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Autopsy Manifestations of Deaths Suspected of Acute Allergic Reactions

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ABSTRACT

Aims: To outline the prevalence of postmortem manifestations of anaphylaxis at necropsy after suspected fatal acute allergic reaction.

Materials and Method: Data were registered from archives at the Medico-legal Directorate, ten cases were examined within two years from January 2021 to January 2023, seven males and three females with age a group in between 5-75 years, and average was forty years. Mast cell tryptase (MCT) was measured in laboratories of both Medico-Legal Directorate and Baghdad Medical City. Further information were gathered from histopathological assessment, witnesses at the scene, police report with suspected positive family or personal history of drug allergy.

Results: All ten victims gave a past history of fainting after contracting with allergen. All patients have had a respiratory problem in their life. Most victims passed away within one hour of acute allergic reaction (seven victims developed sudden rapid deaths) and delayed in three cases (up to one month).All cases have had previous allergic reaction to drugs. Iatrogenic reactions were seen in four cases. Five cases gave history of penicillin intake, three with NSAIDS (Nonsteroidal anti-inflammatory drugs) and two with combination drugs intake. Most drugs were given by intramuscular way (five patients), three with intravenous and two with oral routes. Most patients died without obvious reason. Lung swelling and congestion both were the most common finding in all necropsies.

Conclusion: Most cases of deaths related to suspected acute allergic reaction present with no diagnostic cutline signs and symptoms at necropsy specially if anaphylactic .The absence of specific signs and symptoms of allergic reaction or negative clinical history does not deny the presence of fatal allergic reaction.

Keywords: *Autopsy; Anaphylaxis; Mast Cell Tryptase*

INTRODUCTION

Sudden anaphylactic (or anaphylactoid like) reaction is rare but still a remarkable cause of abrupt death (1). Allergic response can lead to a wide grade of signs and composites of symptoms such as widespread redness, itching, angioedema, regurgitation, loose bowel motion, conjunctivitis, runny nose, sniffing, and coughing; sometimes associated with fainting and deterioration and may affect awareness as a sequence of shock, or difficulty in breathing as a

result of respiratory passages obstacles of either upper or lower pathways (2).

Vigorous anaphylactic response may cause lung and/or heart cessation. Bronchial spasm and mucous accumulation, edema of pharynx and larynx, all may lead to either upper and/or lower air passages occlusion and asphyxia which may cause death. Heart stoppage may follow pulmonary arrest and sometimes may occur alone as a straight effect of allergic mediators or severe abrupt shock resulting from decrease in the fluid volume within the circulation as a consequence of angio-edema (2, 3).

Sometimes not all features or stages of anaphylactic shock may not appear especially if the shock developed rapidly after beginning of the reaction. Many cases of anaphylactic positive history may lack any specific finding in spite of adjuvant clinical history that may agree with anaphylaxis and it is difficult to estimate the stages or the spectrum of anaphylactic reaction at autopsy (1, 3, 5).

METHODS

Data were registered from archives at the Medico-legal Directorate for cases died as a result of fatal anaphylactic shock at necropsy of suspected drug culprit as a major cause of anaphylaxis, ten cases were examined within two years from January 2021 to January 2023, seven males and three females with age groups in between 5-75 years, and average was forty years. Mast cell tryptase (MCT) was measured in laboratories of both Medico-Legal Directorate and Baghdad Medical City. Further information were gathered from histopathological assessment, witnesses at the scene, police report with suspected positive family or personal history of drug allergy.

All ten cases were accepted as deaths resulted from anaphylactic reactions. Five cases died from air passages occlusion and respiratory failure and two from shock and heart arrest, three cases died as a result from combination of the previous causes. Intra-cardiac epinephrine was administered in five cases before arrest and two cases during revival. MCT was measured in all postmortem victims.

RESULTS

All ten victims gave a past history of fainting after contracting with allergen. Depending on past medical history, all patients have had a respiratory problem in their life. Most victims passed away within one hour of acute allergic reaction (seven victims developed sudden rapid deaths) and delayed in three cases (up to one month).

All cases have had previous allergic reaction to drugs. Iatrogenic reactions were seen in four cases. Five cases gave history of penicillin intake, three with NSAIDS (Nonsteroidal anti-inflammatory drugs) and two with combination drugs intake. Most drugs were given by intramuscular way (five patients), three with intravenous and two with oral routes. Most patients died without obvious reason , so mode of death was regarded as iatrogenic in five patients ,three with respiratory seize but without shock ,two with both shock and respiratory arrest and only one developed shock without respiratory arrest.

