Henoch-Schönlein Purpura

Definition

Diffuse systemic hypersensitivity vasculitis of uncertain aetiology that affects small blood vessels, producing a characteristic palpable purpuric rash, often associated with joint swelling and abdominal pain.

Criteria

Formal diagnosis dependent on having 2+ of the following criteria (sens 87.1%, spec 87.7%):

- Palpable purpura
- Age of onset less than 20
- Bowel angina (abnormal pain after meals or bowel ischemia usually with bloody diarrhoea)
- Granulocytic infiltration of vessel walls

Epidemiology

Incidence: Most common childhood vasculitis. 10-30/100,000 school-aged children per year
Geography: UK>USA>Scandinavia
Age: Usually <20yrs. 50% are <6yrs, 90% <10yrs
Sex: Probably M=F (until recently thought 1.5-2.0M:1F in children)
Seasonal: More common in winter, spring, and fall.
Racial: Most common in Whites, Asian, and Native Americans. Low incidence in Blacks.
Genetics: susceptibility factors are likely but not yet determined. Weak associations with HLA-B35 and HLA-DR4- DQW4.

Pathophysiology

- Probably Type III immune complex reaction involving abnormal IgA.
- Some stimulus e.g. infection→IgG against abnormal IgA→large IgA- immune complexes that are unable to be degraded in liver.
- Deposited in skin capillaries, arterioles, & venules, GIT, kidneys, joints, occ CNS & lungs.
- Renal nephritis histological appearance identical to IgA nephropathy (Berger's Disease).
- Rheumatoid factors and IgA autoantibodies can be produced.
- Complement activation may occur.
- Possible other factors: IL-1 & IL-6, TNF-α, TGF-β, PAF, PDGF, platelet factor IV & plts

Aetiology

~75% associated URTI or GI infection in preceding 1-3wks
Infectious agents implicated:

- Staphylococcus, Group A β-Haemolytic Streptococcus
- Parainfluenza, parvovirus B19, adenovirus,
- Mycoplasma
- EBV, Hepatitis B or C, Varicella
- Campylobacter, Salmonella, Yersinia, Shigella, Legionella

Other associations:

- Vaccinations
  - Typhoid, Measles, Cholera, Yellow fever, H1N1 influenza A
- Drugs or food
  - Thiazides, ampicillin, erythromycin, penicillin, quinidine, quinine, ACEI
- Exposure to cold
- Insect bites

Clinical Features

Prodrome

- Fever
- Headache
- Anorexia

Characteristic symmetric rash (100%)

- Extensor surfaces of arms and legs, especially ankles, buttocks, and elbows.
- The face and trunk are less often involved.
- Rapid progression from urticaria through maculopapular lesions to petechiae and purpura which is often palpable.
- Some lesions coalesce and become necrotic.
- Resolution occurs over 2-4 weeks.
- Fresh crops can frequently appear.

Joint involvement

- 75% case have these transient symptoms.
- Usually large joints – knee, ankle and hip most frequently.
- Elbows, hands and feet may also be involved.
- Arthralgia is more common than serous effusions of joints.
- Joint symptoms may precede the rash in 25% of cases.

Abdominal pain

- Occurs in 60-70% of cases.
- >50% have occult blood in stools, diarrhoea (with or without blood), or haematemesis.
- Usually colicky pain, often post-prandial, caused by oedema/damage to the GIT vessels.
- Intramural haematomas may cause obstruction or intussusception (<5%).
- Rarely bowel infarction, perforation or massive haemorrhage.

Renal disease

- Complication in 25% of children <2yrs, but 50% of older children.
- Spectrum of severity:
    - Microscopic haematuria
    - Mild proteinuria
    - Acute glomerulonephritis or nephrotic syndrome
    - Oliguria and renal failure
- The most common manifestation of renal disease is haematuria.
- Generally becomes apparent within 1-6 months of the rash onset.
- Renal histopathology may include minimal change to severe GN that is indistinguishable from IgA nephropathy.

Uncommon features

- GUS: Scrotal swelling – orchitis, torsion, priapism
- CNS: Headaches, behavioural changes, seizures, focal deficits
- PNS: Guillain-Barre, poly- and mono-neuropathies
- GIT: Hepatosplenomegaly, hydrops of gallbladder, pancreatitis
- CVS: Myocardial infarction
- RS: Pulmonary haemorrhage or pleural effusion

Differential Diagnosis

- Platelet disorder e.g. ITP, TTP
- Sepsis/infection: meningococcemia, Rocky Mountain Spotted Fever
- Leukaemia
- Coagulopathies, DIC
- Other primary and secondary vasculitides: PAN, Wegener granulomatosis
- Drug reactions
- Bruising: Trauma, NAI

Investigations

Urine: Cells, casts, protein, culture

Bloods:

- FBC: Hb usually normal, WCC can be raised, Platelet count normal or elevated
- ESR: normal or elevated
- Clotting: normal
- UEC: urea and creatinine elevated with renal involvement

Special bloods:

Serum total IgA: ↑ in only 50% but galactose-deficient IgA1 level may predict nephritis.
Serum C3: normal (decreased in post-streptococcal GN and SLE)
Antinuclear antibody: negative (elevated in SLE)

Throat swab: For Group A Beta-Haemolytic Strep: positive in up to 75% of cases

Imaging:

- CXR: May show interstitial lung disease.
- AXR/USS/CT: If abdominal pain severe/persistent
- Air or contrast enema: in diagnosing/treating intussusception.

Renal Biopsy: if severe renal involvement

Management

Usually resolves spontaneously with rest, supportive therapy and monitoring for Cx.

Analgesics and NSAIDs: (care in renal impairment) for joint pain.

