Endocrine Fever

Sanjay Kalra[1], Saptarshi Bhattacharya[2], Atul Dhingra[3], Jaideep Khare[4], Sushil Jindal[5]

Abstract

Fever is usually thought to be of an infectious or inflammatory etiology. In this brief communication, we explore the multifaceted connections between fever and endocrine dysfunction. Impaired resistance to infection often leads to fever in conditions like diabetes and Cushing's syndrome. Additionally, several endocrine disorders, including hyperthyroidism, subacute thyroiditis, carcinoid syndrome, and pheochromocytoma, can manifest as fever. Furthermore, fever can be an adverse effect of various endocrine treatments, such as bisphosphonates and antithyroid drugs. We refer to these scenarios as 'endocrine fever.' Increased awareness of these clinical associations can aid in prompt diagnosis and management of these conditions.

Keywords: Fever, infection, immunity, adverse effect, diabetes, thyrotoxicosis

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Introduction

Fever is a common symptom of various illnesses and infections. It indicates the body is fighting off an infection or responding to an inflammation. The mechanism of fever involves complex processes in the body's immune and thermoregulatory systems. Endocrine disorders can disrupt these pathways and refashion the febrile response. Fever or pyrexia can be presenting features of several endocrine conditions. Various unique infections are characteristically associated with specific endocrinopathies. Understanding these interactions is crucial for effective medical management. In Table 1, we list various ways in which fever intersects with endocrine praxis.

[1]Department of Endocrinology, Bharti Hospital, Karnal, India; University Center for Research & Development, Chandigarh University, Mohali, India; [2]Department of Endocrinology, Apollo Indraprastha Hospitals, New Delhi, India; [3]Department of Endocrinology, Bansal Gangaram Hospital, Sriganganagar, India; [4]Department of Endocrinology, People's Medical College, Bhopal, India; [5]Department of Endocrinology, People's Medical College, Bhopal, India.

Correspondence: Sanjay Kalra. e-mail: brideknl@gmail.com

ORCID ID: 0000-0003-1308-121X

Table 1: Endocrine fevers

- Fever as a symptom of endocrine disease
  - Hyperthyroidism: Graves' disease, other causes of hyperthyroidism, hyperpyrexia in thyroid storm
  - Subacute thyroiditis
  - Lymphocytic hypophysitis
- Fever mimetics in endocrine practice
  - Carcinoid syndrome
  - Menopausal hot flushes
  - Pheochromocytoma due to interleukin-6 production
  - Fever in hyperparathyroidism
  - Fever in Addison's disease
- Fever due to endocrine gland infection
  - Adrenal tuberculosis
  - Adrenal histoplasmosis
  - Mastitis, breast abscess
  - Orchitis, testicular torsion
  - Ovarian torsion, tubercular endometritis, oophoritis
- Chronic febrile illnesses with multiple endocrine dysfunction
  - Long-COVID following COVID-19 infection
  - Tuberculosis
  - Leprosy
- Fever due to concomitant illness
  - Autoimmune illness, e.g., rheumatoid arthritis, systemic lupus erythematosus
  - Paraneoplastic syndromes
- Predisposition to fever
  - Uncontrolled diabetes
  - Low cortisol state
  - High testosterone (more prone to influenza)
- Fever due to endocrine therapy
  - Thyroxine overdose
  - Intravenous bisphosponate
  - Steroid withdrawal
  - Urinary tract infection due to SGLT2 inhibitor
  - Adverse effect of propylthiouracil and methimazole
- Endocrine effects of fever
  - Stress hyperglycaemia
  - Depressed spermatogenesis
  - Masking of diseases such as hypothyroidism
- Confounding factors in endocrine practice
  - Leukocytosis without fever in diabetic ketoacidosis
  - Leukocytosis without fever in Cushing's syndrome
  - Lymphopenia with saxagliptin
  - Neutropenia with anti-thyroid drugs
- Fever due to infections that are pathognomic of endocrine disease
  - Malignant otitis externa
  - Emphysematous pyelonephritis
  - Emphysematous cholecystitis
  - Rhino cerebral mucormycosis
  - Diabetic foot

- Necrotizing fasciitis

Masking of fever in endocrine disease

- Hypothyroidism
- Cushing's syndrome
- Panhypopituitarism

Endocrine drugs for management of fever

- Steroids in pyrexia of unknown origin from inflammatory causes, meningitis
- Bromocriptine in neuroleptic malignant syndrome
- Tamoxifen in Reidel's thyroiditis
- Menopausal hormonal therapy in women with recurrent pruritis vulvae/urinary tract infection after menopause

Functional fever due to hyperresponsive endocrine system

- "Spring fever"
- "Heartbreak fever"
- "Saturday night fever"
- "Examination fever"

Endocrine disorders presenting as fever

Pyrexia can be the presenting feature of certain thyrotoxic states. Fever is not a typical features of Graves' disease and should prompt a search for infections.[1] Thyroid storm, an extreme form of thyrotoxicosis is associated with high grade fever and multiorgan dysfunction and is a medical emergency.[2] Subacute thyroiditis, an important differential of thyrotoxic state, is a common cause of pyrexia of unknown origin. Lymphocytic hypophysitis, another inflammatory endocrinopathy, can manifest as fever.[3]

Fever mimetics in endocrine practice

Flushing and pyrexia are characteristic of carcinoid syndrome.[4] Similar symptoms can also occur during menopausal transition. Pheochromocytoma, though rare, may present with fever as an atypical symptom, possibly due to tumour secretion of interleukin-6.[5] Prolonged fever has been reported to occur with hyperparathyroidism and fever can be also associated with Addison's disease.[6]

Fever due to endocrine therapy

Factitious or iatrogenic thyrotoxicosis can manifest as fever. Bisphosphonates especially when given through intravenous route elicit an acute phase response and induce fever.[7] Propylthiouracil has been reported to provoke autoimmune reaction and hypersensitivity presenting as fever and multiorgan dysfunction.[8] Urinary tract infection is a recognized side effect of sodium-glucose cotransporter-2 (SGLT2) inhibitors, and should be used with caution in those who are at risk.

Infectious causes of fever in endocrine disorders

Endocrine disorders such as diabetes and Cushing's syndrome are linked to impaired innate and adaptive immune response increasing susceptibility to various infections. Conditions such as malignant external otitis, rhino cerebral mucormycosis, emphysematous cholecystitis and pyelonephritis are characteristically seen in diabetes.[9] Cushing's syndrome predisposes to opportunistic infections like cryptococcosis, aspergillosis, nocardiosis, and pneumocystis, necessitating appropriate prophylaxis.[10] Endocrine glands are also prone to endemic fungal infections such as histoplasmosis, coccidioidomycoses and paracoccidiodomycoses.[11]

Functional fever due to hyperresponsiveness of enodcrine system

Sometimes, the term 'fever' is poetically linked to other endocrine phenomena, such as 'fever of the heart' or 'heartbreak fever' in Indian literature. Colloquially in English, the term 'fever' is used to describe heightened excitement, as seen in phrases like 'spring fever' or 'Saturday night fever.'

Summary

Fever and endocrine axes are closely intertwined. This article serves as a valuable checklist for both practitioners and students. It underscores the need for vigilance in clinical practice and the importance of considering endocrine diseases in individuals with fever, particularly when it is prolonged or of unknown origin. We also stress the significance of obtaining a fever history in individuals with endocrine conditions, where applicable.

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