Lung swelling and congestion both were the most common finding in all necropsies, present in five cases (50%).Characteristics suggestive of anaphylaxis were seen in seven (70%) of cases and in all cases of iatrogenic causes with rapid immediate death (five cases with 100%). Three cases 30%) developed skin rashes with itching, edema of larynx was shown in three samples (Thirty percent) and of pharynx in five samples (Fifty percent), Upper respiratory edema was seen in only three cases (30%).Four cases with immediate death (40%) shoed features of lung extreme inflation with mucous blockage suggestive of underlying asthmatic problem during life also the presence of tiny petechial hemorrhages on the surface of the lung was seen in all ten cases (100%).Seven cases (70%) presented with cerebral swelling suggestive of cerebral hypoxia.

Other pathologic finding encountered during autopsy were the presence of coronary artery diseases, carcinoma and lung emphysematous changes in five (50%), two (20%) and one (10%) respectively.

All ten cases suspected of anaphylactic cause of death underwent thorough gross and microscopic

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examination, regarding histopathologic changes, all cases presented with upper air passages obstruction showed remarkable eosinophilia with mucosal edema and inflammatory changes, and grossly epithelial sloughing with mucosal obstruction. MCT enzyme was determined in sera of all victims and was elevated in only seven cases, the sample was measured as soon as possible after arrival to the mortuary but the exact time of death is unknown in most cases. Immunoglobulins study was not performed because of lack of specific kits for suspected allergen.

DISCUSSION

The current issue in Iraq was focused to declare suspected fatal anaphylactic deaths. A lot of deaths referred to the mortuary gave clinical history of anaphylactic and anaphylactoid reactions prior to death. Most of the cases were of iatrogenic origin (6).

The present study outlined that four of all ten acute allergy victims examined were without obvious gross autopsy signs of acute allergy this is because it is difficult to identify positive postmortem anaphylactic findings at necropsy so most cases present with negative findings against acute allergic reactions(7).

A research study of forty three fatal medications related reactions, Delage and others after examining the autopsy results, mentioned that upper air passages edema with mucous obstruction of bronchi to be present in only twenty two percent and twenty five percent of victims, respectively. It is hard to ascertain the reason of anaphylactic interaction in spite of causing no death (5,7). Elements that assume acute allergic reactions may involve a sudden previous contact with an allergen recognized to induce abrupt anaphylaxis, signs and symptoms of acute allergic reaction, a preceding history of response to similar or cross-reactive allergens, the precise immune gamma globulins type E antibodies to the allergen expected as a cause of the interaction, and increase in measures of byproducts of an allergy such as NMH (N-methyl histamine) in urine or blood MCT(8-10).In cases of victims of suspected fatal anaphylactic reactions, skin tests of culprit allergens are useless and impossible but serum tests of antibodies are amenable and specific since IgE antibodies elevations may stay in blood for respectable period after death(11).IgE antibodies can also be measured for some common drugs such as penicillins and some cross reactive drugs and also for thiocholine epitope which is a common antigen that is similar and cross reacts with a wide spectrum of muscle relaxants suspected as a cause of iatrogenic fatal acute allergic reactions(12).

In some occasions, Mast cells popularity and predominance may mimic anaphylactic reaction in spite of absence of IgE antibodies. MCT is an enzyme that is either 'beta' which is a protein delivered from specific granules of 'active' mast cells degranulated during active allergic reactions or 'alpha' which is delivered from 'resting' MC and increased in mastocytosis.MCT is fairly steady for many days in blood of victims died as a result of acute anaphylaxis and can be measured (10-13).

Discussions were running among scientists to rule out the benefits of testing and measuring the level of beta MCT since this enzyme may be raised in some natural deaths and fatalities without anaphylactic origin and on the reverse were within normal ranges in some deaths of acute asthmatic anaphylaxis, but with no doubt that beta MCT is certainly elevated in acute allergic interactions specially if associated with shock (14, 15).

Beta MCT was measured in all ten victims encountered in this study and was elevated in eight cases. In two negative victims, death was elapsed for at least twelve to fourteen hours, in this period , already increased values of MCT might restored to baseline within a period of time; after peak values that attained in the first few hours of an interaction, blood MCT levels decline, with a half-life around three to five hours (16).

Immunoglobulins type 'E' and MCT measurements are not performed in most instances and the main reason is ignorance even that these tests are available (17).

CONCLUSIONS AND RECOMMENDATIONS

Most cases of deaths related to suspected acute allergic reaction present with no diagnostic cutline signs and symptoms at necropsy specially if anaphylactic .The absence of specific signs and symptoms of allergic reaction or negative clinical history does not deny the presence of fatal allergic reaction. In all victims with suspected allergic reactions as suggestive cause of death even with no specific findings at autopsy, it is highly recommended to perform tests for IgE antibodies and MCT as routine tests of anaphylaxis. In cases of sudden onset of death, fatal anaphylaxis should be one of highly suspected cause and blood specimens from such victims should be kept for later testing of antibodies and MCT. The results of MCT and antibodies testing, medical history and autopsy findings with immunological consultation should all be interpreted together because in most cases of fatal anaphylactic deaths the diagnosis is difficult and uncertain and the causation of death as anaphylaxis in most cases is a matter of exclusion.

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