CIS CME

Clinics India School of Continuing Medical Education

Quick Case Work-up

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Fever Without Localisation

History

A 5-year-old male (Weight: 18 kg; Height: 105 cm) presented with fever of four days duration. The child was apparently well prior to fever onset. Initially, the fever was mild to moderate and responded to paracetamol, although it recurred every 4-6 hours. By day 4, the fever was high and the child appeared sicker. There was no history of cold or cough or any other significant symptoms. There was no history of any major illness or disease in the family.

On physical examination, the child's temperature was 104°F, pulse was 130/min, and the respiratory rate was 28 per min. The child looked sick, was irritable and exhibited a cold periphery. Examination of the abdomen revealed mild gaseous distension. The liver was 2F+, soft, not tender, and the spleen was not palpable. There was no lymphadenopathy, skin rash, or icterus and ENT was normal.

Physical examination at a glance

Weight	: 18 kg	**Lymph nodes**	: No lymphadenopathy
Height	: 105 cm	**Skin**	: No rash
Temp	: 104°F	**ENT**	: Normal
PR	: 130/min	**Abdominal**	: Mild gaseous distension; Liver: 2F+, soft, non-tender; Spleen: not palpable
RR	: 28/min		
Looks	: Sick, irritable		
Icterus	: No	**Other systems**	: Normal

What is the best management approach?

Select one or more.

1. Antibiotic – if so, which?
2. Antipyretic – if so, which?
3. Urinalysis and urine culture, sensitivity
4. CBC and PS
5. Chest x-ray
6. Other tests

CASE DISCUSSION

It is optimal to analyze the child's past history in order to arrive at a provisional diagnosis. This helps guide a focused physical examination and specific laboratory tests to confirm the diagnosis.

PATIENT HISTORY

Fever at the onset of illness invariably denotes an acute infection. Although many non-infective disorders such as systemic inflammatory disease and malignancy may also begin with fever, they are rare and the correct diagnosis in such diseases usually evolves over time.

In the absence of respiratory or GI symptoms, it is unlikely that the patient is suffering from a viral infection. A high fever at the onset of illness usually suggests a disease developing at the site of entry of organisms such as occurs in acute tonsillitis, bacillary dysentery or urinary tract infection (UTI). The patient had mild to moderate fever that began to rise after a few days. This suggests a bacterimic origin of the disease that may eventually localize to an organ. However, even on day 4, there are no obvious symptoms of localization such as cough indicating pneumonia or headache and vomiting suggesting meningitis or dysuria denoting lower UTI. Clinically non-localizing bacterial infections include typhoid/paratyphoid fever and pyelonephritis. In general, pyelonephritis is a result of a congenital malformation of the urinary tract and presents early in life. As this child had no significant disease prior to the present illness, it is unlikely to be a UTI. Thus, we must consider typhoid or paratyphoid fever in this child. Both diseases are clinically indistinguishable. It is not true that paratyphoid fever is a milder version of typhoid fever. Malaria is unlikely in this patient as this child presents with a rhythmic fever that increased by day 4.

Conclusion. The patient is suffering from an acute non-localizing bacterial infection, most likely typhoid or paratyphoid fever.

PHYSICAL EXAMINATION ANALYSIS

This child has a normal body weight and height indicating that he was healthy prior to illness onset. This rules out the presence of an acute or chronic disease. A sick appearance and irritability suggests a toxic condition. A cold periphery in a febrile child indicates peripheral vasoconstriction most likely in an attempt to achieve a high fever. The patient has a proportionate rise in pulse and respiratory rate. A higher respiratory rate may have suggested developing pneumonia. Gaseous abdominal distension may indicate a developing intra-abdominal pathology although it may also be a non-specific sign. The liver is generally not palpable or just palpable at the age of 5 years in a healthy child. A 2 finger palpable liver in this child may suggest an evolving disease. A soft, enlarged liver is indicative of recent onset. As the liver is not tender, hepatitis is ruled out although it may suggest reticuloendothelial cell hyperplasia. There is

no evidence of splenomegaly. One would expect splenomegaly in malaria or typhoid fever although it is usually at the end of a week that the spleen becomes palpable in typhoid fever while it is palpable early in the course of malaria. Other systems are normal in this child.

