrome with ureteral or vesical involvement, like the classical form of Henoch–Schönlein syndrome, might be found in all age groups, but occurs most often between the ages of 5 and 9 years with a male to female ratio of approximately 2:1 [1]. The discussion focuses on the presentation and the management of Henoch–Schönlein syndrome with ureteral involvement.

In Henoch–Schönlein syndrome, ureteritis, like in other systemic vasculitides, characteristically causes luminal obliteration (owing to wall inflammation or to bleeding with clot formation) or, more rarely, ureteral rupture [34–36]. Henoch–Schönlein ureteritis is likely underappreciated (and its diagnosis delayed) because it occurs rarely and, more importantly,

because its clinical symptoms, namely colicky abdominal pain and gross hematuria, are mostly attributed to intestinal or renal disease. On the other hand, some reported cases of proximal ureteral obstruction might actually be a congenital ureteropelvic junction obstruction that is unrelated to this vasculitis syndrome. Although in Henoch–Schönlein patients abdominal pain is almost always caused by submucosal or subserosal bleeding and swelling within the intestine, abdominal ultrasound examination is currently often performed to exclude intussusception [1]. Combining abdominal with renal tract ultrasound is a rather simple and non-invasive tool that would likely prevent a delayed diagnosis of ureteral obstruction. This diagnostic technique appears warranted at least in patients with abdominal pain and hematuria. The diagnosis of ureteral stenosis, which is suspected on ultrasound, currently deserves confirmation either by scintigraphy or by magnetic resonance urography. Compared with scintigraphy, magnetic resonance urography could have the potential to provide equivalent information about renal function, but superior information regarding morphology [37].

Controlled trials are not realistic with rare and heterogeneous conditions such as ureteral and vesical involvement in Henoch–Schönlein syndrome. With these limitations in mind, the data of the present analysis prompt us to shortly address both medical and surgical management of ureteral involvement. Corticosteroids in the acute phase of Henoch–Schönlein syndrome do alleviate and treat extra-renal symptoms [38, 39], but these studies, like the present review, do not give data on their efficacy on ureteral (or vesical) involvement. Controversy has remained as to whether corticosteroids can prevent the development of kidney disease and reduce its severity [40], but recent data suggest that early corticosteroid treatment does not prevent kidney disease [41, 42]. Since stenosing ureteritis is self-limited in some instances (and occasionally [43] ameliorates on corticosteroids), surgery other than pyelostomy deserves consideration in patients with persisting ureteral stenosis or a rather low disease activity. Traditional operative reconstruction has been mostly used. Balloon dilatation or stenting, which have been recently used in kidney transplant recipients affected by ureteral stenosis, may be a further option [44, 45].

Conclusions

This review confirms that ureteral or vesical involvement is very unusual and likely underappreciated in Henoch–Schönlein syndrome. Improved recognition and wider appreciation of ureteral and vesical involvement could help avoid the substantial associated morbidity. The management must be individualized for each patient. A multidisciplinary approach may be of value in planning medical treatment, surgical intervention, and follow-up.

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