DISSEMINATED INFECTIONS AS CAUSE OF DEATH DETECTED AT ORGAN AUTOPSY- 2-YEAR STUDY
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ABSTRACT

BACKGROUND
Tuberculosis and Malaria are among the leading causes of infectious disease-related deaths worldwide. Plasmodium falciparum is almost always responsible for the most severe cases of malaria, leading to multi organ failure and higher mortality rates among the plasmodium species. India has the highest burden of TB in the world, an estimated 2 million cases annually, and accounting for approximately one fifth of the global incidence. Despite the availability of effective treatment for most cases, tuberculosis is still a cause of death in our environment; as in some cases, the diagnosis of tuberculosis may not be established until after the patient had died and an autopsy has been performed.

MATERIALS AND METHODS
The present prospective study includes 93 cases of medico legal organ-autopsies reported at Osmania General Hospital/Osmania Medical College during a period of 2 years. Of these, cause of death in 3 cases was attributed to disseminated tuberculosis involving multiple organs and one rare case of disseminated Plasmodium falciparum malaria was reported involving multiple organs such as heart, brain, liver, kidneys and spleen in a 26-year-old male who presented with a brief history of fever and vomiting.

RESULTS
The presence of unspecific symptomatology, insufficient cost-effectiveness of the diagnostic tests and precocious death, are identified as the most frequent causes of undiagnosed cases of deaths due to infectious aetiology.

CONCLUSION
Infectious diseases are under-recognized cause of sudden death, usually autopsy can help in identifying the cause of death in such cases.

KEYWORDS
Tuberculosis, Malaria, Autopsy.


BACKGROUND
Despite decreasing autopsy rates in many parts of the world, autopsy retains its value for determining the cause of death, for detecting clinically unknown lesions, as a quality assurance tool, and for providing accurate information for death certification. Disseminated TB, characterized by the involvement of multiple organs is defined as tuberculosis infection involving the blood stream, bone marrow, liver or 2 or more non-contiguous sites, or miliary TB which is an acute form of TB that results from widespread hematogenous dissemination of tubercle bacilli.1

Of the 4 species of human malarial parasites, Plasmodium falciparum is the most common cause of severe complicated malaria. Although the risk of death due to mild, uncomplicated malaria is low, infection occurring in individuals with insufficient immunity can progress to life-threatening disease when untreated or inadequately treated.

MATERIALS AND METHODS
The present study highlights 4 rare cases of infectious diseases identified incidentally among 93 organ autopsies conducted at department of pathology at our institute over a period of 2 years between January 2016 to December 2017. The organs removed at autopsy were preserved in 10% neutral buffered formalin fixative and sent for examination. Microscopic sections were made from tissues obtained at autopsy and were reviewed histologically. Special stain for Acid fast bacilli with Ziehl-Neelsen and Malarial parasite with Giemsa was performed for identification of infectious agents.
RESULTS
In our study, three cases of tuberculosis were diagnosed with findings of caseating tuberculous granulomas and one case of disseminated falciparum infection in multiple organs diagnosed at organ autopsy incidentally. These 4 cases represent 4.30% of all organ autopsies (n=93) performed at our hospital during two-year period from 2016 Jan -2017 Dec.

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Clinical Info</th>
<th>Organs Received</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>42 years Female, known case of tuberculosis under treatment had a sudden collapse and died.</td>
<td>Heart, part of lung, part of liver</td>
<td>Lung - caseating granulomatous lesions.</td>
</tr>
<tr>
<td>2.</td>
<td>21 years male, apparently healthy young male with sudden death.</td>
<td>Heart, mediastinal structures, liver, lung</td>
<td>Disseminated tuberculosis – lung, liver and heart</td>
</tr>
<tr>
<td>3.</td>
<td>26 years male with brief history of fever and vomiting.</td>
<td>Brain, heart, kidney, spleen, part of liver</td>
<td>Disseminated cerebral malaria - Trophozoites of plasmadium falciparum detected in brain, heart, kidney, spleen and liver.</td>
</tr>
<tr>
<td>4.</td>
<td>32 male, generalized weakness and fever</td>
<td>Liver, lung</td>
<td>Granulomatous infection – Koch’s aetiology</td>
</tr>
</tbody>
</table>

Table 1. Clinical Information

The patients ranged in age at the time of death from 21 to 42 years. One of the patients was diagnosed of TB before death and was undergoing treatment. The presence of numerous tuberculous granulomas corresponding to miliary TB was defined as macroscopic dissemination of millet seed-sized lesions in pulmonary areas and pathologic evidence of lesions with an active granulomatous reaction in at least 2 organs. (Figure 1)

Histopathology of one case revealed severe sequestration of Plasmodium falciparum-infected erythrocytes in brain microvasculature through cytoadherence to endothelium, along with dissemination in other organs including heart, liver, kidneys and spleen. (Figure 2)

Figure 1
1. TB: lung- Gross- cut section shows cut open bronchus along with enlarged multiple hilar lymph nodes measuring 3X2 cms each, grey-tan, areas of caseous necrosis noted. Adjacent lung parenchyma showed consolidation with miliary foci.
2. Liver – cut section of liver showed areas of congestion grossly.
3. Heart- thickened pericardium with adhesions.

