Fever of Unknown Origin in PEDs

Background
1. Definition
   o Fever >101.1°F [38.4° C] in a child
     ▪ Lasting >7–14 days
     ▪ H&P and preliminary lab eval fail to reveal a probable cause for fever
   o In contrast, fever w/o source (FWS) is =< 7 days
2. General information
   o Most children w/FUO have uncommon presentations of common illnesses, rather than rare or exotic dz
   o 3 most commonly identified causes of FUO are:
     ▪ Infectious dz
     ▪ Rheumatologic disorders
     ▪ Malignancies

Pathophysiology
1. Pathology of dz
   o Dependent upon underlying etiology
2. Incidence/ prevalence
   o No data available on frequency of FUO in children
3. Risk factors
   o Immunodeficiency
   o Chronic medical conditions/ challenges
     ▪ "Children w/Special Healthcare Needs"
   o Exposures to infectious dz
   o Travel to developing countries
4. Morbidity/ mortality
   o 40% of children w/FUO have serious, long-lasting sequelae
   o Cause-related mortality ranges from 9-17%

Diagnostics
1. History
   o Clinical approach to any child w/FUO should be individualized
   o Fever: method of measurement, duration, height and pattern
     ▪ Is fever real or not?
     ▪ Is fever persistent or are there periods of complete cessation between episodes?
   o Other associated symptoms
     ▪ Location
     ▪ Length of time involved
   o Contacts
     ▪ People: ill contacts, carriers
     ▪ Animal: dog, cat, rodent, exotic pets, others
     ▪ Insect: mosquitoes, ticks, others
   o Travel hx
     ▪ Especially foreign, w/in past 12 mos
2. Medications
   - Current medications
   - Consider any meds which could cause drug fever
   - Consider herbal and OTCs

2. Ethnicity/ family hx
2. Past medical hx
   - Immunization status
   - Transfusion hx

2. Physical exam
   - General assessment
     - Documented fever? Oral, tympanic or rectal?
     - Growth curves: poor wt gain or wt loss? Decr linear growth?
   - Thorough and complete PE
   - Specific PE areas to focus on
     - Skin lesions, rashes
     - Eyes
     - Sinuses
     - Oropharynx
     - Chest
     - Heart
     - Abdomen
     - Bone/ joint exam
     - Rectal, genital exam, pelvic exam if sexually active

3. Diagnostic testing
   - Laboratory eval
     - 1st tier
       - (Ordered together, as a group)
       - CBC and peripheral smear
       - Blood cultures
       - Urinalysis and urine culture
       - Chem-12
       - ESR
       - PPD
       - HIV serology
       - ANA
       - Stool culture and O&P if diarrhea present
     - 2nd tier
       - (Considered individually, if 1st tier labs and H&P do not reveal etiology)
       - CRP
       - Quantitative immunoglobulins
       - Stool culture and O&P (if not already done)
       - EBV/ CMV serologies, and other appropriate serologies
       - LP, if indicated
   - Diagnostic imaging
     - 1st tier
       - CXR
       - Sinus imaging
- 2nd tier
  - Bone scan
  - Nuclear tagged WBC scan
  - Echocardiogram
  - U/S vs. CT vs. MRI
- Other studies
  - Bone marrow biopsy
  - Other biopsies
    - Liver
    - Lymph node, etc.

**Differential Diagnosis**

1. Infectious, Systemic
   - Benign "nonspecific" viral syndrome
   - EBV
   - CMV
   - Viral hepatitis
   - HIV
   - Spirochete infections
     - Lyme
     - Cat Scratch
     - Leptospirosis
   - Rickettsial infections
   - Tuberculosis
   - Salmonellosis
   - Brucellosis
   - Tularemia
   - Malaria
   - Toxoplasmosis
   - Fungal infections
2. Infectious, localized
   - Sinusitis
   - Otitis media
   - Pneumonia
   - Bacteremia
   - Tonsillitis
   - UTI
   - Meningitis
   - Osteomyelitis
   - Septic arthritis
   - Endocarditis
   - Occult abscesses
   - Other focal bacterial infection
3. Connective tissue dz
   - JRA
   - SLE
   - Acute rheumatic fever
   - Vasculitis
4. Malignancies
   - Leukemia
   - Lymphoma
   - Neuroblastoma
   - Hepatoma
   - Rhabdomyosarcoma
   - Atrial myxoma

5. Miscellaneous
   - Factitious fever
   - Kawasaki Dz
   - Familial Mediterranean fever
   - Behcet syndrome
   - Drug fever
   - CNS dysfunction ("central")
   - Immunodeficiency
   - Inflammatory bowel dz
   - Sarcoidosis
   - Subdural hematoma/ effusion
   - Thyroiditis
   - Diabetes insipidus
   - Idiopathic

**Therapeutics**
1. Acute tx
   - ABCs
   - Supplemental oxygen if hypoxic
   - Empiric antibiotics not recommended until dx established, unless pt critically ill

2. Further mgmt
   - See dx above
   - Based upon specific etiology of fever

**Follow-Up**
1. Return to office
   - Time frame for return visit
     - At least every 2-3 days until dx found, or fever resolves
   - Recommendations for earlier follow-up
     - Sooner, if any clinical change.
       - Worsening clinical status
       - New complaint

2. Refer to specialist
   - Consider ID consultation
   - Consider Hematology/ Oncology consultation

3. Admit to hospital
   - No formal recommendations exist on when to admit
     - However if pt is unstable or there is concern for factitious fever, consider admission
Prognosis

1. Most causes of FUO self-limited or treatable
2. 10 - 20% of FUO cases spontaneously resolve
3. 40% w/long-term morbidity
4. Cause-related mortality ranges from 9-17%

References


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