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Case Report

A case of sudden death due to pulmonary embolism of bone marrow origin, masked as acute drug toxicity: A rare case in a bewildering clinical scenario

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ABSTRACT

Introduction: Sudden death is unexpected death within 24 hours from the onset of symptoms with or without known preexisting conditions. Respiratory pathologies are the second most common cause of such deaths.

Brief History of Case: 39 years old male patient with a history of mental illness for the last 10 years and on regular treatment with antipsychotic medications, suffered sudden deterioration of higher functions and was admitted to the Medical College, and Hospital, Kolkata with a provisional diagnosis of drug toxicity. He succumbed to his condition within 24 hours of admission and the dead body was referred to Kolkata Police Morgue for a medicolegal autopsy.

Gross autopsy findings: Shows multi-system involvement in the form of Pulmonary Oedema, consolidation, broncho-pneumonic changes and subpleural petechiae, Cardiomegaly due to biventricular hypertrophy, Cerebral Oedema, Enlarged kidneys with loss of cortico-medullary differentiation and streaky cortico-medullary haemorrhages. Stomach findings were unremarkable.

Salient findings in ancillary investigations: 1) Toxicological Examination of blood, bile, vitreous and routine viscera was negative for any poison or pharmacological agents. 2) Histopathological examination with routine H&E staining showed Pulmonary oedema with lymphocytic infiltration and the presence of fat and hematopoietic precursor cells in pulmonary vessels, Interstitial Oedema and focal glomerulosclerosis and Periportal inflammation in the liver.

1. Introduction

Even with remarkable advancement of the of modern medicine, sudden death remains as a major concern for clinicians, and forensic pathologists. There are various definitions and diagnostic criteria, available for sudden death in the literature. But the recognized definition is based on the duration of time between the onset of symptoms and death.[1,2] The World Health Organization (WHO) definition of sudden death according to the International Classification of Diseases, version 10 (ICD-10) is death, non-violent and not otherwise explained, occurring less than 24 hours from the onset of symptoms.[2] Among the various causes of sudden death, cardiovascular, respiratory and neurological diseases contribute the majority, pulmonary pathologies being the 2^{nd} most common cause following cardiac ailments. Pulmonary embolism is the most common cause of such pulmonary pathologies. Though pulmonary thromboembolism is a fairly frequent finding during autopsies of sudden death, fat and marrow embolism is extremely rare. According to the established literature,

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microscopic fat globules with hematopoietic bone marrow cells can be found in pulmonary vasculature following fractures of long bone, soft tissue trauma, burns, severe cardiopulmonary resuscitation.

Antipsychotic drugs are mainly prescribed for psychiatric and behavioral diseases. They are known to cause various neurological and/or metabolic adverse effects on long term users. Also, these drugs are notorious as means of overdosing in psychiatric patients.

Though there are few reports of pulmonary thromboembolism in antipsychotic users; there are no reports on fat and marrow embolism following long -term antipsychotic therapy in available literature either locally or internationally.

In the following report, we present this case, which was suspected to be a case of drug toxicity, but following meticulous dissection and ancillary investigation, it was found out to be case of pulmonary embolism of fat and bone marrow origin.

2. Case History

A 39 years old male patient with history of mental illness, was on regular treatment with anti-psychotic medications e.g.; Sertraline, Aripiprazole, Haloperidol, Alprazolam, Risperidone etc for last 10 years. He experienced sudden deterioration of higher functions e.g., irritability, agitation followed by progressive drowsiness for last 4/5 days. On advice of his treating psychiatrist, the antipsychotic medications were stopped for 2 days. As there was further deterioration of his condition, he was admitted with provisional diagnosis of drug toxicity in the Medical College and Hospital, Kolkata. He was treated symptomatically and ultimately, he succumbed to his conditions within 24 hours of admission. As the emergency doctor suspected this case to be a case of drug toxicity, it was booked as medicolegal case. So, following the demise of the subject, the dead body was referred to Kolkata Police Morgue for medicolegal autopsy.

2.1. Findings

2.1.1. Autopsy findings

Routine medicolegal autopsy was conducted after around 15 hours of death.

2.1.2. External

A well-built, moderately nourished male subject with length of 175 cm and weight being 65 kg. Rigor mortis was well developed all over the dead body, Bluish-purple hypostatic stains present over back except the areas with contact pallor/flattening. Pupils were bilaterally dilated equally and fixed. No external injuries were detected.

2.1.3. Internal

On dissection, after opening up the thoracic cavity, we found pulmonary oedema, patchy consolidation, broncho-pneumonic changes and subpleural petechial hemorrhage on both the sides. There was also evidence of cardiomegaly (Wt-425 gm) due to biventricular hypertrophy. On exploring the abdominal cavity, kidneys were found to be enlarged (Wt- Lt-135gm; Rt- 145gm) with evidences of loss of cortico-medullary differentiation with streaky cortico-medullary hemorrhage on the both sides. Cranial cavity was also examined meticulously and evidences of cerebral oedema noted (Wt of brain-1550 gm). No other abnormality was detected elsewhere in the body.

