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Lessons from the GRAND ROUNDS 1

A Pediatric Approach



YK Amdekar
RD Khare
RR Chokhani

3rd Edition

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37 CASE

Fever for 2 Weeks with Constitutional Symptoms

HISTORY

A 10-year-old child was presented with a fever and loss of appetite and weight for 2 weeks. There were no other symptoms. The fever was moderate to high, temporarily responding to paracetamol with a normal interfebrile period. He was prescribed two sets of antibiotics without any diagnosis; his complete blood count (CBC), urinalysis, and chest X-ray were normal. He had suffered from a viral infection a few days prior to the onset of this fever which had settled by itself without any treatment; otherwise, he had been a healthy child.

Analysis

History suggests an acute onset of probably a **noninfective disease** as evidenced by a normal interfebrile period, absence of localizing symptoms, and failed antibiotic therapy. **Partially treated infections** can be kept in mind, especially acute bacterial infections that present without any localizing symptoms like subacute endocarditis. In case it is a noninfective illness, one should look out for any clinical features that suggest **rheumatological** diseases (arthritis, mouth ulcers, and skin rash) or **hematological** diseases (pallor, petechiae, and lymph node swellings). The history of (H/o) having suffered a recent viral infection may be relevant in the sense that immune complications of such infections are known to appear after an interval of a few days. However, there is no clue to any specific organ involvement yet.

PHYSICAL EXAMINATION

Sick look

Temp. 102°F	HR 112/m	RR 28/m	BP 115/75 mm Hg
Moderate pallor		No purpura	No skin rash

No lymphadenopathy or joint swelling or tenderness

Liver 2 cm, soft, not tender, span 9 cm	Spleen 2 cm

Other systems normal

Analysis

A sick look with moderate anemia suggests a progressive disorder of inflammatory origin. Splenomegaly without any significant hepatomegaly favors a hematological disorder either a hemolytic disorder or an infiltrative disorder of the marrow. The absence of jaundice almost rules out a hemolytic process; and therefore, bone marrow infiltration is the likely possibility

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(leukemia or other similar disorders). Malaria is unlikely as the fever has gone on for 2 weeks, the child looks sick, and yet there don't seem to be further complications.

INVESTIGATIONS

Hb 7 g% WBC 12,000/cmm P 52 L 43, M 3 E 2 PC 50,000/cmm
S ferritin 2,500 ng/mL S triglycerides 500 mg/dL S fibrinogen 80 mg/dL
PS no abnormal cells
Bone marrow: Hemophagocytosis

Analysis

Bicytopenia with marrow showing hemophagocytosis, raised ferritin and triglycerides and reduced fibrinogen favor the diagnosis of hemophagocytic lymphohistiocytosis (HLH) which is further proved by high CD-25 and low NK cells.

Final Diagnosis

Hemophagocytic LymphoHistiocytosis (HLH) (probably secondary to the viral infection that this child suffered in the recent past).

KEY MESSAGES

Prolonged fever without localizing symptoms is mostly, not due to acute bacterial infection; subacute infections such as tuberculosis, brucellosis, Epstein–Barr virus (EBV) or *Cytomegalovirus* (CMV) viral infections, toxoplasmosis, and kala azar may be considered. Besides, noninfective inflammatory disorders (rheumatological or hematological) also have to be considered. Anemia and splenomegaly favor hematological diseases.

RELEVANT INFORMATION

Hemophagocytic lymphohistiocytosis is an immune-mediated disorder secondary to many triggers; such as infections of all types, autoimmune disorders, malignancy; and drugs such as anticonvulsants and antibiotics (cotrimoxazole and vancomycin). Rarely HLH may be due to a primary immune defect—perforin deficiency, that is genetically determined. It may be present very early in life and is often fatal. Diagnosis is suspected when there is a persistent fever without any clue to infections, in the presence of bicytopenia or pancytopenia, and splenomegaly with or without hepatomegaly. Occasionally, it may also be present as specific organ affection. Macrophage activation syndrome is similar to HLH though it presents as a complication of a rheumatological disorder and not as a primary hematological disease. Clinically, a high index of suspicion is necessary; once suspected, it has to be followed by further confirmatory tests which may pick up typical laboratory findings as in this child. The treatment consists of etoposide, steroids, cyclosporine, and if necessary other chemotherapeutic drugs. A bone marrow transplant can also be considered.

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A Pediatric Approach

Back to School
HISTORY
can often define the route
(GEOGRAPHY)
to reach a diagnosis based on
SCIENCE
with the accuracy of
MATHEMATICS

Encouraged by the overwhelming response to our earlier editions, we present our third edition of this book. While the basic format remains the same, we have added new cases in various sections, thereby widening the spectrum of areas covered.

This unique book is different in the sense that it is all about the art of clinical analysis. It comprises 92 actual cases as they presented with their varied symptom complexes, encompassing a wide clinical spectrum in different subspecialties. To begin with, it briefly discusses the basic concepts of symptoms and signs pertaining to a system, before proceeding with representative cases, which are listed according to the presenting symptoms. It describes how a sequential analysis of every point in the history, clinical examination, and investigations leads to the correct diagnosis. While reading through the cases, the keywords are highlighted, facilitating a quick revision. Each case ends with key messages that convey critical concepts of clinical medicine. Thus, this book is one of its kind; it does not intend to teach pediatrics at all; it purely stimulates the reader to develop a fine sense of rational thinking that facilitates clinical diagnosis in the field of pediatrics, through a self-learning, totally case-based format. This book is ideal for undergraduate and postgraduate medical students, practicing pediatricians, teaching faculty in the field of pediatrics, and family physicians who also deal with children.

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