Original Article

Role of HRCT in detection and characterization of pulmonary abnormalities in patients with febrile neutropenia

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ABSTRACT

Background: Fever is of grave concern in the management of patients with neutropenia with early detection of a focus of infection being the major goal. As lungs are the most common focus, chest imaging is of vital importance. This Institute Review Board approved prospective study was undertaken to assess the usefulness of high resolution computed tomography (HRCT) in early detection and characterization of pulmonary abnormalities in febrile neutropenia. **Materials and Methods:** A total of 104 consecutive patients (M:F:75:29, age range 11-66 years) with fever of 38.2°C or more with an absolute neutrophil count <500/μl underwent HRCT chest. HRCT diagnosis was compared with final diagnosis based on ancillary investigations. **Results:** HRCT could detect pulmonary abnormalities in 93 patients (89.4%) with air space consolidation being the predominant finding ($n = 57$), followed by ground-glass opacities (Ground glass opacity (GGO), $n = 49$) and nodules ($n = 39$). HRCT could correctly characterize the infective lesions in 76 patients (81.7%). Presence of random or pleural-based nodules >10 mm with or without surrounding GGO or cavitations was sensitive (95.23%) and specific (96.7%) for fungal infection, while small (1-4 mm) random or centrilobular nodules with tree-in-bud appearance was sensitive (90%) and highly specific (97.02%) for tuberculosis. Diagnosis of pyogenic infection based on presence of air-space consolidation, pleural effusion, GGO or centrilobular nodules showed a sensitivity of 84.78% and specificity of 93.84%, whereas patchy or diffuse GGO, interstitial thickening and/or air-space consolidation showed high sensitivity (86.7%) and specificity (96.8%) for *Pneumocystis jiroveci* pneumonia. **Conclusion:** HRCT chest is an excellent modality in the diagnostic work-up of patients with febrile neutropenia allowing early detection and characterization of pulmonary abnormalities.

KEY WORDS: Febrile neutropenia, high resolution CT, imaging, pulmonary infections

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INTRODUCTION

Neutropenia is defined as an absolute neutrophil count (ANC) more than two standard deviations below the normal mean. Patients with severe neutropenia (count <500/μL) are susceptible to life threatening infections. Fever is a common problem with these patients and febrile neutropenia is defined as fever of 38.2°C or more with an ANC of 500 or less the same day or day after.[1-3]

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The causes of neutropenia may be extrinsic or intrinsic to bone marrow myeloid cells. Cytotoxic chemotherapy and radiotherapy are being increasingly used to treat different types of cancers and hematological malignancies. These, along with the underlying malignancy cause neutropenia and associated compromise of the cellular immunity and thereby, predispose the patients to a much greater risk of infection than other causes of isolated neutropenia. Neutropenia is also encountered in conditions requiring long-term steroid and/or immunosuppressive therapy including transplant recipients, connective tissue disorders, etc. In long-term (>10 days) neutropenia, this risk rises to more than 85%.[1-3]

Bacterial pathogens, mainly Gram-positive (65-75%) are responsible for approximately 90% of the infections in the early phase of neutropenia.[3] The nature of these infections is serious and if left untreated, have a high mortality rate (up to 100%).[4] Empirical broad-spectrum

antibiotics have been accepted as a standard treatment protocol in febrile neutropenic patients. However, they are not targeted to a specific organism, and are associated with increased side effects and risk of super added fungal infections. Moreover, many infection mimics such as graft versus host disease, radiation or drug toxicity, pulmonary hemorrhage or leukemic infiltrates are underestimated by empirical antibiotics. High cost of antibiotics is another consideration.[3,4]

The lungs are the most common organ to be infected in febrile neutropenic patients.[5] The chest radiograph is the standard initial investigation to look for pulmonary changes. However, the sensitivity of chest radiographs for the detection of pulmonary abnormalities has been shown to be very low.[6,7] High resolution computed tomography (HRCT) chest can detect the abnormality with a high degree of accuracy, as well as differentiate between different types of infections.[5] It is extremely useful in early detection or exclusion of a focus of infection and characterization of the focus. Exact etiological diagnosis is not possible in most of the cases, but identification of broad category of infective causes itself is very important for the appropriate therapy. Pattern identification adds significantly to the improved management of the patients. The use of HRCT with subsequent guided bronchoalveolar lavage (BAL) has been recommended as the most sensitive technique for the detection of pneumonia.[5]

