ARDS in Scrub Typhus
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Introduction
Scrub typhus is a mite-borne infectious disease caused by Orientia tsutsugamushi. It is an acute febrile illness which generally causes non-specific symptoms and signs. The clinical manifestations of this disease range from sub-clinical disease to organ failure to fatal disease. Deaths are attributable to late presentation, delayed diagnosis, and drug resistance. Acute respiratory distress syndrome (ARDS) is a serious complication of scrub typhus. The mortality rate for the scrub typhus patients with ARDS can range up to 25% (1).

Recently with increasing trend of outdoor recreation activities, mountaineering, urbanization into rural areas, even physicians those who are not in the endemic areas may encounter the disease and should be aware of its symptoms and complications.

If there is delay in the initiation of the appropriate antimicrobial therapy patient may present with serious complications when diagnosis is delayed or patient is not treated with appropriate antibiotic, the scrub typhus can present with serious complications such as renal failure, myocarditis, septic shock, meningoencephalitis and rarely acute respiratory distress syndrome that may lead to death. The pulmonary manifestations of scrub typhus are varying grades of bronchitis and interstitial pneumonitis progressing to ARDS (1). Acute respiratory distress syndrome is defined as an acute and persistent lung inflammation with increased vascular permeability and is most often associated with sepsis syndrome, aspiration, primary pneumonia, or multiple traumas (2).

Pathology of ARDS
The pathologic progression of ARDS reflects the sequentially occurring exudative, organizing (fibroproliferative) and fibrotic stages. There are reports of diffuse alveolar damage in the organizing stage without evidence of vasculitis (3). Pathological findings in ARDS patients on gross inspection reveal oedematous and haemorrhagic lungs. Microscopic examination revealed diffuse alveolar damage with hyaline membrane formation and interstitial pneumonitis with infiltration of inflammatory cells. Immunohistochemical stain showed O. tsutsugamushi antigen depositions in the endothelial cells. It is also possible to demonstrated iNOS in the alveolar macrophages and lung tissue debris in both cases. Thus, direct endothelial cell invasion of the organism and marked iNOS expression may be involved in the pathogenesis of ARDS associated with scrub typhus (4).

Clinical Studies with ARDS
A retrospective study in Taiwan, China reviewed the medical records of 72 patients diagnosed with scrub typhus from January 1998 to August 2006. Patients with ARDS were included in study while patients without ARDS served as controls. Mortality rate was found to be 25%. The study highlighted that significant predictors of ARDS are initial presentations of dyspnea and cough, white blood cell count, hematocrit, total bilirubin, and delayed used of appropriate antibiotics while albumin, prothrombin time, and delayed use of appropriate antibiotics are independent predictors of ARDS. Identification and keeping these relative risk factors in the mind may help clinicians to evaluate & identify clinical cases of scrub typhus with ARDS early (5).

In the same study group the biochemical parameters were studied in detail, which indicated that WBC counts of the ARDS group were significantly higher than those of the control group, which reflects the seriousness of infection in the ARDS group. Hematocrit in the ARDS group was significantly lower than that of the control group, which suggested that the ARDS group was more anemic than the control group. Although all liver enzyme levels (AST, ALT, ALP, and total bilirubin) were increased in both the ARDS and control groups, only the total bilirubin level was significantly higher in the ARDS group than in the control group. Therefore, a scrub typhus patient with severe infection, anemia and jaundice may be considered to be at high risk for developing ARDS (5).

In general, fever for more than one week was the only common manifestation in patients clinically and serologically confirmed to have scrub typhus. At times, it may present without the typical symptom of high fever, as in case of an aged patient in Japan and subsequently developed the complication of ARDS but improved dramatically on timely intervention with minocycline and supportive measures (6).

In another study, scrub typhus patients presented in

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emergency with acute respiratory distress syndrome and
history of fever for more than one-week duration and were
positive for Weil Felix reaction. All these patients with scrub
 typhus and ARDS responded dramatically to doxycycline
and the fever subsided after five days (7).

Interstitial pneumonia is the most frequent chest
manifestation of scrub typhus. The presence of interstitial
pneumonia is closely associated with morbidity and severity
of disease for patients with scrub typhus. The physician
should recognize the presence of interstitial pneumonia as
being the important determining factor for predicting the
clinical course and prognosis for patients with scrub typhus (8).

Chest radiography should be included in the initial
evaluation of patients with suspected scrub typhus. Bilateral
reticular infiltration, with or without cardiomegaly or
congestive heart failure are the most frequent radiographic
finding of scrub typhus. The pulmonary manifestations of
scrub typhus include interstitial pneumonia, interstitial
edema, and hemorrhage caused by vasculitis. Interstitial
pneumonia (IP) frequently occurs in patients with scrub
 typhus and is closely associated with severity of the disease.
The recognition of the presence of Interstitial Pneumonia
is an important determining factor for predicting the clinical
course and prognosis for patients with scrub typhus.

Bilateral diffuse areas of reticulonodular opacity and
septal lines are the most common findings (1, 2). Airspace
consolidation is relatively uncommon and generally appears
in the lower zone of both lungs (1, 2). Unilateral or bilateral
hilar enlargement and pleural effusion are common
radiographic features, found in 25%-27% and 12%-43%
of patients, respectively (1, 2).

Ground-glass opacity, interlobular septal thickening and
pleural effusions are common findings at thin-section CT,
whereas bronchial wall thickening, centrilobular nodules
and axial interstitial thickening are less common.

HRCT of lower lung zones shows interlobular septal
thickening, bronchial wall thickening, diffuse ground glass
opacities in the dependent lung zones, increased vascular
diameter may also be present.

Doxycycline would be an appropriate initial antimicrobial
treatment in patients who develop cardiovascular
involvement shown by chest radiography as been depicted
in a study and azithromycin & rifampicin in resistant cases
(9,10).Meticulous respiratory supportive care must then
be provided .Treatment of the hypoxemia seen in ARDS
usually requires tracheal intubation and positive-pressure
mechanical ventilation.

The public health importance of this disease is under-
estimated due to difficulties in clinical diagnosis and lack
of laboratory methods in many geographical areas. Scrub
typhus is known to occur all over India and therefore
physicians should be aware of this potentially serious but
easily treatable disease. This strategy, if meticulously
followed, by all practitioners will surely help to bring down
the occurrences of ARDS associated with scrub typhus.

Conclusion

Scrub typhus is a mite-borne infectious disease caused
by Orientia tsutsugamushi. Acute respiratory distress
syndrome (ARDS) is a serious complication of scrub typhus.
The mortality rate for the scrub typhus patients with ARDS
can range up to 25%. Initial presentations of dyspnea and
cough, white blood cell count, hematocrit, total bilirubin,
and delayed used of appropriate antibiotics are significant
risk factors of ARDS. Identification of these relative risk
factors with timely and aggressive treatment of this fatal
complication may help clinicians to reduce related mortality
associated with Scrub Typhus

References