Steroids: Used for painful cutaneous oedema and abdominal pain. No evidence that they prevent more serious renal disease. Pulsed methylprednisolone used in severe GN/nephrotic syndrome.

Immunosuppressants: Generally disappointing results with azathioprine, cyclophosphamide, and plasmaphoresis. Cyclosporin A possibly helpful to achieve remission.

Other treatments:

- Prophylactic antibiotics have no proven value but sometimes used with recurrent cases.
- ACEI & ARBs if persistent proteinaemia & may retard renal disease in GN patients.

Complications

- End stage kidney disease (acute or as a late sequela)
- Persistent hypertension
- Protein losing enteropathy
- Strictures of the oesophagus
- Bowel perforations and infarctions
- Pseudomembranous colitis
- Appendicitis
- Skin necrosis
- Subarachnoid, subdural, and cortical haemorrhage and infarction

Prognosis

- Generally excellent – settling in 2-6 weeks.
- Better prognosis associated with younger age.
- About 33% have a recurrence (most within the first 6 weeks).
- Most have only one to three episodes of purpura; however, a few will continue to experience symptoms for months or years.
- Persistent renal involvement is the most serious long-term morbidity.
- However <5% of cases progress to end-stage renal disease
- Predictors for persistent/ES renal disease:
    - Rash persistence.
    - Bloody stools.
    - Chronic recurrence.
    - Age>6yrs.
    - GN with glomerular crescent formation on biopsy.
    - The presence of proteinuria and haematuria
    - Combination of nephritis-nephrotic symptoms – 50% develop end-stage disease after 10 years.

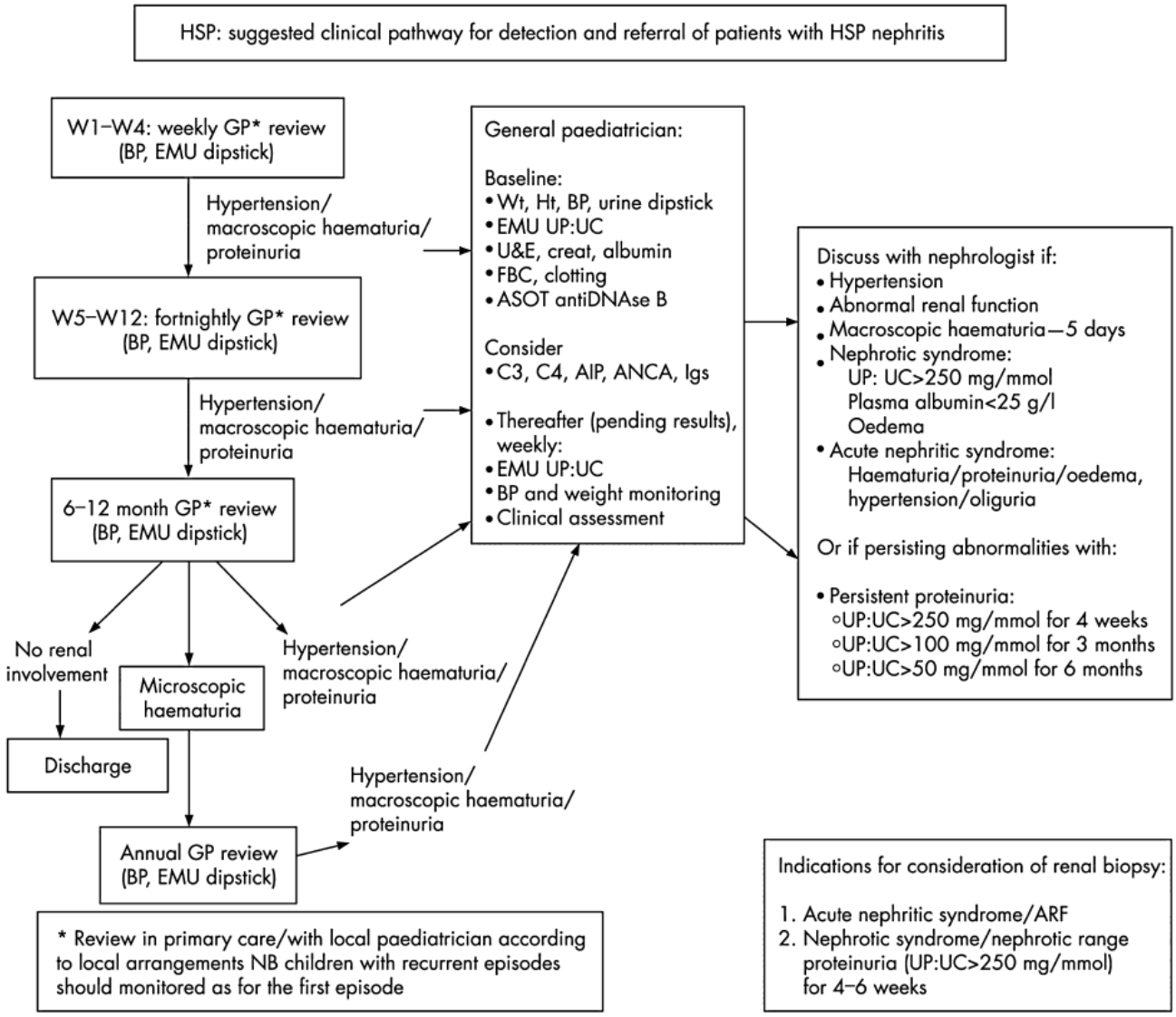

Fig. 7 Suggested clinical pathway for detection and referral of patients with HSP nephritis. This pathway has been adapted from local guidelines developed by Dr D Hothi and Bristol Paediatric Nephrologists, and reprinted with permission from reference 50. Abbreviations: EMU – early morning urinalysis; UP:PC – urine protein/creatinine ratio.