Henoch-Schönlein Purpura (HSP)

See also HSP (Peds)

Background

1. Definition
    - Autoimmune, IgA-mediated, self-limiting, systemic, small-vessel vasculitis
2. Synonyms:
    - Hemorrhagic capillary toxicosis
    - Allergic purpura
    - Anaphylactoid purpura
    - Rheumatoid purpura
    - Anaphylactoid vasculitis
3. General information:
    - Occurs in children and adults
    - Main distinctions:
        - Children:
            - The most common systemic vasculitis
            - Associated with serious GI vasculitis resulting in intussusception
        - Adults:
            - More serious renal disease
            - Intussusception is rare

Pathophysiology

1. Pathology of disease
    - No single etiologic cause
    - Deposition of IgA immune complexes in affected organs
    - In HSP capillaries, arterioles and venules affected as opposed to Polyarteritis nodosa, and Wegener's granulomatosis which involve small and medium size arteries
    - Biopsy shows:
        - Skin: leukocytoclastic vasculitis
        - Kidney: endocapillary proliferative glomerulonephritis involving mesangial region
2. Incidence, prevalence
    - Children: 9-20/100,000 aged 2-14 yrs in the US
        - Highest between 6 months and 8 years of age, peaking at 4-6 yrs
    - Adults: less common
    - More common in late fall/early winter and spring
    - Male: female ratio is 2:1
    - Race: white, asian > blacks
3. Risk factors
    - Recent infections:
        - Viral URI, EBV, varicella, parvovirus B12, and Campylobacter enteritis, group A Streptococcus, Staphylococcus, or Mycoplasma
    - Recent vaccinations
        - Typhoid, measles, cholera, yellow fever
    - Drug allergies

- Penicillin or sulfonamides
- Insect bites
- Family Hx of inherited IgA or complement deficiency disorders

4. Morbidity / mortality
   - Initial phase:
     - Due to GI complications
     - 50% develop GI manifestations
     - Complete recovery in 94 % of children and 89 % of adults
   - Long-term:
     - Due to renal disease
     - More common in adults than in children
     - <1% children develop End Stage Renal Disease (ESRD)
     - 11% adults develop ESRD
     - 13% severe renal insufficiency (creatinine clearance <30 cc/min per m2)

Diagnostics

1. History
   - Constitutional:
     - Fever
     - Malaise
     - Recent URI, hepatitis, strep infection.
   - Skin:
     - Classic dark-red and purple rash on legs and buttocks
     - Swelling of hands and feet, eyelids
   - Gastrointestinal:
     - Abdominal pain, nausea vomiting, abdominal distension
     - Hematemesis, hematochezia, or melena
   - Musculoskeletal:
     - Hx of joint pain and swelling
     - Involve hips, knees, and ankles
     - Less commonly elbows, wrists, and hands
     - Precedes rash in 25% of cases
   - Renal involvement:
     - Hx of gross hematuria
   - Genital involvement:
     - Hx of scrotal swelling, testicular pain
2. Physical exam
   - Vital signs:
     - Low grade fever
     - Hypertension
   - Skin: 100% of patients
     - Ecchymotic (>1 cm) or petechial (pin point hemorrhages <2 mm), and palpable purpuric (2-10 mm) symmetrically distributed rash
     - Commonly involve:
       - Buttocks, knees, and ankles