Till date, no radiological data is available that identifies and characterizes the spectrum of infections and defines the HRCT pattern of pathogen profile in patients of febrile neutropenia in the Indian population. We therefore undertook this study to assess the usefulness of HRCT chest in the early detection and characterization of pulmonary abnormalities in patients with febrile neutropenia and to attempt to correlate the HRCT pattern with the etiological agent. To the best of our knowledge, our study is first of its kind to be conducted in our country.

MATERIALS AND METHODS

In this Institute Board approved prospective study, 104 consecutive patients with febrile neutropenia due to any cause were enrolled after informed consent. These patients included were those with malignancy with or without anticancer therapy, and those receiving immunosuppressive therapy for organ transplants, bone marrow transplants, etc. All patients with febrile neutropenia, that is, fever of 38.2°C or more with ANC of <500/μL the same day or day after were included if they presented to this hospital within 48 hours from the onset of fever.

Methodology

Following a detailed questionnaire related to pulmonary symptoms and coexisting disorders, a detailed clinical examination was conducted and a hemogram obtained. HRCT chest was done using 1.25 or 1 mm collimation at 10 mm intervals using a high frequency algorithm on a 4 slice (Light speed Qxi plus, GE medical systems, Milwaukee, WA) or a 16 slice (Somatom sensation 16, Siemens medical systems, Forscheim, Germany) CT scanner. Standard kVp (120) and mAs (200-250) were used. The CT scans were interpreted by an experienced chest radiologist.

Patients were kept on regular follow up and the details of investigations like sputum examination, blood cultures, BAL/transbronchial lung biopsy (TBLB), etc., were recorded. Records of the clinical status and the details of treatment were maintained. Positive results of sputum/blood/BAL, etc., and/or clinical response to particular drugs were taken as the criteria for final diagnosis.

RESULTS

A total of 104 patients (75 males and 29 females) were enrolled in the age group of 11-66 years with a mean age of 39.7 years. The vast majority of patients were suffering from hematological malignancies who developed febrile neutropenia during or after treatment. There were 18 patients with acute myelogenous leukemia (AML), 12 patients with chronic myelogenous leukemia (CML), 16 patients with acute lymphocytic leukemia (ALL), 6 patients with chronic lymphocytic leukemia (CLL), 9 patients with non-hodgkins lymphoma (NHL), 4 patients with myelodysplastic syndrome, 4 patients with aplastic anemia, 4 patients with myelofibrosis, 3 patients with hairy cell leukemia, 1 patient with carcinoma breast, 16 patients were postrenal transplant, 4 cases of systemic lupus erythematosus (SLE), and 4 constituting the miscellaneous category in our study. There were also four human immunodeficiency virus (HIV) positive patients.

Besides fever, dyspnea and dry cough were the predominant symptoms. The mean delay of onset of symptoms in the patients with malignancies after initiation of therapy was 3 weeks. However, onset of symptoms in the noncancer immunosuppressed group was significantly later with a mean of 8 months.

Chest X-ray findings

Most of the patients had a normal chest X-ray (68.26%). Of the 71 patients with a normal chest radiograph, subsequent HRCT chest showed pulmonary abnormalities in 61 patients. The remaining chest X-rays showed air space consolidation in 19 (18.2%), nodules in 3 (2.8%), cavitation in 4 (3.84%), reticulonodular shadows in 2 (1.9%), bronchiectasis in 2 (1.92%), pleural effusion in 7 (6.7%), and lymphadenopathy and fibrotic band in 1 X-ray (0.96%) each.

