HENOCH-SCHOENLEIN PURPURA

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Henoch-Schoenlein Purpura (HSP) is predominantly a disease of children characterized by non thrombocytopenic purpuric rash, abdominal pain, arthritis and nephritis due to vasculitis of small blood vessels.[1,2] These characteristic clinical manifestations, however, may appear in any sequence making the diagnosis difficult. HSP is also known as anaphylactoid and rheumatoid purpura; leukocytoclastic vasculitis and allergic vasculitis.[1,2]

HSP is more common in male children (male to female ratio of 1.5-2: 1). The disease is very rare in adults but occurs with similar frequency in both sexes. Seventy five percent of children with HSP are from 2-11 years.[1,3] HSP is rare in children younger than 2 years and has milder course with less frequent renal and gastrointestinal (GI) involvement.[3] HSP is less common in black than white children.[4] In 75% cases, the disease is preceded by upper respiratory tract infection including streptococcal sore throat. Cases of HSP may present in clusters and more cases occur in spring and autumn months.

ETIOLOGY AND PATHOGENESIS

The cause of HSP is unknown. Streptococcal pharyngitis, Yersinia, Legionella, Parvovirus, Adenovirus, Epstein-Barr virus, Varicella and Mycoplasma infections have all been reported to precede the clinical syndrome of HSP.[3] The disease has also been reported following exposure to drugs such as penicillin, ampicillin, erythromycin, quinine, quinidine, vaccines of typhoid and paratyphoid, measles, cholera, yellow fever certain foods, cold and insect bites.[1] Allergic basis for the illness has also been described.[3]

Vasculitis of small blood vessel is the basic pathogenetic lesion of HSP. Small vessels are surrounded by an acute leukocytoclastic inflammatory reaction and infiltrated by lymphocytes, polymorphs, circulating immune complexes, IgA, C3 and fibrin. Capillaries are most frequently involved but arterioles and venules may also be affected. Skin, kidneys, synovium, central nervous system (CNS) and GI system may be involved. Intussusception may result from vasculitis and edema of intestinal wall. Perforation of gut may also occur.[1,2]

Renal lesion of HSP consists of focal and segmental increase in mesangial cells and matrix. Generalized mesangial involvement occurs in some cases. Diffuse necrotizing glomerulitis with crescent formation is rare. Immunofluorescence studies show IgA deposits. Histopathologically, the renal lesion of HSP is identical to that of IgA nephropathy. There are other similarities between these two diseases including increase production of IgA and circulating immune complexes of IgA, deposits of IgA on immunofluorescence microscopy in skin lesions, decreased Fc receptor mediated immune clearance, progression to end stage renal disease and recurrence after renal transplantation. Renal involvement occurs in 20-50% cases of HSP, while 30% patients

with IgA nephropathy have skin rash and arthralgia. HSP occurs in younger patients while IgA nephropathy is common in older individuals.[1,2,4]

CLINICAL MANIFESTATION

Typically, there is an urticarial and purpuric rash on the buttocks and lower limbs, arthritis or arthralgia and abdominal pain. The presentation, however, may be extremely variable. Different manifestation of the disease may occur simultaneously, sequentially or in different combinations.

Cutaneous Manifestation

Skin lesions are present in 100% of cases. In 50% cases, however, skin lesion may not be the presenting feature. The typical lesions of HSP are urticarial wheals, erythematous maculopapules or large palpable echymotic rash. They blanch on pressure initially but become petechial or purpuric and non blanchable later on. They change from red to purple, then rusty and fade away. The lesions appear in crops and give a polymorphic appearance. The rash may be pruritic, last for weeks, be short lived and may recur.[1,2]

Skin manifestations of HSP may be atypical. They usually involve the buttocks and lower extremities. Face, trunk and upper limbs be may also involved. The typical distribution of skin lesions may be completely absent. HSP has also been described with orofacial lesion alone. Vesicular eruption, various patterns of erythema multiforme and erythema nodosum may occur as presenting features of HSP.[1,2,7] Non pitting angioedema of lips, eye lids, hands, feet, back, scrotum and perineum is common and especially striking in children younger than 3 years. Rarely the entire limb or a segment of limb such as forearm may be transiently swollen and tender.[1,2]

Gastrointestinal Tract Involvement

Colicky abdominal pain, which may be severe and associated with vomiting, is the commonest complaint. GI symptoms appear in 30-80% cases and are the most frequent manifestation after skin and joints involvement. Skin rash precedes the visceral involvement in majority of cases; however, in 14% patients visceral manifestation appears before the skin rash. This may lead to difficulty in diagnosis and unnecessary laparotomy for acute abdomen. Abdominal pain in most cases is due to submucosal and intramural extravasation of fluid and blood into the gut wall leading to mucosal ulceration. This may be associated with diffuse arterial inflammation and fibrinoid necrosis due to mesenteric vasculitis.[1] Peritoneal exudates and enlarged mesenteric lymph nodes may also be present. Other GI manifestations are intussusception with obstruction, infarction with intestinal perforation, pancreatitis and hydrops of gall bladder. In patients with HSP, a sudden onset or increase in abdominal pain may be secondary to these GI complications.[1,2] Most surgical complications occur after the skin rash. Abdominal pain that appears before the skin rash may be severe but is unlikely to be due to perforation or infarction of gut.[8]

