HENOCH-SCHONLEIN PURPURA: THE CHANDIGARH EXPERIENCE

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Objective: *To determine the clinical profile of children with Henoch-Schonlein purpura (HSP).* ***Design:*** *Hospital based descriptive follow-up study. Subjects: 45 patients attending the Pediatric Rheumatology and Immunology clinic over the last 4 years.* ***Results:*** *The patients were aged between 2.5-12 years with a male to female ratio of 2:1. All cases had palpable purpura. Gastrointestinal involvement was seen in 38 patients, with abdominal pain in 35 (78%) and lower GI bleed in 21 (47%). Large joint arthritis occurred in 60%. Renal involvement was seen in 14 subjects (31%). Major renal involvement occurred in 9 patients, with nephritic syndrome in* 6 *and nephrotic syndrome in 3 cases. Five patients had minor urinary abnormalities; 6 patients with major renal involvement and crescentic glomerulonephritis were treated with high dose pulse steroid therapy followed by oral prednisolone and azathioprine for 12-18 months. Normalization of urinary abnormalities occurred in these patients over 4-8 months and presently all are normotensive and off antihypertensive drugs. Conclusions: HSP in children is a common form of vasculitis. Though short term results in HSP nephritis have been good, long term prognosis in those with major renal involvement would remain guarded.*

Key words: *Henoch-Schonlein purpura, Nephritis.*

HENOCH-Schonlein purpura (HSP) is a multisystem disorder affecting predominantly the skin, joints, gastrointestinal tract and kidneys, although involvement of other organs can occur rarely. It is one of the most common causes of systemic vasculitis in children the world-over(l-4), though racial or ethnic variations in the incidence of disease are described(5,6). Indian data on HSP are scanty and the condition is thought to be less frequent than other rheumatological conditions like juvenile rheumatoid arthritis (JRA) and systemic lupus erythematosus (SLE)(7-9). Bagga *et al.(10)* reported a series of 47 patients with HSP from Delhi observed over a period of 17 years. We, however, have seen 45 cases of HSP over a short period of 4 years, implying that the condition is perhaps as common in our country as it is in the West.

Subject and Methods

All patients of HSP diagnosed and treated in the Pediatric Rheumatology and Immunology Clinic of Postgraduate Institute of Medical Education and Research, Chandigarh between January 1993 and December 1996 were included in this analysis. Diagnostic criteria included the

characteristic purpuric rash, most prominent on the buttocks and/or lower legs and with at least one of the following: (i) hematuria and/or proteinuria, (ii) abdominal-pain, *(iii)* arthralgia with or without arthritis.

Hematuria was defined as more than 5 RBCs/HPF in centrifuged urine; proteinuria as timed urinary protein excretion >4 mg/m^2/hour or positive dipstick test. Nephrotic syndrome, nephritic syndrome or renal impairment was defined using standard criteria(3).

Laboratory investigations included a hemogram, serum electrolytes, blood urea and creatinine, total and differential serum proteins, serum cholesterol, complement (C_3), antinuclear factor (ANF), antistreptolysin-O (ASO), C-reactive protein (CRP), coagulogram and timed urinary protein estimation. In addition repeated urinalysis were undertaken to pick up renal involvement. Skin biopsy from the involved skin was subjected to light microscopy and direct immunofluorescence studies.

Percutaneous kidney biopsy was done in patients who had major renal involvement *i.e.,* those with nephrotic or nephritic illness. Pathological changes on routine microscopy were graded according to the classification of the International Study of Kidney Disease in Children(11): Grade I: Minor glomerular abnormalities; Grade II: Focal or diffuse mesangial proliferation; Grade III: As II but with crescentric/segmental lesions (sclerosis, necrosis) in less than 50% glomeruli; Grade IV: As III but with crescents/segmental lesions in 50-75% glomeruli; and Grade V: As III but crescents/segmental lesions in more than 75% glomeruli.