HRCT findings

A total of 93 patients showed abnormal imaging findings on HRCT. In 11 cases, HRCT was normal. Air space

consolidation was the commonest finding present in 57 (54.8%) cases, being multifocal in 43 cases and unifocal in 14 cases. Twelve patients had patches of fibrosis and collapse. Nodules were seen in 39 (37.5%) patients. Both small and large nodules, measuring from 2 mm to 2.5 cm were encountered. Small nodules were centrilobular in distribution in 12 cases with tree-in-bud pattern in 5 cases. Majority of the larger nodules were random and peripheral in distribution. A halo of ground glass opacity was seen around the nodules in 11 cases with eccentric cavitation in 6 cases.

Ground glass opacity (GGO) was the second most common finding seen in 49 (47.1%) patients. Bilateral diffuse GGO was seen in 10 cases. In 28 cases, the GGO was patchy and in another 11 cases it was seen around the nodules as a halo. Bronchiectatic changes were seen in 10, mosaic perfusion in 3, septal thickening in 18, lymphadenopathy in 20, and pleural effusion in 33 patients. Table 1 summarizes the findings on HRCT chest.

HRCT findings were highly suggestive of specific pulmonary infection in 77 patients. In 16 of these cases, ill- and well-defined nodules with spiculated margins were seen with a surrounding halo of GGO in 11 cases. In six cases, nodules showed eccentric cavitation and in four patients, air-crescent sign was positive. In all of these patients, a HRCT diagnosis of fungal pneumonia was suggested [Figure 1]. BAL was positive for *Aspergillus* in eight patients, while blood culture was positive for *Candida albicans* in one patient. In the remaining seven cases, antifungal therapy was started based on the HRCT findings with favorable clinical response.

In 12 cases, HRCT showed patchy or diffuse ground glass haze associated with interlobular and/or intralobular septal thickening in eight cases. Pulmonary cysts were present in four cases. The GGO was associated with discrete and/or confluent areas of consolidation in seven cases. In all these cases, a diagnosis of *Pneumocystis jiroveci* pneumonia (PCP) was offered [Figure 2]. In five of these patients, BAL confirmed the diagnosis and the remaining seven patients responded to cotrimoxazole therapy.

A diagnosis of tuberculosis was offered in nine cases based on the HRCT findings of centrilobular nodules [Figure 3], consolidation and pleural effusion in varying combinations. Of these, sputum for AFB was positive in five patients. In one patient, there were multiple, small (1-4 mm) randomly distributed nodules associated with right pleural effusion and bilateral upper lobe consolidation. Three patients showed centrilobular nodules with a tree-in-bud appearance at places in two cases. One of these cases also had multifocal patchy consolidation and bilateral pleural effusion. In all these four cases, a HRCT diagnosis of tuberculosis was offered. Antitubercular therapy was given empirically based on

Table 1: HRCT chest findings

Radiologic abnormality	No. of patients	Frequency (%)
Air-space consolidation	57	54.8
Nodules/nodular shadows	39	37.5
Fibrosis	12	11.5
Bronchiectasis	10	9.6
Emphysematous changes	5	4.8
Cavitation	8	7.6
Septal thickening	18	17.3
Interlobular only	8	7.6
Intralobular only	2	1.9
Both	8	7.6
Ground glass opacity	49	47.1
Mosaic perfusion	3	2.8
Lymphadenopathy	20	19.2
Hilar only	1	0.9
Mediastinal only	14	13.4
Both	5	4.8
Pleural effusion	33	31.7
Air cysts	6	5.7

HRCT: High resolution computed tomography

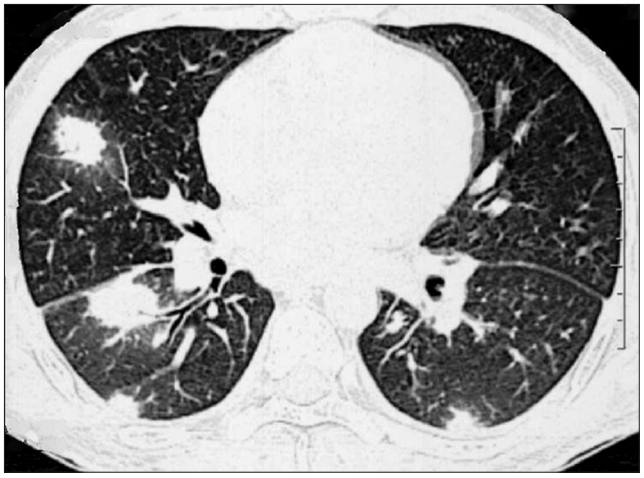

Figure 1: A case of NHL with ANC of 360/μl. HRCT chest shows multiple large nodules in both lungs with halo sign evident in most of the nodules suggestive of fungal pneumonia. Fungal serology was positive for aspergillus

