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Original Article

HRCT Lung in a Follow up Patients of Bone Marrow Transplant with Cough and their Pathological Correlation

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ABSTRACT

Introduction: *Bone marrow transplantation is today's procedure of choice for management of various malignancies and immunologic disorders. HRCT is the common technique in the diagnosis of such recipient's with respiratory symptoms. This study we will target the accuracy of the modality and its pathological correlation.*

Aim *To study the role of HRCT in transplant patients with respiratory symptoms and their pathological correlation.*

Material and Methods *Patients are screened for pre transplant chemotherapy, clinical examination, lab investigations including blood and biochemical examinations, radiological examinations and a follow up for post transplant infections and complications with 16 slice Siemens CT scan.*

Result *Study included total 52 patients The patients presented early symptoms (<30 days) and findings were associated with prolonged neutropenia and later excluded due to non-engraftment.*

Conclusion: *Study claims pick up of findings on the HRCT which were not seen on routine chest radiograph and confirmed pathologically. This study suggests use of HRCT for early diagnosis.*

Keywords- *immunosuppression, pneumonia, algorithms.*

Introduction

Bone marrow transplantation (BMT) is an emerging management of various hematopoietic malignant and severe immunologic disorders haematological disorders[1].

Types Depending upon the donor, the transplantation is called allogeneic, autologous syngenic[1].

Procedure: The recipient and donors undergoes matching for HLA, blood group, complete blood counts, microbiological examination to rule out

any active infection and biochemical investigate-ons. After matching recipient requires immunosuppression. Mobilization consists of use of growth factors or chemotherapy agents for collecting enough stem cells from donor. These harvested stem cells are then cryopreserved and then infused after thawing. In vitro manipulation is done primarily to reduce the relapse and GVHD. The conditioning is primarily aimed for eradication of the recipient clone.

Pulmonary complications of HSCT

The complications can be in the form of infections, graft versus host disease and regimen related toxicities like interstitial pneumonitis, bronchiolitis obliterans, diffuse alveolar haemorrhage etc[5].

High-resolution computed tomography (HRCT):

HRCT is a non contrast CT acquisition and reconstruction method which produces highly detailed images of very high resolution due to acquisition of thin slices of 0.5 to 1mm with high frequency reconstruction algorithms[10].

The study was conducted from October 2013 to March 2015 after formal permission from the hospitals ethical committee. This was a prospective observational study where 52 patients who had undergone hematopoietic stem cell transplantation (HSCT) between this period in the hospital. All patients underwent complete clinical examination and laboratory investigations include-ing biochemical and radiological investigations, baseline HRCT on Philips Brilliance multiphasic 16 slice HRCT chest, post transplant HRCT when suspected clinical abnormalities and confirmed by either BAL (broncho-alveolar lavage) or sputum examination of the patients.

Methodology

Patients were screened for pre transplant chemotherapy. Thorough clinical examination, Lab investigations includes: complete blood count, serum biochemistry and any culture in suspected cases. Radiological examination includes ultrasound abdomen, chest radiography and HRCT chest.

Patients were followed for any post transplant complications by the help of 16 slice Philips CT scan in prone position hw supine position kept reserved for critically ill patients not able to proceed for prone position. Acquisition of 1 mm slice thickness helical scan taken from the thoracic inlet to the diaphragm with a pitch of 1.0 and image reconstruction at 0.5 mm intervals with high frequency reconstruction algorithm for lung and soft tissue algorithm.

The radiological findings were reported by two junior radiologists of 4 years of experience and reviewed by a senior radiologist of 26 years of experience and confirmed pathologically by a pathologist of 4 years of experience. The pathologist is kept blind for the study.

Study protocol HRCT acquisition is taken from the thoracic inlet till the diaphragm. The values and parameter taken in this study of Philips Brilliance 16 slice CT scanner. Statistical Analysis: With the help of Chi square method the different parameters were studied as age group, patients chief complaints, sputum analysis and brocho-alveolar lavage (BAL) correlation, ultrasound and routine investigations findings, personal history and biochemical parameters with the radiological findings.

Results

Out of the 52 patients 35 were male and 17 were female with age variation from 1 to 72 years. Total deaths in the study were 5.

Most common finding in the study was normal HRCT followed by nonspecific finding as fibrosis, consolidation with sterile bronchial fluid, bronchiectatic changes, chronic GVHD (graft versus host disease), tuberculosis, bacterial pneumonia and viral pneumonia. Most of these findings were not observed on the conventional radiograph.