Results

Forty five patients were diagnosed as having HSP. There were 30 boys and 15 girls (male-female ratio 2:1). The mean age at presentation was 7.6 years (range 2.5-12 yr) with majority (71%) being older than 5 years. Mean duration of symptoms before diagnosis was 26 days (range 2-90 days). More than half of these patients (24/45) had symptoms for over one month before the diagnosis was established. The presenting symptoms were skin rash in 42 (93%), abdominal pain in 34 (75%) and joint symptoms in 22 (49%). Fever occurred in one third of the patients.

Systemic Manifestations

Skin was the most frequently affected organ system *(Table I).* The characteristic purpuric rash occurred in all patients. Subcutaneous edema involving scalp, face, extremities and penoscrotal area occurred in 21 (47%) patients. It was more common

TABLE I—*Comparison of Clinical Features of Henoch-Schonlein Purpura in Various Series*

Clincial features	Present study (n=45)	Bagga (10) (n=47)	Allen (4) (n=131)	Sterky (12) (n=224)
Age Mean	7.6 yr	8.5 yr	4 yr	3.5 yr
Range	2.5-13 yr	3-12 yr	6 mo-16y	2-5 yr
Male: Female	2:1	2.6:1	2:1	1.6:1
Purpuric rash (%)	100	96	100	100
Abdominal pain (%)	78	64	66	77
Arthritis (%)	60	47	68	38
Nephritis (%)	31	51	40	22

in children below 6 years (9/13) as compared to those above 6 years (12/32). Gastrointestinal tract (n=38) was the second most common system involved and manifested as abdominal pain in 35 (78%), lower GI bleed in 21 (47%), upper GI bleed in 10 (22%) and vomiting in 7 (16%). Four patients had loose stools and ascites occurred in 2 cases. One subject had clinical and sonographic evidence of intussusception and laparotomy revealed ileocolic intussusception with gangrenous caecum. Two patients had been opearated elsewhere with an erroneous diagnosis of acute abdomen (appendicitis was suspected in one and Crohn's disease in the other). One patient developed shock following massive GI bleed and required resuscitation with blood transfusions.

Transient arthritis/arthralgias involving large joints occurred in 27 (60%) of the patients. Knee joints were most frequently affected (n=16), followed by ankles (n=9) and other joints.

Renal involvement (HSP nephritis-HSN) was seen in 14 (31%) patients. The mean age at onset was 9.3 years. All our patients with HSN were older than 6 years. There were 9 boys and 5 girls. Renal involvement occurred within 2 months of onset of disease in all the patients. The manifestations of HSN included asymptomatic hematuria and/or proteinuria in 5, nephritic syndrome in 6 and nephrotic syndrome in 3. Nine patients had hypertension. Out of these, 6 patients were having concomitant major renal involvement. One patient had hypokalemia with electrocardiographic changes and required emergency management.

Kidney biopsy was done in 8 patients. Histological involvement in relation to clinical findings is shown in *Table II.* Three patients had grade III involvement and 3 had more than grade III involvement. Direct immunofluorescence examination revealed the presence of IgA and C_3 in the mesangium and capillary wall.

CNS involvement was noted in 2 patients. One had generalized tonic-clonic convulsions while the other had findings suggestive of Guillain-Barre syndrome (GBS). Other manifestations of HSP seen in our patients included hepatosplenomegaly (n=5), lymph node enlargement (n=4) and orchitis (n=l). Two patients had radiological evidence of pleural effusion and pulmonary infiltrates.

Recurrence of symptoms was observed in 4 (8.8%) patients and it occurred within 1-3 months of initial illness. Symptoms included skin rash in all, and GI symptoms in one. One patient had aggravation of renal symptoms associated with the recurrence of skin rash.