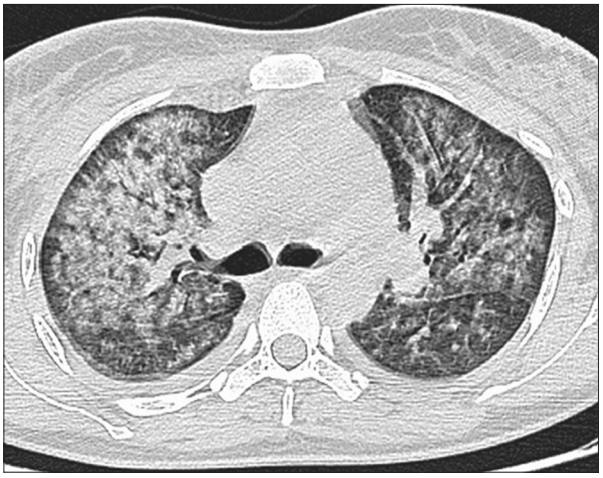

Figure 2: A case of AML with ANC of 200/μl, presented with high grade fever and dyspnea. HRCT chest reveals bilateral diffuse GGO with air space consolidation and subpleural sparing and a few air cysts classical of *Pneumocystis jiroveci* pneumonia

the symptomatology and the HRCT findings. All patients showed good response to therapy.

Pyogenic infection was considered a first choice diagnosis based on unifocal or multifocal consolidation in 36 cases. Associated pleural effusion was present in 21, GGO in 15, centrilobular nodules in 5, and cavitation in 3 cases. Microbiological proof could be obtained in 22 cases, (Group A β hemolytic streptococci in 13 cases, coagulase positive staphylococci in 8 cases and *Klebsiella* in 1 case) by means of Gram staining of sputum, sputum culture, and blood culture [Figure 4].

In three cases, a diagnosis of mixed pyogenic and fungal infection was offered based on presence of air space consolidation as well as nodules and pleural effusion. Sputum examination revealed Gram positive cocci in all three cases. The absence of clinical response to antibiotics alone prompted the addition of antifungals and the patients showed improvement. In one patient, possibility of mixed infection with *P. jiroveci* and fungi was considered based on bilateral diffuse GGO, consolidation and nodules. However, the patient responded to cotrimoxazole alone.

In a patient of carcinoma breast with post chemo-radiation therapy, HRCT was suggestive of radiation fibrosis and no organism was grown from sputum or blood culture. In two patients nonspecific GGO was seen in the lungs, while sections through the lung bases showed hepatic lesions suggestive of abscesses. Blood culture revealed group A β hemolytic streptococci. In two patients of chronic myeloid leukemia, multiple discrete and conglomerate lymph nodes were seen in the mediastinum and hila with bilateral pleural effusion. We suggested lymphoma as the diagnosis. Subsequent CECT abdomen showed retroperitoneal lymphadenopathy, biopsy from which proved lymphoma.