        - Less commonly:
            - Face, trunk, upper extremity
        - Angioedema of the scalp, peri-orbital region, ears, dorsum of the hands and feet, back, scrotum, and perineum
    - Gastrointestinal: 50% of patients
        - Abdominal tenderness (2/3 of cases)
        - Hepatosplenomegaly may be present
        - Signs suggestive of GI bleeding, intussusception (ileal) or bowel infarction and bowel perforation
        - Rarely acute pancreatitis, gall bladder involvement, and, protein-losing enteropathy(children)
    - Musculoskeletal: 43 to 82 % of patients of patients
        - Involved joints are tender, swollen, with limitation of motion
        - Symmetrical, non-migratory, Polyarticular, and non deforming arthritis
        - Erythema or warmth are uncommon
        - Hx of Pain may be out of proportion to external findings
    - Renal involvement: 21 to 54% of patients
        - Usually no physical signs
        - Signs suggestive hematuria and/or proteinuria without any abnormality in renal function or nephritis or nephrosis with renal insufficiency.
        - Causes 15% of all childhood glomerulonephropathies
        - Severity correlates generally w/severity of clinical Sx
        - Usually seen days to 4 weeks after systemic Sx
    - Genital: 13 % of patients
        - Tenderness and swelling of the involved testicle and/or scrotum
        - may mimic testicular torsion
    - CNS: 1 to 3 % of patients
        - Seizures, focal neurologic deficits, ataxia, intracerebral hemorrhage, and central and peripheral neuropathy
    - Eyes:
        - Keratitis and uveitis
3. Diagnostic testing
    - Clinical diagnosis
        - No specific labs and imaging indicated
        - Tests may be useful to exclude other potential Dx
    - Lab evaluation
        - Urinalysis:
            - Hematuria and proteinuria
        - Stool guaiac:
            - Positive in GI involvement
        - BMP (electrolytes, BUN/creatinine):
            - Elevated in renal involvement
        - Lipase:
            - Elevated in GI involvement
        - CBC with diff, platelet count:
            - Leukocytosis, eosinophilia, normal platelet count
        - ESR & CRP:
            - Elevated

        - PT/PT:
            - Normal, to r/o hemorrhagic disorders
        - Serum immunoglobulin:
            - IgA-elevated and IgG & IgM- normal
        - Serum complement factor 3 & 4 levels:
            - Normal (decreased in streptococcal GN)
        - ASO and anti-DNase titers:
            - To diagnose preceding streptococcal infection
        - Throat swab:
            - May be positive for group A beta-hemolytic streptococci
    - Diagnostic imaging
        - Abd US:
            - To rule out intussusception, testicular torsion.
        - Abd x-ray:
            - To identify small bowel obstruction or intussusception.
        - Abdominal CT:
            - If intussusception is suspected and abdominal ultrasound is inconclusive
        - Barium enema: not indicated for suspected intussusception
    - Other studies
        - Skin or renal biopsy:
            - IgA deposits on immunofluorescence microscopy
4. Diagnostic "Criteria"
    - Characterized by tetrad of clinical manifestations:
        - Palpable purpuric rash in patients with neither thrombocytopenia nor coagulopathy (mandatory finding)
        - Arthritis/arthralgia
        - Abdominal pain
        - Renal disease
    - Develops in any order and at any time over a period of several days to several weeks
    - Biopsy with predominant IgA deposition

Differential Diagnosis

1. Key DDx
    - Idiopathic thrombocytopenic purpura
        - Purpuric rash with severe thrombocytopenia
        - No renal or musculoskeletal involvement
    - Meningococcal septicemia
        - Pt acutely ill with profound hemodynamic alterations
        - Septic appearance
        - Purpuric rash with thrombocytopenia
    - Rocky Mountain Spotted Fever
        - Hx of tick bite, high fever, severe headache unresponsive to antipyretics
        - Purpuric rash with thrombocytopenia
        - Commonly involve CNS
    - Polyarteritis nodosa
        - Similar Sx of HSP

        - But fails to follow typical course or recurs multiple times
        - Multiorgan involvement
        - Biopsy medium and small vasculitis
    - Rheumatoid arthritis (including juvenile form)
        - Musculoskeletal Sx predominant
        - No rash or GI or renal involvement
    - Systemic lupus erythematosus
        - Uncommon in children
        - Purpuric rash rare
        - Photosensitive rash with butterfly distribution
        - Renal and hematological involvement common
        - ANA and anti-dsDNA are positive
    - Hemolytic uremic syndrome
        - Preceded by diarrhea
        - Present with acute onset of ARF
        - Hemolytic anemia and thrombocytopenia present
    - IgA nephropathy
        - Frequently affects adults
        - Renal involvement similar to HSP
        - No rash, GI tract and joint involvement
    - Acute hemorrhagic edema of infancy (AHEI)
        - Occurs in children <2 yrs
        - Skin lesions involve trunk, face and upper extremities
        - No kidney or GI tract involvement
    - Hypersensitivity vasculitis
        - Hx of exposure to drugs or infection, or without an identifiable trigger
        - Present with fever, urticaria, lymphadenopathy, and arthralgias
        - No renal involvement
2. Extensive DDx
    - Churg-Strauss syndrome
        - Age of onset 15-70 years and more common in men
        - Triad of
            - Allergic rhinitis, asthma, and peripheral blood eosinophilia
        - Biopsy shows granulomatous pANCA-associated small vessel vasculitis
    - Wegener's granulomatosis
        - Onset at any age, with peak in 4th decade
        - More common in males
        - Triad of
            - Upper respiratory tract, lungs, and kidneys involvement
        - Biopsy shows granulomatous cANCA-associated small vessel vasculitis
    - Microscopic polyangiitis
        - Age of onset 40-60 years and more common in men
        - Skin (palpable purpura)
        - Renal and lung involvement common
        - Biopsy shows non -granulomatous pANCA-associated small vessel vasculitis