The most common duration following the HSCT for such patients were >100 days then <100 and <30 days respectively. The patients presented

early symptoms (<30 days) and findings were associated with prolonged neutropenia and later excluded due to non-engraftment. The patients who died in the study had consolidation as the commonest lung finding. Most common cause of death among the patients in the study was due to sepsis followed by low counts of all cell lines except one patient died due to gastrointestinal tract symptoms with venous occlusive disease (VOD).

Table 1: Chief complaints * post transplant HRCT (Radiological Findings)

Respiratory Symptoms		post transplant HRCT(radiological Findings) PT1	PT2	PT3	PT4	PT5	PT6	Total	Chi-square value	p-value
Fever (number of patients)	Yes	3	8	1	0	4	4	20	8.95	0.111
	No	3	4	4	4	12	5	32		
Total		6	12	5	4	16	9	52		
wt(number of patients) loss	Yes	2	7	2	2	2	2	17	7.67	0.176
	No	4	5	3	2	14	7	35		
Total		6	12	5	4	16	9	52		
Cough(number of patients)	Yes	5	10	4	4	15	5	43	6.86	0.231
	No	1	2	1	0	1	4	9		
Total		6	12	5	4	16	9	52		
duration of R/F from transplant(days)	31-100	2	1	1	1	0	1	6	6.06	0.3
	>100	4	11	4	3	16	8	46		
Total		6	12	5	4	16	9	52		

The table 1 describe chief complaints with statistical correlation between post HSCT –HRCT radiological findings.
PT 1- stands for fibrotic changes. PT 2- stands for consolidation.
PT 3- stands for cavities PT 4- stands for bronchiectatic changes and tree in bud appearance
PT 5- stands for normal. PT 6- stands for ground glass opacities and ill defined opacities.

Table 2:
Sputum/brochial fluid analysis * post transplant HRCT(radiological Findings)

		post transplant HRCT(radiological Findings) 1	2	3	4	5	6	Total	Chi-square value	p-value
sputum/bronchial fluid analysis	1	4	7	4	4	15	9	43	27.01	0.029
	2	2	0	1	0	0	0	3		
	3	0	3	0	0	1	0	4		
	4	0	2	0	0	0	0	2		
Total		6	12	5	4	16	9	52		
Final diagnosis	1	2	1	3	3	15	8	32	42.8	0.002
	2	2	1	2	0	0	0	5		
	3	0	2	0	0	1	0	3		
	4	0	2	0	0	0	0	2		
	5	2	6	0	1	0	1	10		
Total		6	12	5	4	16	9	52		

The table 2 describes the statistical significance between the bronchial fluid analysis and the final diagnosis. The sputum fluid/ Bronchial fluid analysis are coded in five groups;
Group 1 for sterile and non specific. Group 2 for tuberculosis.
Group 3 for bacterial origin. Group 4 for viral markers positive.
Group 5 for fungal origin.

After the pathological correlation about 1/3rd of the patients had fungal lesion associated in the patients were Angioinvasive aspergillosis (figure1 a,b,c). Five patients were found positive for

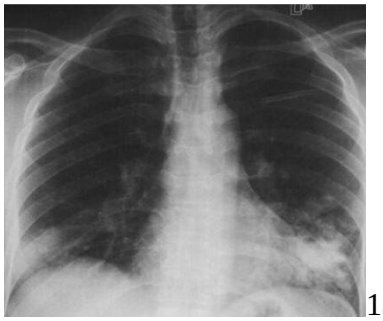
pulmonary tuberculosis (figure 2 a,b,c). Three patients were found positive for pneumococcal pneumonia (figure3 a,b,c). Two patients found positive for CMV(figure4a,b,c). These findings were not specific without pathological analysis. Many lesion found sterile with significant radiological findings taken in group 1.

The most common findings among all these are for group 1 i.e. non specific and sterile with radiological findings of group 5 i.e. normal. The correlation for this finding is strongly statistically significant (p value=0.029).In the final diagnosis the most common findings were of group1 of bronchial fluid analysis associated with group 5 of radiological findings. The final diagnosis is strongly statistically significant with these findings (p value 0.02).

llustrated cases with representative images

Case 1.[figure1a, b(Radiological correlation) and pathological correlataion 1c]

A 13 yr old female, case of ALL, had chief complaints of tachypnoea and abdominal pain, radiological findings 3 days after the transplant, this patient was diagnosed invasive aspergillosis. This patient died one day later due to fungal pneumonia and septicemia.

