

Review Article

A Study on Drug Fever in Patient during Treatment

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Abstract: It is a common condition which is not frequently diagnosed. Drug fever is a febrile response that coincides temporally with the administration of a drug and disappears after the discontinuation of the offending agent. It is important for clinician to suspect drug as a cause of fever of unknown origin. Drug fever is usually suspected when no other cause of the fever can be elucidated, sometimes after anti-microbial therapy has already been started. Most commonly appears after 8-11 days of drug administration and immediately disappears after discontinuation of a drug. In appropriate and potentially harmful and expensive diagnostic and therapeutic intervention may be reduced by early diagnosis. This article expresses awareness about the temporary febrile reactions occurring after administration of certain drugs.

Keywords: Drug Fever, Clinical Features, Hypersensitivity reaction, Treatment.

INTRODUCTION

Drug fever is a common condition that is frequently misdiagnosed. It becomes problematic when it occurs during the course of an infection, since drug fever can mislead the clinicians to believe that a successful course of therapy is failing. Drug fever differs from fever of other causes in that it reverses once the offending drug is discontinued. Clinicians have the responsibility to maintain an index of suspicion for the possibility of drug fever and we aware of the most common offending agents in order to avoid expensive diagnostic work-up for further evaluation, incorrect treatment with antibiotic therapy, possible adverse effects and prolonged hospital stays. A variety of drugs can cause drug fever like antimicrobials, anticonvulsants, anti-arrhythmic agents, and other cardiac agents. To get a better understanding of the diagnosis, mechanism, management and to increase awareness among clinicians to conduct a literature search using various data bases like MICROMEDEX, MEDLINE, MEDSCAPE etc. It have been estimated that 12-18% of drug fever occurs in in-patients in united states This article reflects an idea about the unexplained fever occurring during a therapy and disappears after the stoppage of same therapy [1, 2].

Diagnosis

Diagnosis could be made after a detailed review of a patient's clinical presentation, drug therapy and laboratory values. Fever can be a characteristic of many disease processes other than infection other than

infection including malignancy thrombo embolic disease, cerebrovascular accidents, collagen vascular disease, acute gou, surgery, trauma. If fever is unexpected, particularly in a situation when a patient is otherwise clinically well improving, then drug fever should be considered in the differential diagnosis . A definite diagnosis that can be made only when fever determined after discontinuing the implicating agent. Returning of fever after the rechallenge of suspected agent solidifies diagnosis of the drug fever but it is a more dangerous practice that should be avoided [3].

Clinical Features

Drug fever may occur at any time with drug therapy and there is a significant variation in different drug classes. The drug fever can experience with in 7-10 days of drug therapy start. Anti neoplastic and antimicrobial agent produce drug fever within short interval , and drugs like cardiovascular drugs, CNS agents shows the longest interval between the initiation of drug therapy and onset of fever.

Different type of drug fever can experience with individual patient that can be depends up on the patient condition, drug therapy, etc. The different types of fever include continuous fever, intermittent fever, remittent fever, hectic fever. Hectic fever is a common type of fever and that can be controlled by using antipyretic drugs and cooling blankets. Degree of temperature can be vary from 99⁰F (low grade

temperature) to 109⁰F (high grade temperature), but most common elevated temperature is 102-104⁰F.

Patient with drug fever is not a problematic condition. During drug fever the patient experience bradycardia. 18-29% patient with drug fever shows hypersensitivity reaction and also generalized rashes occur with minority of patients. Hypersensitivity reaction causing drug fever when offending agent is not discontinued, the patient may experience drug rashes [4, 5].

Laboratory Tests

Differential leukocyte count should be performed with suspected patients. Eosinophills levels are elevated but eosinophilia is uncommon. Erythrocyte sedimentation counts (100mm/hr or more) also elevated with drug fever. Hepatic transaminase level shows mild to moderate elevation, lactic dehydrogenase also show the moderate elevation in the drug fever. These types of laboratory tests and patients physical examination are to be helpful for identification of the drug fever [6].

Risk Factors

Drug fever is occurring in all age group but the priority is in women's and older population due to the use of drug like antibiotic. Patients with drug allergies can increase the risk of drug fever.

Mechanism

There are mainly important mechanisms for drug fever. Hypersensitivity reaction and altered thermoregulatory mechanism reaction that are directly related to the administration of drug [1]. Pharmacologic action of a drug, idiosyncratic mechanism occurs from antimicrobial agent.

Hypersensitivity reaction

The most common mechanism is hypersensitivity reaction. The most probable mechanisms are mediated by a humoral response. The drug acts either as a complete antigen or a hapten [1]. Haptens are small molecules that can elicit an immune response only when attached to large carrier protein to form functional antigen [13]. The presence of antibodies in the serum does not prove hypersensitivity reaction since they can be present in patients who demonstrate no signs of a drug reaction. The formation of circulating antibody-antigen complexes along with complement can stimulate the release of pyrogen from granulocytes that leads to drug fever [1].

Altered thermoregulatory mechanism

Many of the drugs can either increasing heat production or limiting heat dissipation they will alter thermoregulatory mechanism [1]. For example, Levothyroxine sodium. It increases metabolic rate that will directly increases heat production. It is the direct effect of the drug regardless of the patient's thyroid state.

3,4-methylene dioxy methamphetamine, amphetamine and cocaine are the sympathomimetic agent that causes drug fever .

Anticholinergic drugs such as tricyclic antidepressants, antihistamines, buterophenone tranquilizers etc. all will reduce heat loss through controlling sweat gland secretion,ultimately leads to drug fever [14] .

Drug Administration-related fever

This can be due to contamination or due to the intrinsic effect of the drug itself. Pyrogens not removed during manufacturing process may contaminate some antibiotics, chemotherapy agents and streptokinase. Vancomycin at one time used to contain impurities and was a well known source of drug fever. Administration related fever may also occur with injection as a result of phlebitis from the infusion of irritating solutions such as cephalosporin and Vancomycin [7, 8].

Fever related to pharmacologic action of the drug

Mainly due to the release of endotoxins from killed or dying organism resulting in drug fever. Endotoxin is an integral part of cell wall of gram negative bacteria and it releases when neutrophil digest the organism. After initiating therapy, fever occurs within 8-10 hours [9].

Idiosyncratic reactions

Malignant hyperthermia, a disease characterized by elevated temperature of >106 F, tachycardia , muscular rigidity occurs in patients undergoing treatment with inhaled anaesthetic agent. The mechanism is genetic defect resulting in abnormal release of calcium ions in to muscle myoplasm that will induce catabolic reactions which ultimately leads to production of large amount of heat.

Drug fever from antimicrobial agent

Mainly the beta lactams causes the drug induced fever. Fever induced by non beta lactum antibacterials rarely occurs [10, 11].

TREATMENT

The main approach is to discontinue the offending agent .there is no standard approach for the treatment and is very difficult to determine appropriate agent. It may be favourable to stop all suspected drugs or to stop recently added agents or a drug with a high index of suspicion. Discontinuation should be done carefully since benefit of continued therapy may outweigh the risk of continued fever in some clinical practice [12].

CONCLUSION

When drug fever is suspected clinician should outweigh the risk and benefit of discontinuing

suspected agent. In patients whose fever disappears after removal of several agents that are not urgently necessary, these drugs should be restarted individually and carefully to identify the causative agent of drug fever. In such case an agent having high index of suspicion. Of causing the fever should be stopped if possible. The management must be based on patient's situation, severity of illness and other conditions of the patients. The pharmacist also plays a valuable role in the identification of agent that causes drug fever and also its management.

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