- Systemic-onset Juvenile idiopathic arthritis (Still's disease)
  - Evanescent, salmon colored macular rash on trunk and extremities
  - Associated with fever, hepatosplenomegaly and lymphadenopathy
  - Polyarticular joint pain, swelling and morning stiffness
  - ANA, RF factor and anti-dsDNA are positive
- Subacute bacterial endocarditis
  - HX of heart problems
  - No associated GI or Renal involvement
  - Skin lesions are splinter hemorrhages localized to digits
  - Asymmetric arthritis affecting up to 3 joints
- Septic arthritis
  - Common in children aged 1-3yrs
  - Typically involves 1 or 2 joints
  - Associated with marked joint effusion, erythema, warmth and tenderness
- Toxic synovitis
  - Common cause of Hip pain in children aged 3-10 years
  - HX of Recent respiratory infection or trauma
  - Mono articular joint involvement
  - No systemic involvement
- Rheumatic fever
  - Migratory arthritis affecting large joints
    - Knees, ankles, wrists and elbows
  - Skin lesions are pale red macules or papules on the trunk and proximal limbs (erythema marginatum)
  - Associated Sx of
    - Chorea, subcutaneous nodules, carditis
  - Raised or increasing streptococcal antibody titer
- Mixed cryoglobulinemia
  - Palpable purpura limited to lower extremities
  - Hx of hepatitis C
  - Multiple organ involvement, mainly skin, liver, renal, peripheral nerves
  - Systemic vasculitis secondary to circulating immune complex deposition in the small vessels
- Child abuse
  - Presentation incompatible with the stated history
  - Skin rash with bruises of different age and pattern
- Drug reaction
  - Recent HX of new medication use
  - Recurrence of skin rash in same distribution either involving entire body or same distribution
  - No associated GI or renal involvement

Therapeutics

1. Acute treatment
   - Supportive care with bed rest and oral hydration / IV fluids
   - Symptomatic pain management with acetaminophen / NSAIDs
     - Naproxen, 10-20 mg/kg in two divided doses/day, max 1500 mg/day
     - Ibuprofen 400-800 mg PO q 4h-6h, max 3200 mg/day).

- NSAIDs should be avoided in any patient with GI symptoms or renal disease

2. Further management (24 hrs)
   - Monitor for complications:
     - GI: intussusception, bowel infarction or perforation, peritonitis, GI bleeding, pancreatitis.
     - Renal: fluid and electrolyte imbalance, hypertension, nephrotic syndrome, renal insufficiency.
     - CNS: intracranial hemorrhage.
   - Complication needs prompt evaluation including specialist consultation, surgical intervention and/or targeted treatment
   - Systemic corticosteroids:
     - Use is controversial
     - Do not shorten course or recurrence of disease
     - Indications:
       - Severe abdominal pain or GI complications
       - Severe musculoskeletal pain
       - Severe or persistent renal disease
       - Severe orchitis
       - Pulmonary hemorrhage
       - Severe CNS symptoms
     - Dosage
       - Needs tapering
       - Oral Prednisone
         - 1 mg/kg /day for two weeks, 0.5-1 mg/kg /day for 1 week, then 0.5 mg/kg every other day for 1 week., max dose of 80 mg/day, OR
       - Parenteral Methylprednisolone
         - 0.8-1.6 mg/kg/day, max dose of 64 mg/day
     - The following Tx may be beneficial in pts with severe crescentic nephritis:
       - High-dose IV pulse Methylprednisolone (250-1000 mg /day) for 3 days followed by oral Prednisone (1 mg/kg /day) for 3 months, OR
       - High-dose Prednisone with cyclophosphamide (2-3 mg/kg/day PO for 60-90 days or 0.5-1 g/m2 IV monthly for 2-3 months) or azathioprine (2-3 mg/kg/day PO, QD)