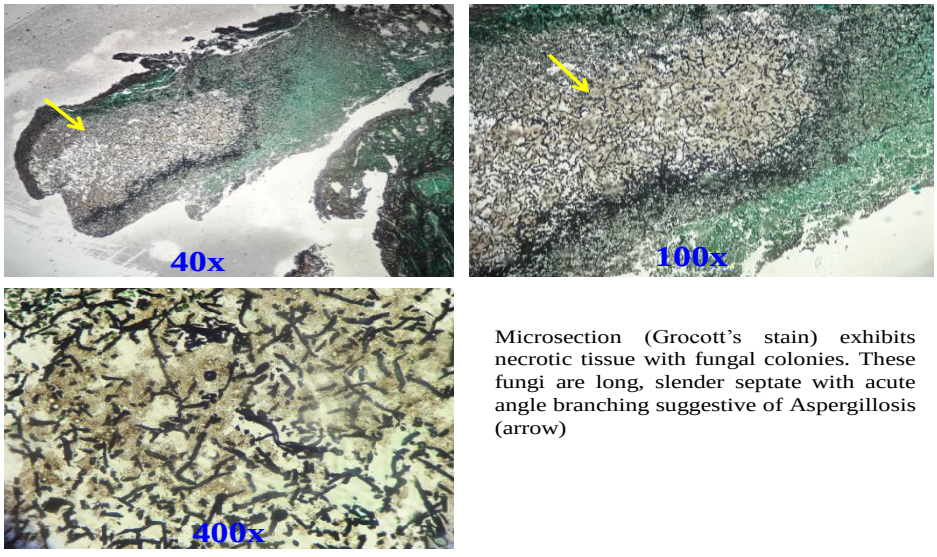


1a

Chest radiograph shows few ill defined irregular non-homogenous soft tissue mass like opacities in both lower lobes.

1b

HRCT in lung window of the patient with invasive aspergillosis showing ground glass opacities, multiple nodular and mass like opacities, cavities and bronchiectatic changes in both t lower lobes.



Microsection (Grocott's stain) exhibits necrotic tissue with fungal colonies. These fungi are long, slender septate with acute angle branching suggestive of Aspergillosis (arrow)

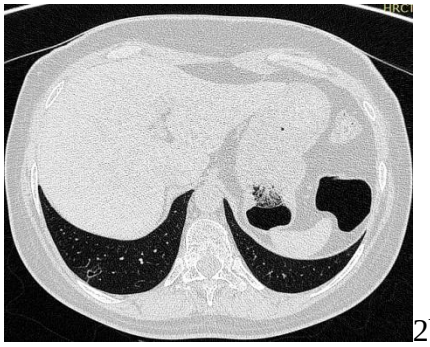
1c

Case 2. (figure 2a, b c)

A 46 yr old female a known case of AML with chief complaints of cough. Radiographic findings 8 months after the transplant. This patient was found positive for acid fast bacilli and confirmed by ZN staining as pulmonary tuberculosis (2c).

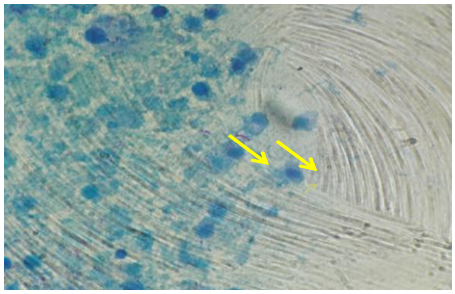
2a

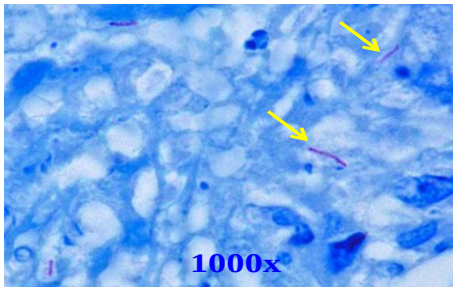
Chest radiograph of this patient appearing normal.



2b

Axial view of a patient of AML with tuberculosis showing small cavity with surrounding ground glass opacities in right lower lobe.





Ziehl Neelsen stain under oil immersion reveals (arrow) bright red, straight or slightly curved beaded rod like organisms compatible with Mycobacterium (2-4 µ in length and 0.2-0.5 µ in width) against a blue or green background.

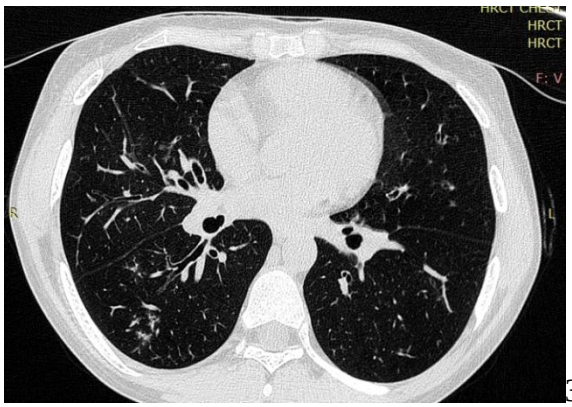
2c

Case 3 (figure3 a, b, c).