TABLE II–*Clinico Pathological Findings in HSP Nephritis*

Clinical features	I	II	III	IV	V
Nephritic syndrome (n=6)*	0	1	3	1	0
Nephrotic syndrome (n=3)	0	1	0	1	1
Asymptomatic hematuria and/or proteinuria (n=5)#	0	0	0	0	0
Total (n=14)	0	2	3	2	1

* Biopsy not done in one, # Biopsy not indicated

Elevated ESR was observed in 19 of 22 patients where it was done. C_3 levels were normal in all 14 patients where this was estimated. ANA was positive (1+, speckled) in 2 of 13 patients. Platelet counts were available in 36 patients. Mean platelet count was 4.0 lac/mm^3 and 56% patients had platelet counts > 4.0 lac/mm^3.

Skin biopsy was done in 36 patients. Of these 34 had histological (leukocytoclastic changes, n=27) and/or immunofluorescent (deposition of IgA with/without C_3 in dermal capillaries, n=18), evidence of vasculitis to suggest a diagnosis of HSP. In 2 patients, however, both histological and direct immunofluorescence studies were negative.

Therapy

Nonspecific symptomatic treatment was given to all patients and included antacids, analgesic drugs, H_2-antagonists and intravenous fluids. A short course (2-3 weeks) of oral prednisolone was given for severe abdominal pain and/or bleeding. Six patients with nephritic or nephrotic illness and histological grade of more than III were given pulse methylprednisolone (n=5) and dexamethasone (n=l) followed by oral prednisolone for 6-12 months and azathioprine for 12-18 months. One patient with nephritic illness, who did not undergo renal biopsy and had concurrent Guillain-Barre syndrome was treated with pulse methylprednisolone followed by oral prednisolone for 8 months. Hypertension was controlled with nifedipine, enalapril and propranolol used singly or in combination.

Follow-up

None of the patients who escaped renal involvement at initial presentation have developed any urinary abnormalities on follow-up. Five patients with minor renal involvement *(i.e.,* asymptomatic hematuria and/or protenuria) have been followed up for a period of 1 month to 33 months and none has any persitent urinary abnormalities. Of the 9 patients with major renal involvement, one was lost to follow up after discharge. The remaining 8 have been followed up for 5-32 months. Normalization of urinary abnormalities occurred over a period of 4-8 months in all. Antihypertensive drugs were used for a period of 4-12 months and presently all the patients are normotensive without drugs. Repeat renal biopsy has not been done in any of these patients. The patient with Guillain-Barre syndrome made full neurological recovery in 8 months. No mortality was seen in the present series.

Discussion

Earlier reports from our country indicated that HSP is relatively uncommon in children(7-10). However our study suggests that it is perhaps as common in India as in the West(l,2). Moreover the present study is the only one from India where the clinical diagnosis has been confirmed by histopathological and /or direct immunofluorescence studies on skin biopsy in majority of the patients.

The mean age at presentation was 7.6 years which is comparable to that reported' earlier(3,10). This is in contrast to lower mean age at presentation observed in sortie series(4,12). Male preponderance is similar to that reported in other series(4,10).

Skin involvement occurred in all patients and included purpuric rash (100%) and subcutaneous edema (47%). Rash appeared as the first symptom at onset of disease in 47% while abdominal pain preceded the rash in 13 (29%) patients. Occurrence of acute abdominal pain, especially when severe, in the absence of skin rash may lead to misdiagnosis of acute

abdomen and unnecessary surgical exploration(3,4). This occurred in 2 of our patients who had undergone laparotomy elsewhere for suspected appendicitis and Crohn's disease, respectively. On reviewing their history, it was evident that arthritis and skin rash were present along with acute abdomen but these had not received due attention. One patient had clinico-radiological evidence of intussusception and required laparotomy which showed intussusception with gangrene of caecum. Intussusception as a complication of HSP is a rare event(3,4,10) and may mandate urgent surgical intervention. Other infrequent manifestations reported in literature and also present in our cases included hepatosplenomegaly, lymphadenopathy and orchitis(10,13).