Intussusception associated with HSP occurs in 2-3% cases. It is often the result of submucosal hematoma. In HSP Intussusception is ileoileal in 65% cases. In contrast, ileocolic Intussusception is the most common type (95%) in general population. Barium enema may miss the ileoileal intussusception of HSP and abdominal ultrasonography (US) is used for the diagnosis.[9] Abdominal US will show rounded mass with echocentric appearance described as a sliced onion". Intestinal wall thickening and abnormal peristalsis - findings highly suggestive of HSP- may also be identified on abdominal US.

Pancreatitis presenting with acute onset of vomiting and raised serum amylase[10], hydrops of gall bladder presenting with right upper quadrant pain and mass,[11] and ileal stricture occurring months after the acute

illness[12] have also been described as unusual GI manifestations of the syndrome. Stress ulceration or use of steroid may lead to massive bleeding from the stomach.[13]

Joints Involvement

Swollen, render and painful joints are common features of HSP. Arthritis, arthralgia or both are present in two third of patients having HSP and is the first presenting sign in 25% cases.[7] Large joints, particularly knee and ankle are most commonly involved whereas fingers and wrist joints are usually spared. Joints involvement is usually periarticular without effusion or hemorrhage. Joints are acutely involved. Complete resolution, however, is the rule with no residual deformity or articular damage. Arthralgia or arthritis may recur during the course of illness.[1,2,3]

Renal Involvement

Renal involvement occurs in 20-50% (variations are in part due to the adequacy of examination) of cases with HSP, usually within 3 months of the onset of skin rash. One percent patients with HSP develop persistent nephropathy and less than 1% progress to end stage renal disease (ESRD).[14] Renal manifestations precede the skin rash in 3% of cases. GI and renal involvement usually occur together. Recurrence of renal disease may be associated with recurrence of skin rash. Persistence of skin rash for 2-3 months is associated with renal involvement.

Renal disease is usually manifested by haematuria with or without casts or proteinuria. Rapidly progressive glomerulonephritis, nephrotic syndrome and nephritic-nephrotic syndrome all make part of the spectrum of renal involvement of HSP. Patients with haematuria alone do not develop ESRD. Fifteen percent of patients having both haematuria and proteinuria progress to ESRD. Nephritic-Nephrotic syndrome in HSP carries the worst prognosis with 50% cases developing ESRD. Children with HSP and Nephritic-Nephrotic syndrome, who become clinically and biochemically normal, do not develop ESRD. The onset of HSP nephritis in children older than 6 years, development of nephrotic syndrome, and crescent formation (in more than 50% glomeruli) are associated with poor prognos and progression to ESRD. Persistence of severe proteinuria is the most accurate predictor of ESRD.[1,2,3]

In HSP vasculitis of genital organ may produce the initial symptoms. Acute scrotal swelling occurs in 25-35% patients with HSP. Scrotal vessel involvement may also lead to the inflammation and hemorrhage of the testes, spermatic cord, epidydimus and scrotal wall. These patients can be treated expectantly, however, prompt surgical exploration is required when investigation of acute painful scrotal swelling can not exclude torsion.[15] Hydronephrosis, calcified ureter, hematoma of the bladder wall, urethritis and hemorrhagic spermatic cord are complications of HSP.[1]

Central Nervous System Involvement

CNS involvement is very rare. The most common symptom of CNS involvement in HSP is headache. Changes in mental status, mood liability, irritability, apathy, hyperactivity, focal deficits such as (aphasia, ataxia, chorea, cortical blindness, hemiparesis, paraparesis, hemiplegia, quadriplegia, subdural hematoma, cortical and intra cerebral bleeding, infarction, peripheral neuropathies (Guillian Barre syndrome, brachial plexus neuropathies) and mononeuraparthies (facial, femoral, sciatic, ulnar and peroneal nerve) all have been reported. Seizures (may be focal, partial, generalized or status epilepticus) are rare but may precede other systemic manifestations. Predisposing factors for seizures in HSP include hypertension (due to renal involvement), electrolyte imbalance (due to GI involvement) and CNS hemorrhage. Tran-

sient electroencephalographic abnormalities may also occur. Sudden changes in behavior or level of consciousness may indicate intracranial complications.[12]

