EDITORIAL

Travel-associated Febrile Illness

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International travel has increased exponentially in the last 20 years with a transient setback during the pandemic. Thereafter, tourism has bounced back with a vengeance in recent times with a 32% increase in number of Indians taking two or more international trips per year. This has led to increased probability of acquiring infections that are not endemic in ones' homeland.

Fever has been reported in 43–79% of travelers returning from developing countries, tropical infections are reported in 36% of cases (malaria being the most common) while non-tropical infections (gastrointestinal infections, respiratory tract infections) and rarely non-infectious causes constitute the rest .

A specific cause for fever might not be identified in ≥25% of returned travelers.

We need to be aware of travel-associated illnesses as the spread of endemic diseases to nonendemic areas have increased due to long distance travel, as well as extensive migration. Moreover, travelers to South and Southeast Asia are at high risk of acquiring multidrug-resistant infections.

Once the patient presents to the physician, the assessment of the stability is foremost.

It is mandatory to check the airway, breathing, circulation, disability and act accordingly.

Thereafter the clue to obtaining a diagnosis rests on three pillars namely:

- A properly obtained history.
- Potential diagnostic clue (PDC) derived from clinical examination.
- Confirmation from focused laboratory investigations.

History Taking

The first step is to characterize the fever, e.g., its onset, pattern and duration and any prodromes.

Some of the classical febrile patterns are:

- High-grade fever – Dengue, Malaria.
- Step ladder pattern – Enteric fever.
- Biphasic pattern – Dengue, Leptospirosis.
- Periodicity – Malaria, Borreliosis.

Knowledge of the incubation period is also vital for assessing probable etiology, for example:

When it is less than 10 days it could be dengue, chikungunya, plague while if within 10–14 days we have to consider malaria, enteric fever, leptospirosis, toxoplasmosis.

History of fever onset after 2 weeks, even at times more than 6 weeks of travel, may be found in:

- Typhoid or paratyphoid fever.
- Malaria (*Plasmodium ovale, P. vivax*).
- Cytomegalovirus, Epstein-Barr virus, HIV (acute).
- Tuberculosis, melioidosis, brucellosis.
- Acute hepatitis B, hepatitis C, hepatitis E.

The list of diseases is extensive and mindboggling which makes it very difficult for the treating physician to pinpoint the diagnosis. In that case we need a meticulous enquiry into other aspects like;

- A personal medical history:
  - Comorbidity.
  - Occupational history.
  - Drug history.
  - Underlying immune suppression.
  - Whether the patient has been visiting friends and relatives (VFR).
  - Childhood vaccinations up to date or not.
  - Status of vaccination/prophylaxis for specific destination risk.
- Details about the travel:
  - Country visited as well as traveled through and its endemicity, e.g., malaria, dengue.
  - Local geography (mountains/lakes/beaches/urban or rural)– where the patient resided.
  - Accommodation (family/hostel/hotel/camping).
  - Information about ongoing outbreaks.
  - What was the patient doing while abroad?
  - Work or vacation.
  - History of sexual contact.
  - Was there any hospital treatment or admission.
  - Any history of insect bites.

The elucidation of symptoms associated with fever is of prime importance because it helps in following the syndromic approach to fever.

Various infections have predilection in producing particular organ involvement – the syndromes commonly encountered in the tropics are:

- Acute encephalitic syndrome.
- Fever with rash.

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- Fever with hepatosplenomegaly.
- Fever with lymphadenopathy.
- Fever with bleeding.
- Fever with abdominal pain.
- Fever with hepatorenal syndrome.
- Fever with arthralgia/arthritis.
- Fever with acute kidney injury.
- Fever with acute respiratory distress syndrome (ARDS).
- Fever with multiorgan failure.

Examination

Once the history gives us a direction to possible system involvement we examine for:

- Pallor, jaundice, lymphadenopathy, sternal tenderness, Temperature – Pulse dissociation.
- Skin and mucosa examination for rashes, bites, eschars, bleeding.
- Cardiopulmonary, abdominal and neurology examination, as well as evidences of medical interventions.

The clinical evaluation is expected to give us a PDC which will give the physician to go for rational and focused investigations.

However three tests are mandatory for all patients of undifferentiated fever including those after travel.

- Rapid diagnostic test (RDT) for malaria.
- ELISA for dengue NS1, IgM.
- Complete blood count (CBC) and examination of blood smears.

The other investigations are according to clinical pointers or febrile syndromes:

- Liver function test (LFT), renal function test (RFT), electrolytes arterial blood gas (ABG), urinalysis, cultures of blood and body fluids, cerebrospinal fluid (CSF) analysis.
- Serology: Dengue IgM (after 5 days of fever), scrub typhus, leptospiral serology, Typhi dot IgM.
- Respiratory viral swab-RT PCR-COVID-19, Influenza.
- C-reactive protein (CRP), ferritin, and creatine phosphokinase (CPK).
- Antinuclear antibody (ANA), antineutrophil cytoplasmic antibodies (ANCA), rheumatoid factor (RF), and anti-CCP antibody (if noninfectious disease suspected).
- Radiological: Chest X-ray, ultrasonography, CT/MRI as indicated.

Management

The management issues primarily focus on patient stabilization and treatment of the cause along with supportive therapy. Infection control considerations by isolation are needed if there is a chance of spread.

However, it is clear to all, that awareness and prevention is the key to effective handling of travel associated illness.

A visit to the local physician is to be highlighted as a necessary step around 4–6 weeks before a planned vacation or tour. The physician needs to take detailed information about the following:

- Destination, personal details, date of trip, itinerary and purpose of visit.
- Personal medical history, including pregnancy, medication, and allergies (e.g., to eggs, vaccines, antibiotics) are not to be missed.
- Advice regarding good quality insect repellents, appropriate clothing is to be given if visit is in remote seaside or forest destinations.
- The traveler needs to be up to date with regular vaccinations and specific vaccines depending on destination (varies from country to country) should be recommended.
- In special situations for foreigners visiting from nonendemic zones, chemoprophylaxis for malaria, leptospirosis, scrub typhus, travelers' diarrhea may be required if they are to stay for a long duration (>1 month) in remote places.

Conclusion

There are many challenges in diagnosing undifferentiated fever after travel, and dates of travel and exposures are key to establishing a timeline for the onset of symptoms and signs.

However, hurdles for diagnosis are posed by atypical or overlapping features, and cross-reactivity in serological investigations.

Therapy is also difficult as there are no drugs for many of the viral infections, coupled with a lack of proper guidelines or algorithm for therapy. Drug resistance in infections like malaria, enteric fever and other bacterial sepsis is another monster to wrestle with.

Thus, there is no doubt that we have to take all precautions before and during travel. Specialized travel clinics that are a regular feature in many countries, need to be set up here, to provide information, counseling and prophylaxis against common infections for the safety and wellbeing of all travelers.

Suggested Reading

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