A 27 year old female known case of AML with chief complaints of cough following 18 months of transplant. This patient was later diagnosed pneumococcal pneumonia on the basis of bronchial fluid aspirate.

3a

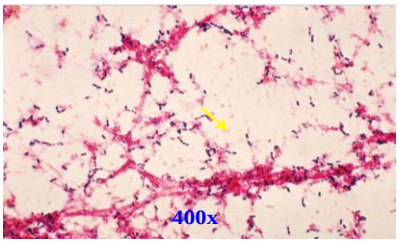
Radiograph chest appearing normal.



3b

Axial view of a known case of AML with ground glass opacities at right middle lobe and right lower lobe and fibrotic changes. This patient was later found positive for Gram positive cocci in bronchial fluid analysis.

Bone window axial view of the patient showing multiple lytic areas in sternum and ribs with fixation of the pathological fractures in dorsal vertebrae.



Small elongated paired cocci arranged as singles, small chains compatible with Pneumococcus (arrow)

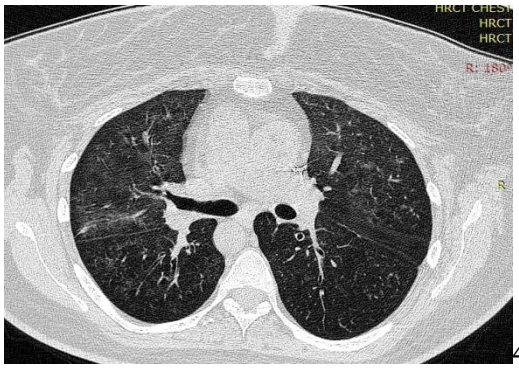
3c

Case 4 (figure 4 a, b, c).

A 25 year old male known case of Aplastic anemia with chief complaints of fever and cough following 3 years of transplant. Patient was found positive for CMV infection in bronchial aspirate.

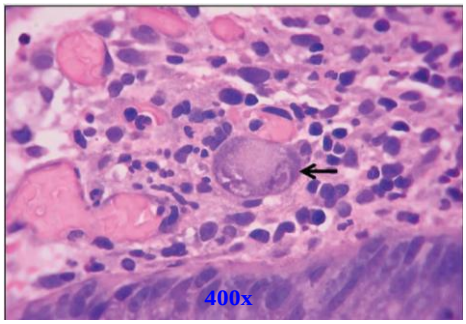
4a

Radiograph chest appearing normal.



4b

Axial section of the lung of a known case of aplastic anemia with CMV markers positive showing extensive ground glass opacities in bilateral lungs and few areas of patchy consolidation in right middle lobe, right lower lobe and left upper lobe.



H&E stained section exhibits a stromal fibroblast containing an microorganism with basophilic cytoplasm and prominent intranuclear basophilic inclusion (arrow) consistent with Cytomegalovirus

4c

Comparison of the studies

1.This study Versus Hatzimichael and Tuthill et al

States that 5 out of 52 death with full healthy follow up statusshows that the death in the studied sample is 9.6%, with survival of 91.4 % of the patient with a healthy status after HSCT. Similarly as the death of one patient is noticed after 3 years it shows that the risk of mortality is high in the recipients these findings matching with the study of Hatzimichael and Tuthill et al .

2.This study versus Coelho LOM, Gasparetto TD, Escuissato DL, Marchiori E et al, states that in our study the most common finding as normal followed by consolidation while Coelho had consolidation as the commonest finding hw they have not mentioned about normal findings in their study.

Conclusion

The patients with tuberculosis (Acid fast bacilli+ve/ high ADA values) have shown cavities, fibrotic changes and ground glass opacities along with lymphadenopathy chiefly involving the upper lobes. Chronic GVHD is noticed in the form of BOOP with consolidation, ground glass opacities tree in bud opacities. Idiopathic pneumonia syndromes were seen as nodular lesion, consolidation and ground glass opacities Bacterial pneumonia (bronchial fluid were positive for the causative organism) were noticed as consolidation, ground glass opacities and ill defined nodular lesions. Viral infection

such as CMV (by H&E stain and positive for CMV PCR test) shows consolidations, ground glass opacities, end arteriolar and peri-bronchial ground glass opacities and consolidations. Various non specific isolated and mixed findings were noticed in the lungs of some patients as bronchiectatic changes, tree in bud appearance, ground glass opacities, calcified granulomas and fibrotic changes. This study states that HRCT lung in cases of BMT recipients is a very important in early diagnosis and management of the pulmonary complications. Similarly pathological correlation gives more proof on the findings.

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Conflicting Interest: Nil

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