2.2. Toxicological analysis

Blood, urine, vitreous humor and bile was sent for toxicological analysis, which came negative for drugs.

2.3. Histopathological examination

1. Lungs–Pulmonary oedema with lymphocytic infiltration, There was presence of fat and hematopoietic precursor cells in pulmonary vessels (Figures 1 and 2).

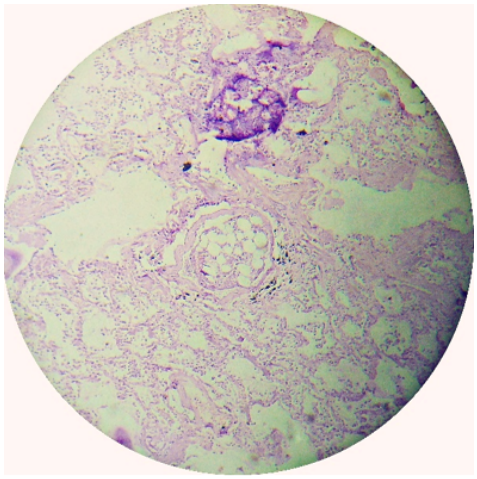

Fig. 1: Lung HPE (H&E stain) 100X

Kidneys—Interstitial Oedema and focal glomerulosclerosis (Figure 3).

Liver–Periportal inflammation, interstitial oedema with loss of cellular structure in the liver (Figure 4).

3. Discussion

This case is a rare presentation of pulmonary fat and marrow embolism in a background of long-term antipsychotic pharmacotherapy. Clinically significant fat embolism is mostly seen following fracture of bones, severe burn, crush injuries, decompression sickness, liposuction, parenteral fat

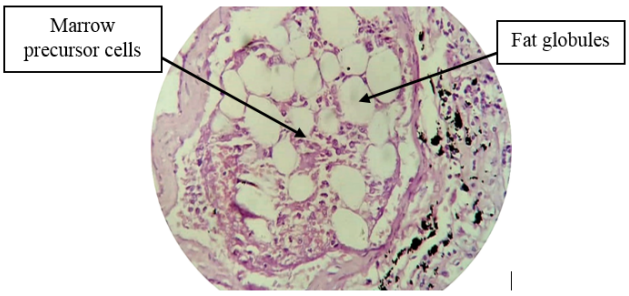

Fig. 2: Lung HPE (H&E Stain) 400X

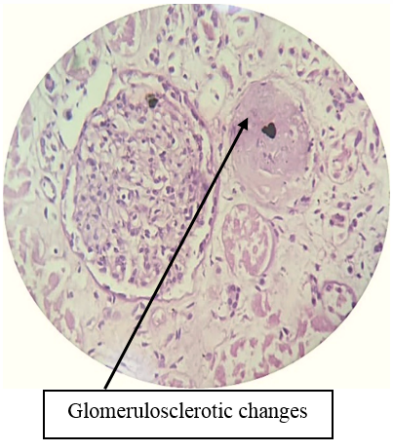

Fig. 3: Kidney HPE (H&E Stain) 400X

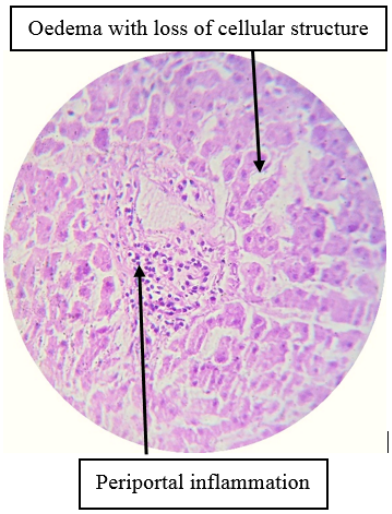

Fig. 4: Liver HPE (H&E stain) 400X

infusion. Clinically these cases usually present with acute onset confusional state, agitation, dyspnoeas, shock.[3,4] Even in those cases, detection of fat emboli either on gross examination or histopathological examination is rare following autopsy. As it is postulated that fat disappears fairly quickly due to action of lipolytic enzymes present in the lung tissues.[4] Bone arrow embolism is even a rarer observation in human beings. Bone marrow emboli only occlude small and medium sized vessels. It is distinct from the fat embolism because of presence of characteristic marrow cells and it is detectable only under microscope unlike fat embolism. According to the various available scientific literature, bone marrow embolism is seen only following trauma to the bones.[5–8]

Though anti-psychotic drugs especially atypical antipsychotics are known to cause cardiovascular side effects e.g., thromboembolism on long term use; it is not known to cause fat and marrow embolism according to available literature.[9,10]

Therefore, this unique findings of this case, gives us a new perspective regarding investigation of cause of death in the cases of sudden death. So, for further exploration, we should keep in mind that even without the history of obvious trauma of extensive soft tissue injury, fat and marrow embolism may occur. In such cases, meticulous dissection along with ancillary investigations especially histopathology would be highly recommended.

4. Abbreviations

HPE- histopathological examination; H&E- Hematoxylin and Eosin; Wt- Weight; Lt-Left; Rt- Right**.**

5. Conflict of Interest

None.

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None.

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