Figure 2
1. TB: lung- Gross- cut section shows cut open bronchus along with enlarged multiple hilar lymph nodes measuring 3X2 cms each, grey-tan, areas of caseous necrosis noted. Adjacent lung parenchyma showed consolidation with miliary foci.
2. Liver – cut section of liver showed areas of congestion grossly.
3. Heart- thickened pericardium with adhesions.
DISCUSSION

Tuberculosis is a notifiable infectious disease in India. Disseminated TB is a potentially lethal form of TB resulting from massive lymphohematogenous dissemination of Mycobacterium tuberculosis bacilli. The emergence of the HIV/AIDS pandemic and widespread use of immunosuppressive drugs has changed the epidemiology of disseminated TB. Impaired cell-mediated immunity underlies the disease's development. Clinical manifestations are non-specific, and typical chest radiographic findings may not be seen.\(^1\) Although extra pulmonary tuberculosis (TB) had been observed for many centuries, the exact incidence of disseminated TB is still unclear.

Disseminated TB is defined as tuberculous infection involving the blood stream, bone marrow, liver, or 2 or more non-contiguous sites, or miliary TB.\(^1\)\(^2\) The name miliary tuberculosis was derived from the Latin word miliarius, meaning related to millet seed to describe the resemblance of gross pathological findings to that of innumerable millet seeds in size and appearance.\(^3\)\(^-\)\(^6\) It results from erosion of mycobacteria laden inflammatory foci into blood vessels with subsequent showering of bacilli into blood stream and seeding into non-pulmonary sites.\(^6\) The symptoms are nonspecific and the duration of symptoms before diagnosis is variable.\(^1\) Therefore, it mimics a variety of diseases and requires a high index of suspicion. Miliary TB accounts for 1% to 2% of cases of tubercle bacillus infection, but the purified protein derivative tuberculin skin test is positive in only 36% of patients with miliary TB. In addition, the miliary pattern is not always evident radio graphically upon presentation of symptoms, and another underlying pulmonary disease may be present.\(^6\) High resolution CT chest and contrast enhanced CT and MRI are useful in identifying miliary lesions at extra pulmonary sites as 50% of chest radiographs are normal in confirmed cases of disseminated tuberculosis.\(^6\)

A lesser encountered manifestation of disseminated tuberculosis in the form of sudden death finds a mention in the literature.\(^7\) In one of the studies it was noted that all-cause mortality rate of TB patients was 12.4%, and this was mainly due to non-TB-related causes (82.7%). Malignancy, liver cirrhosis, renal failure, and miliary and pneumonic radiographic patterns predicted mortality in all TB deaths.\(^6\) Of all cases of tuberculosis cases found at autopsy, progressed rapidly and 33%–80% were missed ante mortem.\(^1\) Moreover, it is often fatal if not promptly treated with delay of a mere 1–8 days.\(^1\)

Although this study comprises of only four cases, of which three were disseminated tuberculosis. In one of the cases, a 21-year-old male deceased on autopsy showed to have disseminated tuberculosis with an unusual involvement of heart muscle. Grossly, pericardium showed numerous grey-white miliary spots with myocardium also showing similar miliary modules of size ranging 1-3 mm. Microscopy revealed numerous caseating granulomas (Figure 3 and 4).

TB should be included in differential diagnoses in patients presenting with severe pneumonia, sepsis or other severe infections such as meningitis. In a study, those patients presented as bacterial pneumonia and died rapidly due to septic shock were later found to have tuberculosis on autopsy. Previously reported TB-related critical conditions were mainly miliary TB with respiratory failure and ARDS.\(^6\)\(^9\)

In the only case of malaria that we encountered, on autopsy various organs showed grossly mild enlargement with slate-grey spleen and brain, liver, heart, kidney showed mild petechial spots. On microscopy, heavy intra-erythrocytic parasitic load in vascular spaces was noted (Figure 5).

Mortality of malaria is often due to by complication of severe P. falciparum infection. The sequestration of Plasmodium falciparum-infected erythrocytes in brain microvasculature through cytoadherence to endothelium, is the hallmark of the definitive diagnosis of cerebral malaria. The effects of sequestration could cause functional disturbance of the organs and lead to organ failure.\(^4\)

CONCLUSION

Infectious diseases are under-recognized aetiology of sudden death and usually autopsy can help in identifying the cause of death in such cases. In our country, tuberculosis and malaria being endemic, a high suspicion for these aetiologies must be considered in cases of fever of unknown origin to reduce the mortality rates due to these infections.

REFERENCES