In 12 patients, the final diagnosis as inferred from clinical outcome and/or various microbiological investigations was not in agreement with the HRCT diagnosis. One patient had patchy GGO with centrilobular nodules. We offered pyogenic small airway disease as the first choice diagnosis and viral infection as the second choice diagnosis. But the patient's sputum was positive for AFB and he responded to antitubercular therapy. Another patient had patchy GGO with interlobular septal thickening which prompted us to suggest *P. jiroveci* pneumonia, however, the patient responded to antibiotics alone. Conversely, based on the presence of patchy consolidation and small centrilobular nodules, we offered tuberculosis as the diagnosis in one patient, but the blood culture grew Klebsiella and the patient responded to antibiotics. One patient had a mass like consolidation with areas of breakdown in the right upper lobe. Our HRCT diagnosis was necrotizing pneumonia but fungal serology was positive for aspergillus and the patient showed clinical response to antifungal therapy. One patient had HRCT features suggestive of a mixed bacterial and fungal infection but the patient responded to cotrimoxazole alone. Another patient had features suggestive of a mixed infection with *P. jiroveci* and fungus, however, the blood culture grew streptococcus. One patient with prior history of tuberculosis had fibrosis with subsegmental collapse in the right middle lobe responded to antibiotics. Another patient with cavitary lesions in both upper lobes with centrilobular nodules diagnosed as tuberculosis on HRCT also responded to antibiotics. One patient with diffuse GGO with air cysts was diagnosed as PCP but also responded to antibiotics. Conversely another patient with patchy GGO with random small nodules diagnosed as pyogenic infection on HRCT responded to cotrimoxazole. In one patient, we reported the HRCT chest as normal, however, BAL showed leukemic infiltrates in this patient. One patient had sub-centimetric mediastinal lymphadenopathy with no parenchymal abnormality, the patient responded to empirical antibiotics. Table 2 shows the comparison of HRCT diagnosis with the final diagnosis while Table 3 summarizes the performance of HRCT chest in diagnosis of infections.

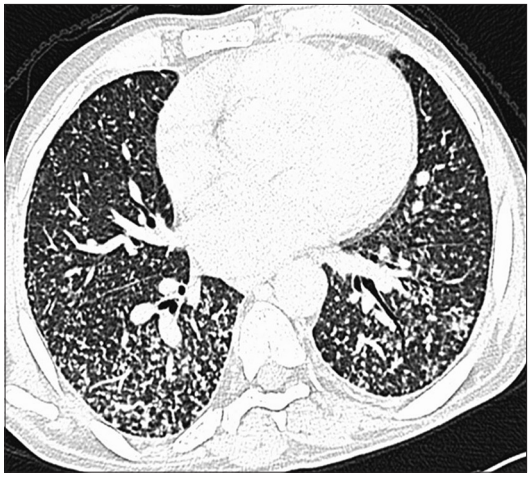

Figure 3: A case of myelofibrosis with ANC of 200/μl. HRCT chest shows multiple small randomly distributed nodules (2-3 mm) in both lungs with tree-in-bud appearance at places suggestive of miliary tuberculosis. Patient's sputum was positive for AFB

DISCUSSION

Lungs are the most commonly affected organ in febrile neutropenia. In a report by Tenholder, up to 98% of leukemia patients who came to autopsy had pulmonary complications.[8] Hence, the initial investigations to

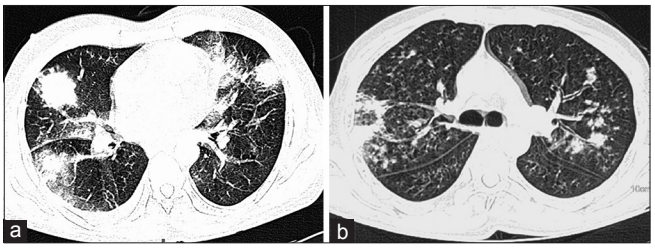

Figure 4: (a, b) A patient of AML (postchemotherapy), with fever and an ANC of 120/μl. HRCT chest shows B/L multifocal consolidation (a) with small nodules in both upper lobes (b) suggestive of pyogenic infection. Sputum was positive for group A streptococcus

Table 2: Comparison of HRCT diagnosis with final diagnosis

Diagnosis	On HRCT	True positive	False positive	False negative	Final diagnosis
Pyogenic	43	39	4	7	46
Fungal	22	19	3	1	20
P. jiroveci	16	13	3	2	15
Tuberculosis	12	9	3	1	10
Postradiation fibrosis	1	1	0	0	1
Lymphoma	2	2	0	0	2
Hepatic abscess	2	2	0	0	2
Nonspecific lymphadenopathy	1	0	0	1	Responded to antibiotics
Normal	11	10	0		10 normal
				1	Leukemic infiltrates
Total	110	85	13	11	107