MANAGEMENT ANALYSIS

OPTION 1

Treatment with an antibiotic is necessary, but not before proper action. Clinical diagnosis of typhoid or paratyphoid fever justifies the use of an antibiotic. However, it is first necessary to perform the relevant laboratory tests so that the diagnosis is confirmed as soon as possible. The choice of an antibiotic depends upon local epidemiology and antibiotic sensitivity. A third generation cephalosporin such as ceftriaxone may be the drug of choice; however, it needs to be administered intravenously and thus requires hospitalization. This is ideal for the sick and toxic child and younger child. Cefixime may be a good alternate oral cephalosporin. Practicality may justify treating the patient with Ceftriaxone until an initial response is achieved and then switching to oral cefixime. Drugs such as chloramphenicol, cotrimaxozole, and ampicillin may exhibit varying sensitivity. Ideally, ciprofloxacin is avoided in children due to possible cartilage damage. Azithromycin is considered to be a good anti-typhoid drug. In addition, it may be a good add-on drug in children when a response to the primary drug is suboptimal. Antibiotics must be continued for 5-7 days after the fever subsides. In general, fever subsides within 5-7 days. The first symptom to improve is general well being, while fever is last to normalize.

OPTION 2

Treatment with an antipyretic is necessary. Any child with fever deserves antipyretic only in case of discomfort caused by fever. Antipyretic is not intended to bring down fever to normal but is used to relieve discomfort caused by fever. Paracetamol is the ideal antipyretic and ibuprofen and mefinimic acid are acceptable alternatives.

OPTION 3

Urinalysis, urine culture, and sensitivity are not necessary. As UTI is most unlikely in this child, urinalysis may not be necessary. In case of doubt, it may be considered, it being a simple and cheap test. If urine microscopy is normal, urine culture should not be asked in this child.

OPTION 4

CBC and PS are necessary. CBC and PS is a good screening test in a febrile child as it may offer a clue to probable diagnosis and is confirma-

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tive in malaria. Neutrophilic leucocytosis with eosinopenia may suggest acute bacterial or viral infection. A constellation of leucopenia, lymphocytosis, monocytosis, eosinopenia and thrombocytopenia is characteristic of typhoid or paratyphoid fever.

OPTION 5

Chest x-ray is not necessary. This child has no symptoms or physical signs of respiratory infection and so chest x-ray is not necessary. Undiagnosed fever in an infant may justify chest x-ray even in the absence of respiratory symptoms or signs.

OPTION 6

Other tests – Blood culture for salmonella species. Since typhoid or paratyphoid fever is the clinical diagnosis in this patient, blood culture is a must. Ideally, a blood sample is sent prior to starting antibiotic therapy so that the diagnosis can be confirmed while treatment is in progress. Every attempt must be made to prove the presence of a bacterial infection by culture and this is especially true for typhoid and paratyphoid fever as it is a bacterimic illness and salmonella species are easy to grow in a culture medium.

Widal test. The Widal test is a serological test that measures O and H antibodies against *S. typhi* and antibodies against paratyphi A and B. There are two methods available, the tube and slide method. The slide method is rapid but it is not reliable. The Widal test has many limitations that confound its interpretation. First, since antibodies develop only after days 5-7 of illness onset, the Widal test should not be ordered during days 1-5 of fever. Since a subclinical infection with salmonella species is common in India, results of the Widal test need to be compared with baseline antibody titres in the population. A rising antibody titre is diagnostic of recent infection but it demands repeat testing after 5-7 days and thus is not practical. Finally, 20% of blood culture +ve patients have a negative Widal test. Therefore, the Widal test is not ideal for a definite diagnosis but may be considered in late first week of illness. In fact, a negative test helps to exclude disease. In infants and toddlers, a positive test may be of significance as exposure to subclinical infection is unusual at that early age.

In summary, this child is suffering from typhoid or paratyphoid fever. Ideally, the diagnosis should be confirmed by blood culture submitted prior to starting antibiotic therapy. The Widal test has limitations. The drug of choice may be either cerftriaxone or cefixime and azithromycin is a good alternate or add-on drug. Antibiotic treatment must be continued for 5-7 days beyond fever remission. Treating typhoid without confirming its diagnosis is not ideal as the choice of antibiotic and duration is specific for a complete cure. Partially treated typhoid is difficult to diagnose and treat. ■