Haematologic

Thrombocytosis is the commonest hematologic manifestation present in two third of cases having abdominal pain and GI bleeding. This is associated with raised ESR and may be the expression of acute inflammation.[16] Vitamin K and Factor VIII deficiency and hypoprothrombinaemia are other haematologic complications that can complicate the course of HSP.[17] Pulmonary hemorrhage with haemoptysis and hemorrhage into large muscles with severe pain have also been described.[18,19]

DIAGNOSIS

Skin rash, arthritis and renal involvement makes the diagnosis very easy in typical cases. In patients presenting with atypical features, when one symptom predominates or multiple system involvement is not recognized, the diagnosis may be difficult. Differential diagnosis include conditions having skin rash (drugs, idiopathic thrombocytopenia, clotting factors deficiency, septicaemia, child abuse), abdominal pain (obstruction, perforation, intussusception), joint pain (rheumatic fever, rheumatoid arthritis, SLE, polyarteritis nodosa), renal involvement (acute glomerulonephritis) and testicular swelling and pain (torsion, orchitis, incarcerated hernia).[1]

LABORATORY INVESTIGATION

In HSP the diagnosis is mainly clinical. Laboratory findings are non specific and non diagnostic. Laboratory tests should be guided by clinical course of the disease. More specific tests include the determination of serum IgA levels and skin biopsy. Serum IgA level may be elevated in 50% patients with HSP. Skin biopsy from a lesion will show leukocytoclastic vasculitis with IgA deposits revealed on immunofluorescence.

Supportive laboratory findings include anaemia (due to acute bleeding), normal or elevated blood counts, leukocytosis with left shift, eosinphilia, thrombocytosis, raised ESR, raised serum amylase (secondary to pancreatitis) and electrolyte changes (secondary to GI involvement). Factor VIII and factor XIII level may be low but prothrombin time and partial thomboplastin time may be normal. Chest radiograph should be obtained in HSP patients presenting with haemoptysis.

Urine should be examined during the acute attack and monthly for 3 months (to detect late onset nephritis) for haematuria, proteinurea and casts. Patients having protienurea should have 24 hour urine measurement of protein excretion. Serum protein, blood urea nitrogen and creatinine should be determined. [12] Patients with HSP and nephritic or nephrotic syndrome should have renal biopsy.[20]. Histopathological changes range from minimal change lesion to severe crescent formation. Light microscopy shows hypercellularity, segmental sclerosis, fibrosis, and infiltration by mononuclear cells. Mesangial, subendothelial and subepithelial deposits are found on electron microscopy. Immunofluorescence studies show diffuse glomerular deposits staining positive for IgA, C3, IgG, and IgM.[1]

Stool for occult blood (guaiac test) is positive in almost half of the patients with HSP. Liver function tests and US should be done in patients with HSP with suspicion of hydrops of gall bladder. Abdominal radiography, US and Barium studies (which will show coil spring appearance due to thickening of ileal folds, thumb printing appearance in the duodenum) should be done to investigate possible intra abdominal involvement where indicated. Computed tomography of skull is indicated if neurological involvement is present. Streptococ-

cal infection, infectious mononucleosis or other infectious agents should be investigated when clinically indicated. Antinuclear antibody and rheumatoid factors (expected to be negative), antistreptolysin O titer (may be raised in 30% cases) and C3 and C4 levels (may be low) should be determined.[1,2]

TREATMENT

Specific treatment for HSP is not available. Supportive care including proper hydration, frequent assessment of vital signs and monitoring and treatment of complications is the most important goal of management. Appropriate supportive management for kidney failure, GI involvement, hemorrhage and CNS disease should be provided.[1,2]

All unnecessary exposure to drugs and other allergen must be avoided. Non steroidal anti inflammatory drugs may be used for arthralgia. Corticosteroid are not indicated for skin rash, arthritis, edema or isolated nephritis. Prednisone 1-2 mg/kg/day for 5-7 days is beneficial in cases of abdominal pain and GI hemorrhage. Other indications for corticosteroids include localized vasculitis in the lungs, testes and CNS.[1,2] Plasmapheresis has been reported to benefit in some cases of HSP with renal failure.[3] Prednisone 1-2.5 mg/kg/day for 21 days given early during the course of illness has been reported to decrease the incidence of nephropathy.[4] Lower levels of Factor VIII correlate with more severe disease particularly abdominal symptoms. Improvement in Factor VIII levels and symptoms has been reported after 3 days administration of Factor VIII.[5]

PROGNOSIS

In children with HSP without CNS and renal involvement, the prognosis is very good. The usual length of illness is 4-6 weeks. Recurrence occurs in almost 50% of cases usually within 6 weeks. Late recurrence upto 7 years may occur necessitating long term follow up. CNS and renal involvement may lead to long term morbidity. Children with renal disease associated with HSP need follow up for progression to ESRD, which may occur many years after the onset of acute illness.

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