

Diagnostic Considerations of Fever of Unknown Origin in Children

Dr. P. R. Sisir

Introduction

The classification of **F**ever of **U**nknown **O**origin(FUO) is best reserved for children with fever documented by a health care provider and for which the cause could not be identified after 3 wk of evaluation as an outpatient or after 1 wk of evaluation in the hospital

Etiology

- The many causes of FUO in children are infections and rheumatologic (connective tissue or autoimmune) diseases.
- **Neoplastic disorders should also be seriously considered**, although most children with malignancies do not have fever alone.
- The possibility of **drug fever** should be considered if the patient is receiving any drug. Drug fever is usually sustained and not associated with other symptoms. Discontinuation of the drug is associated with resolution of the fever, generally within 72 hr, although certain drugs, such as iodides, are excreted for a prolonged period with fever that can persist for as long as 1 month after drug withdrawal.

DIAGNOSTIC CONSIDERATIONS

ABSCESSSES

Abdominal

Brain

Dental

Hepatic

Pelvic

Perinephric

Rectal

Sub-phrenic

Psoas

DIAGNOSTIC CONSIDERATIONS

BACTERIAL DISEASES

Actinomycosis

Bartonella henselae (cat-scratch disease)

Brucellosis

Campylobacter

Francisella tularensis (tularemia)

Listeria monocytogenes (listeriosis)

Meningococemia (chronic)

Mycoplasma pneumoniae

Rat-bite fever (*Streptobacillus moniliformis*; streptobacillary form of rat-bite fever)

Salmonella

Tuberculosis

Whipple disease

Yersiniosis

DIAGNOSTIC CONSIDERATIONS

- Most fevers of unknown or unrecognized origin result from atypical presentations of common diseases.
- In some cases, the presentation as an FUIO is characteristic of the disease, such as juvenile idiopathic arthritis, but the definitive diagnosis can be established only after prolonged observation because initially there are no associated or specific findings on physical examination and all laboratory results are negative or normal.

DIAGNOSTIC CONSIDERATIONS

- The systemic infectious diseases most commonly implicated in children with FUO are salmonellosis, tuberculosis, rickettsial diseases, syphilis, Lyme disease, cat-scratch disease, atypical prolonged presentations of common viral diseases, infectious mononucleosis, cytomegalovirus (CMV) infection, viral hepatitis, coccidioidomycosis, histoplasmosis, malaria, and toxoplasmosis.
- Less common infectious causes of FUO include tularemia, brucellosis, leptospirosis, and rat-bite fever.

DIAGNOSTIC CONSIDERATIONS

- Juvenile idiopathic arthritis (JIA) and systemic lupus erythematosus (SLE) are the connective tissue diseases associated most commonly with FUO.
- Inflammatory bowel disease, rheumatic fever, and Kawasaki disease are also commonly reported as causes of FUO.
- If factitious fever (inoculation of pyogenic material or manipulation of the thermometer by the patient or parent) is suspected, the presence and pattern of fever should be documented in the hospital.
- Prolonged and continuous observation, which can include electronic or video surveillance, of patients is imperative. FUO lasting >6 mo is uncommon in children and suggests granulomatous or autoimmune disease.
- Repeat interval evaluation, including history, physical examination, laboratory evaluation, and roentgenographic studies is required.

Diagnosis

- The evaluation of FUO requires a thorough history and physical examination supplemented by a few screening laboratory tests and additional laboratory and radiographic tests as indicated by the history or abnormalities on examination or initial screening.

History

- The age of the patient is helpful in evaluating FUO.
- Children >6 yr of age often have a respiratory or genitourinary tract infection, localized infection (abscess, osteomyelitis), JIA, or, rarely, leukemia.
- Adolescent patients are more likely to have tuberculosis, inflammatory bowel disease, autoimmune processes, or lymphoma, in addition to the causes of FUO found in younger children.

History

- A history of exposure to wild or domestic animals should be solicited.
- Immunization of dogs against specific disorders such as leptospirosis can prevent canine disease but does not always prevent the animal from carrying and shedding leptospire, which may be transmitted to household contacts.
- A history of ingestion of animal meat might provide a clue to the diagnosis of oropharyngeal, glandular, or typhoidal tularemia.
- A history of tick bite or travel to tick- or parasite-infested areas should be obtained.
- Any history of pica should be elicited. Ingestion of dirt is a particularly important clue to infection with *Toxocara canis* (visceral larva migrans) or *Toxoplasma gondii* (toxoplasmosis).

History

- A history of unusual dietary habits or travel as early as the birth of the child should be sought.
- Malaria, histoplasmosis, and coccidioidomycosis can re-emerge years after visiting or living in an endemic area.
- It is important to identify prophylactic immunizations and precautions taken by the patient against ingestion of contaminated water or food during foreign travel.
- Rocks, dirt, and artifacts from geographically distant regions that have been collected and brought into the home as souvenirs can serve as vectors of disease.
- A medication history should be pursued rigorously. This history should elicit information about over-the-counter preparations and topical agents, including eye drops, that may be associated with atropine-induced fever.

- The genetic background of a patient also is important. Descendants of the Ulster Scots may have FUO because they are afflicted with nephrogenic diabetes insipidus.

Physical Examination

A complete physical examination is essential to find any physical clues to the underlying diagnosis.

The child's general appearance, including sweating during fever, should be noted.

The continuing absence of sweat in the presence of an elevated or changing body temperature suggests dehydration due to vomiting, diarrhea, or central or nephrogenic diabetes insipidus.

A careful ophthalmic examination is important. Red, weeping eyes may be a sign of connective tissue disease, particularly polyarteritis nodosa. Palpebral conjunctivitis in a febrile patient may be a clue to measles, coxsackievirus infection, tuberculosis, infectious mononucleosis, lymphogranuloma venereum, and cat-scratch disease.

Prognosis

- Children with FUO have a better prognosis than do adults.
- The outcome in a child depends on the primary disease process, which is usually an atypical presentation of a common childhood illness.
- In many cases, no diagnosis can be established and fever abates spontaneously.
- In as many as 25% of cases in whom fever persists, the cause of the fever remains unclear, even after thorough evaluation.

THANK YOU