3. Long-term care
   - Monitor for subsequent episodes of HSP
   - Recurrence common in:
     - 1/3 of patients
     - Patients with renal involvement
     - Occurs within four months of the initial presentation
   - Monitor for late renal disease with lab tests

Follow-Up

1. Return to office
   - HSP without renal impairment:
     - Follow with UA and BP monitoring during every visit
   - Weekly or biweekly for first 2 months

- Monthly or every other month until 1 year
- Continued screening during subsequent well-child visits by PCP
- HSP with renal involvement:
  - More frequent and specific monitoring is required with guidance from a nephrologist

2. Refer to specialist
   - When general condition is worsening or conventional Tx is inadequate
   - Nephrology
     - Patients with persistent microscopic hematuria, proteinuria, hypertension, or abnormal BUN and/or creatinine levels, or renal insufficiency
3. Admit to hospital
   - Inability to maintain adequate hydration with oral intake
   - Signs of shock present
   - Mental status changes
   - Severe abdominal pain
   - Signs of acute abdomen
   - Significant GI bleeding
   - Severe joint involvement limiting ambulation and/or self-care
   - Renal insufficiency (elevated creatinine), hypertension, and/or nephrotic syndrome
   - Differential Diagnosis cannot be excluded
     - Sepsis (meningococcal septicemia)
     - Severe septic arthritis

Prognosis

1. Excellent in children
2. Recurrent disease may not predict worse long term outcomes
3. Excellent renal prognosis if transient hematuria and proteinuria resolves within several months.
4. Poor renal prognosis with:
   - Nephrotic syndrome
   - Renal insufficiency
   - Hypertension
   - Crescentic glomerulonephritis (>50%)
   - Tubulointerstitial nephritis

Prevention

1. No effective preventive measures

Patient Education

1. Handout from
   - http://familydoctor.org/online/famdocen/home/children/parents/special/birth/312.html
   - http://www.aafp.org/afp/980800ap/980800b.html
   - http://www.chw.org/display/PPF/DocID/21657/router.asp

References

1. Incidence of Henoch-Schonlein purpura, Kawasaki disease, and rare vasculitides in children of different ethnic origins. Gardner-Medwin JM; Dolezalova P; Cummins C; Southwood :Lancet 2002 Oct 19;360(9341):1197-202
2. Henoch-Schonlein purpura in adulthood and childhood: two different expressions of the same syndrome. Blanco R; Martinez-Taboada VM; Rodriguez-Valverde V; Garcia-Fuentes M; Gonzalez-Gay MA : Arthritis Rheum 1997 May;40(5):859-64.
3. Henoch Schonlein purpura in childhood: epidemiological and clinical analysis of 150 cases over a 5-year period and review of literature. Trapani S; Micheli A; Grisolia F; Resti M; Chiappini E; Falcini F; De Martino M: Semin Arthritis Rheum. 2005 Dec;35(3):143-53.
4. Seasonal distribution of Henoch-Schonlein purpura. AU Atkinson SR; Barker DJ SO Br J Prev Soc Med. 1976 Mar;30(1):22-5.
5. Circulating IgA-immune complexes in Henoch-Schonlein purpura. A longitudinal study of their relationship to disease activity and vascular deposition of IgA.. Kauffmann RH; Herrmann WA; Meyer CJ; Daha MR; Van Es LA :Am J Med 1980 Dec;69(6):859-66.
6. Small-vessel vasculitis. Jennette JC; Falk RJ : N Engl J Med 1997 Nov 20; 337(21):1512-23. AD Department of Pathology, University of North Carolina, Chapel Hill 27599-7525, USA. PMID 9366584
7. Henoch-Schonlein purpura in children from northwestern Spain: a 20-year epidemiologic and clinical study. Calvino MC; Llorca J; Garcia-Porrua C; Fernandez-Iglesias JL; Rodriguez-Ledo P; Gonzalez-Gay MA : Medicine (Baltimore) 2001 Sep;80(5):279-90
8. Intra-abdominal manifestations of Henoch-Schonlein purpura. Choong CK; Beasley SW: J Paediatr Child Health 1998 Oct;34(5):405-9
9. Recurrent Henoch-Schonlein purpura in children. Prais D; Amir J; Nussinovitch M: J Clin Rheumatol. 2007 Feb;13(1):25-8
10. Chang, WL, Yang, YH, Lin, YT, Chiang, BL. Gastrointestinal manifestations in Henoch-Schonlein purpura: a review of 261 patients. Acta Paediatr 2004; 93:1427.
11. Connolly B, O'Halpin D. Sonographic evaluation of the abdomen in Henoch-Schonlein purpura. Clin Radiol 1994;49:320-3.
12. Schwab, J, Benya, E, Lin, R, Majd, K. Contrast enema in children with Henoch-Schonlein purpura: J Pediatr Surg 2005; 40:1221
13. Gastrointestinal and renal involvement in vasculitis: management strategies in Henoch-Schonlein purpura. Szer IS :Cleve Clin J Med. 1999 May;66(5):312-7
14. Allen, DM, Diamond, LK, Howell, DA. Anaphylactoid purpura in children (Schonlein-Henoch syndrome): review with a follow-up of the renal complications. Am J Dis Child 1960; 99:833.
15. A randomized, placebo-controlled trial of prednisone in early Henoch Schonlein Purpura [ISRCTN85109383]. Huber AM; King J; McLaine P; Klassen T; Pothos M: BMC Med. 2004 Apr 2; 2:7.
16. Early prednisone therapy in Henoch-Schonlein purpura: a randomized, double-blind, placebo-controlled trial. Ronkainen J; Koskimies O; Ala-Houhala M; Antikainen M; Merenmies J; Rajantie J; Ormala T; Turtinen J; Nuutinen M : J Pediatr. 2006 Aug;149(2):241-7.
17. Weiss PF, Feinstein JA, Luan X, Burnham JM, Feudtner C, Effects of corticosteroid on Henoch-Schönlein purpura: a systematic review. Pediatrics. 2007 Nov; 120(5):1079-87.