Mixed infection was diagnosed on HRCT in 6 and proved in 3 cases. HRCT: High resolution computed tomography

Table 3: Performance of HRCT chest for diagnosis of infections

Etiology	Sensitivity %	Specificity %	PPV %	NPV %
Pyogenic	84.78	93.84	90.69	89.7
Fungal	95.23	96.7	86.36	98.98
P. jiroveci	86.7	96.8	81.25	97.89
Tuberculosis	90	97.02	75	98.98

HRCT: High resolution computed tomography

localize the site of infection should focus on the lungs. Noninvasive investigations like chest X-ray and HRCT have inherent advantages over invasive ones.

Chest X-rays are readily available, cheap, and have advantage of portability. But the diagnostic yield in terms of sensitivity and specificity is very low. None of the previous studies have shown the X-rays to have a high diagnostic value.[3,5-7,9] In the study by Donowitz *et al.*, only 40 (22%) out of 187 chest X-rays had abnormal findings during episodes of febrile neutropenia.[6] Similar studies carried out by Katz *et al.* and Roy *et al.* showed a sensitivity of 20% and 38%, respectively.[7,10] In our study also, chest X-rays of only 33 (31.74%) patients showed abnormal findings. Hence, we also concluded that chest X-rays are not a very fruitful investigation in the initial diagnostic work up of febrile neutropenic patients. HRCT chest can very aptly fill this void because of its superior sensitivity and specificity in detection and characterization of lesions in these patients.

In our study, HRCT could correctly diagnose 92 cases. Using a pattern approach, 77 cases were correctly ascribed to the infectious etiology, which included 39 bacterial, 19 fungal, 13 *P. jiroveci*, 9 tubercular infections and 3 patients with mixed infections, while 10 scans were correctly read as normal.

Consolidation was the predominant finding in pyogenic infections ($n = 32$). In one case, there was a large rounded area of mass-like consolidation in right upper lobe with associated cavity formation [Figure 5]. We considered the first diagnosis of necrotizing pneumonia and second of nocardia. However, fungal serology was positive for aspergillus. When confronted with a similar radiological picture later in the study [Figure 6], our diagnosis of fungal infection was subsequently proven right.

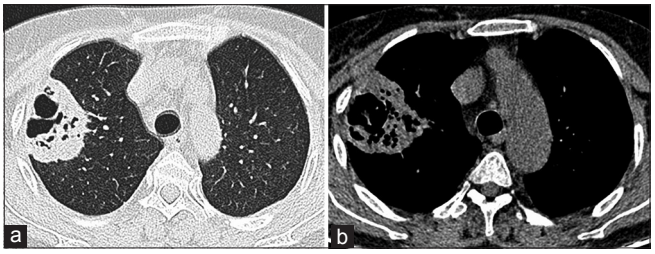

Figure 5: (a, b) A renal transplant recipient with fever and cough with expectoration (ANC of 120/μl). HRCT (a) lung and (b) mediastinal window shows consolidation with areas of cavitation in right upper lobe. HRCT diagnosis was necrotizing pneumonia. However, BAL yielded aspergillus

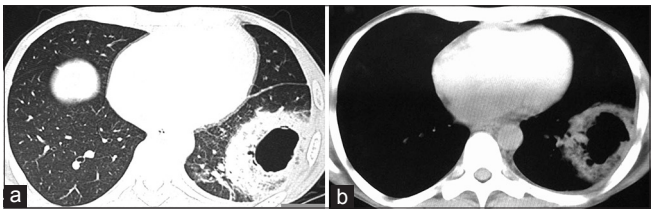

Figure 6: (a, b) A patient of AML (postchemotherapy), presented with fever and dyspnea (ANC of 200/μl). Rounded, mass-like consolidation is seen in the left lower lobe with cavitation. HRCT diagnosis in this case was invasive aspergillosis, which was subsequently confirmed

GGO was the second most common finding seen in 49 cases, but it is very nonspecific and can be seen in a variety of infective and noninfective conditions. GGO was associated with other findings including consolidation ($n = 7$), nodules ($n = 10$), lymphadenopathy ($n = 20$), pleural effusion ($n = 33$), cysts ($n = 4$), and mosaic perfusion ($n = 3$).