Neurological manifestations are also an unusual accompaniment of HSP and include coma, subarachnoid hemorrhage, seizures and Guillain-Barre Syndrome(13,14). The latter two were also seen in 2 of our patients. The patient with Gullian-Barre syndrome made complete neurological recovery on follow up. Two patients had radiological evidence of pleural effusion and consolidation. In one of them it occurred in post-operative period following laparotomy (for suspected Crohn's disease). Though these resolved with antibiotic treatment and were therefore presumed to be of bacterial etiology, these could also possibly be pleural hemorrhage(15) and pulmonary hemorrhage(16), respectively.

Elevated ESR and normocomplementemia (C_3) are the usually observed parameters in HSP. Thrombocytosis seen in 56% of our patients is a well documented feature of HSP and helps in distinguishing this form of purpura from that caused by thrombocytopenia(l/17). The degree of thrombocytosis is believed to correlate with severity of illness(17) though this could not be documented in our patients.

We performed skin biopsy in 36 of our patients with HSP. Findings of leukocytoclastic vasculitis with deposition of IgA and C_3 seen on direct immuno-flourescence (seen in 34 cases) help in confirming the clinical diagnosis especially in difficult or atypical cases(l,18). The two patients where both histology as well as direct immuoflourescence were negative, however had clinical features suggestive of HSP. It is known that an occasional patient may have negative results on skin biopsy(16,19,20). Also characteristic histological and immunoflourescence features may not be observed if biopsy is done late in the course of the disease(20).

"Nephritis is potentially the most worrisome feature of HSP and occurs in 20-50% of the patients usually within first 2-3 months of the diseases(21-23) and its incidence is higher in older children(3,10,23). We found a lower incidence (31%) of renal involvement in our patients. All our patients with HSP nephritis were older than 6 years and renal involvement occurred within first two months of onset of illness. Majority of children have minor urinary abnormalities while major renal involvement occurs only in small percentage of patients(3,10,23,24). However, major renal involvement was more frequent (64%) than mild degree of renal involvement (36%) in our series. The low incidence of nephritis with frequent major renal involvement seems to be due to low incidence of minor renal disease. The latter may be transient and is likely to be missed if repeated urinalysis are not carried out(3,22). This could have occurred in our patients because most of them were referred cases and it was not certain whether the urine was examined repeatedly before referral.

We have followed up our patients with major renal involvement for a mean period of 17.5 months (range 5-32 months). None have persistent urinary abnormalities, hypertension or raised creatinine. Since the number of patients is small and period of follow up short, meaningful conclusions are not possible at this stage. None of our patients with minor degree of renal involvement is having persistent urinary abnormalities.

Although corticosteroids are used for treatment of the acute abdominal pain, and hemorrhage(l,2,23), recent studies do not demonstrate any distinct advantage of prednisolone over supportive therapy(25). The role of corticosteroids in preventing renal disease is controversial(26,27). Treatment of HSP nephritis poses even more difficulties. Patients with minor renal involvement are managed conservatively. For children who have clinical or histological evidence of severe renal disease, corticosteroids with or without other immunosuppressants have been used, but a proven effective and accepted therapy for severe HSP is not available(22,28). However, it is recommended that because of poor long term prognosis in patients with severe HSP nephritis a trial of such therapy is reasonable to slow/arrest the progression of disease(23). We have used oral prednisolone and azathioprine (cyclophosphamide was not used because of gonadal toxicity) in patients with major renal involvement. In addition pulse high dose corticosteroids (dexamethasone in one and methylpred-nisolone in five) was used in those having crescentic glomerulonephritis. Though short term results have been favorable, long term follow-ups are needed before definite conclusions can be drawn regarding the renal outcome in our patients.

To conclude Henoch Schonlein purpura appears to be as common in our country as it is in the West. The clinical features in our patients are somewhat different from the previously published studies. In addition, we have also resorted to skin biopsy in majority of cases to confirm the diagnosis. Renal involvement was found to be less common, but when it occurred it was more severe. The short term outcome appears to be favorable even in those with major renal involvement. However, the long term prognosis in such patients would remain guarded.

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