18. Flynn JT, Smoyer WE, Bunchman TE, Kershaw DB, Sedman ABTreatment of Henoch-Schönlein Purpura glomerulonephritis in children with high-dose corticosteroids plus oral cyclophosphamide.: Am J Nephrol. 2001 Mar-Apr;21(2):128-33
19. The adult kidney 24 years after childhood Henoch-Schonlein purpura: a retrospective cohort study. Ronkainen J; Nuutinen M; Koskimies O: Lancet 2002 Aug 31;360(9334):666-70.
20. Prognosis of Henoch-Schonlein nephritis in children. Counahan R; Winterborn MH; White RH; Heaton JM; Meadow SR; Bluett NH; Swetschin H; Cameron JS; Chantler C: Br Med J 1977 Jul 2;2(6078):11-4
21. Henoch-Schonlein purpura in children. Report of 100 patients and review of the literature. Saulsbury FT :Medicine (Baltimore) 1999 Nov;78(6):395-409.
22. Henoch-Schonlein Purpura in adults: outcome and prognostic factors. Pillebout E; Thervet E; Hill G; Alberti C; Vanhille P; Nochy D J Am Soc Nephrol 2002 May;13(5):1271-8.
23. Kawasaki Y, Suzuki J, Sakai N, et al. Clinical and pathological features of children with Henoch-Schoenlein purpura nephritis: risk factors associated with poor prognosis. Clin Nephrol 2003;60:153-60
24. Henoch-Schönlein Predictors of outcome in Henoch-Schonlein nephritis in children and adults. Coppo R; Andrulli S; Amore A; Gianoglio B; Conti G; Peruzzi L; Locatelli F; Cagnoli L: Am J Kidney Dis. 2006 Jun;47(6):993-1003.
25. Purpura: A Review by Debra M. Kraft, M.D., Denise McKee, M.D., and Carol Scott, M.D. [http://www.aafp.org/afp/980800ap/kraft.html] American Academy of Family Physicians, August 1998.
26. Leung AK, Chan KW. Evaluating the Child with Purpura: Am Fam Physician 2001; 64:419-28 http://www.aafp.org/afp/20010801/419.html.
27. Junnila JL, Cartwright VW. Chronic musculoskeletal pain in children: part I. Initial evaluation. Am Fam Physician 2006;74:115-22 http://www.aafp.org/afp/20060701/115.pdf
28. Junnila JL, Cartwright VW. Chronic Musculoskeletal Pain in Children: Part II. Rheumatic Causes. Am Fam Physician 2006;74:293-300 http://www.aafp.org/afp/20060715/293.pdf

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