Nodules were the third most common finding seen in our study ($n = 39$). In the context of febrile neutropenia, the differential diagnoses to be considered are fungal infections, miliary tuberculosis, endobronchial spread of tuberculosis, pyogenic infections and viral (cytomegalovirus; CMV) infections. Distribution of the nodules assisted in the diagnosis in many cases. Scattered and/or peripheral distribution was suggestive of fungal infections, whereas small, random, or centrilobular distribution suggested tuberculosis. Presence of tree-in-bud appearance further added confidence in this setting for the diagnosis of tuberculosis.

In febrile neutropenic patients, pyogenic infections are the most common cause of fever. Up to 75% of the infections are caused by Gram positive cocci.[3] In the present study, there were a total of 46 cases of pyogenic infections of which, 39 could be prospectively diagnosed (true positive) on HRCT. There were four false positive HRCT diagnosis of pyogenic infections, while we had seven cases in which the pyogenic infection could not be prospectively diagnosed. One case showing consolidation, patchy GGO, and small centrilobular nodules prompted us to suggest a pyogenic infection, which, however, showed a clinical response to antitubercular therapy. GGO in TB is uncommon, but has been previously reported in literature.[11]

Fungal infections are an important and common cause of neutropenic fever. In our study, *Aspergillus fumigatus* was the predominant fungal pathogen with only one case of *Candida albicans* infection. Fungal pneumonias generally occur in the late phase of neutropenia with granulocytopenia being the most important predisposing factor. The presence of large nodules and visualization of halo sign are most suggestive of fungal infection.[8,12,13] Reichenberger *et al.* concluded that invasive pulmonary aspergillosis (IPA) should be suspected whenever pulmonary changes develop in neutropenic patients having antibiotic resistant fever. The appearance of hemorrhagic pulmonary nodules termed 'halo sign' were considered typical of IPA. The halo is present over a short period of 5-14 days after the onset of IPA. The specificity of the CT halo sign for the diagnosis of IPA was 80% and the sensitivity of air crescent sign was 48.68% in their study. They recommended HRCT as the most sensitive radiological modality to detect early changes of IPA.[14]

According to Kuhlman *et al.*, CT provides a noninvasive method for establishing or substantiating the early diagnosis of the IPA when chest X-rays are nonspecific, fungal cultures are negative and biopsy procedures are prohibited by thrombocytopenia.[15] HRCT directly affected patient management in 7 of 10 cases in their study. CT halo sign was positive in eight out of nine cases and air crescent formation in five out of seven cases in their study.

In the present study, we prospectively diagnosed 19 febrile neutropenic patients as having fungal etiology (true positive) on HRCT chest. Halo sign was present in 11 cases and air-crescent sign was seen in 4 cases. The low frequency of air crescent sign lends support to the theory that crescent sign is a late feature occurring when the patient is actually recovering from neutropenia. HRCT specifically aided in the management of seven cases where clinical suspicion of fungal pneumonia was not so strong and thereby helped change the therapy from antibacterials to antifungals. HRCT further altered the management in five cases. In three cases, the dosage of amphotericin was escalated and in another two cases decision to add fluconazole was taken. Overall, the sensitivity of HRCT for detection of fungal pneumonia was 95.23% and specificity was 96.7%.

According to Heussel *et al.*, *P. jiroveci* pneumonia is not very common in febrile neutropenic patients except in the late phase after allogenous transplantation together with chronic GVHD.[5] HRCT is a valuable means for predicting this infection and is a reliable method for differentiating *P. jiroveci* from other infectious processes.[16,17] A combination of GGO and intralobular septal thickening with sparing of the subpleural space (i.e., perihilar distribution) are highly suggestive of *P. jiroveci* pneumonia.

Kuhlman *et al.* reviewed CT scans of the chest in 39 patients to determine the spectrum and frequency of CT manifestations of *P. jiroveci* pneumonia. Three CT patterns of involvement were identified. A ground-glass pattern in 10 of 39 (26%), a patch work pattern in 22 of 39 (56%), and an interstitial pattern in 7 cases (18%). Atypical CT features of *P. jiroveci* pneumonia included nodules and nodular components in seven cases (18%) and cavities in three cases (8%). Associated CT findings included cystic spaces and bullae in 15 cases (38%), pneumothorax in 5 cases (13%), and adenopathy in 7 cases (18%).[18] The identification of cavities or nodular components in addition to infiltrates should raise the suspicion of a second disease process or mixed infection affecting the lungs.[19] In the present study, a total of 15 (14.42%) febrile neutropenia patients had *P. jiroveci* pneumonia. We could prospectively diagnose 13 out of these 15 cases based on HRCT findings. In our study, the HRCT findings of *P. jiroveci* pneumonia included GGO ($n = 13$), diffuse in seven cases and patchy in eight cases. All but one case had subpleural sparing. Intralobular septal thickening was present in two cases and both intra- and interlobular septal thickening in eight cases. Cysts measuring 5 mm to 1 cm were present in four cases (30.4%). Associated pleural effusion and lymphadenopathy were seen in one and two cases, respectively. We did not encounter any case with pneumothorax.

Tuberculosis as such, is not very common in febrile neutropenic patients. According to Heussel *et al.*, it is a rare but relevant diagnosis to be considered in these patients.[5] In these patients more widespread lymphatic and hematogenous dissemination can occur and therefore, the clinical course might be fulminant. TB may mimic or exist along with other infections such as pulmonary aspergillosis or systemic candidiasis. On HRCT, a peribronchial distribution (resulting in 'tree-in-bud' sign) of small, sometimes cavitated ill-defined nodules may be seen. Most of these patients, however, exhibit a primary form of disease with inhomogenous consolidation and necrotic mediastinal or hilar lymphadenopathy.[3]

In the present study, we encountered 10 patients of tuberculosis (9.6%). Of these, one patient was HIV positive and one was a case of ALL receiving steroids in addition to other chemotherapeutic drugs. Out of the 10 patients of tuberculosis, we could prospectively diagnose 9 cases based on the HRCT appearance. Based on the HRCT findings of patchy GGO with centrilobular nodules, we

had given a diagnosis of pyogenic small airway disease. However, this patient was detected to have AFB in sputum.

The confirmed cases of tuberculosis had the HRCT findings of airspace consolidation (n = 6), cavitation (n = 4), centrilobular nodules (n = 5), 'tree-in-bud' sign (n = 3), randomly distributed nodules (n = 4), pleural effusion (n = 4), lymphadenopathy (n = 2), septal thickening (n = 2), and GGO (n = 2).

CMV is an important and not very uncommon viral infection in febrile neutropenic patients. It is in fact, the commonest viral infection in the setting of organ transplantation.[20] In the present study, we did not encounter any CMV pneumonia. Based on the findings of patchy and diffuse GGO in two cases, we had given the second choice diagnosis of CMV, the first choice diagnosis being *P. jiroveci* infection. Both these cases were confirmed to have *P. jiroveci* (one was BAL positive, another responded favorably to cotrimoxazole).

We had 11 patients in whom HRCT was normal. Out of these, no organism could be isolated from sputum or blood in 10 patients. In one patient, BAL revealed leukemic cell infiltrates.

There were a few limitations in our study. First, the causative organism could not be isolated in all the cases. Another was the lack of viral pneumonias in any of the patients. Although no specific clinical investigations were done for isolating viruses, the clinical and radiological picture did not suggest a diagnosis of viral pneumonia any of the patients.

CONCLUSION

HRCT Chest is an excellent imaging modality in the diagnostic work up of febrile neutropenic patients to detect and characterize any pulmonary focus of infection or noninfective conditions. An exact etiological diagnosis is often possible based on recognizing a specific pattern with a high sensitivity and specificity. Usually a broad category of infectious etiology like bacterial, fungal, etc., can be listed, which is of paramount importance to the clinician and often alters the management of these patients.

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