The value of computerized tomography of the chest in patients with neutropenic fever

Khudhair A AL-Khalissi *   MRCP (UK)
Ahmed I Shukr **   FIBMS FICM Haem
Azher S AL-Zubaidy***   CABM

Abstract:

Background: Absolute neutropenia in hematological malignancies remains the single most important risk factor for infection, which can be fatal and requires urgent management including radiological procedures and treatment.

Objectives: To compare computerized tomography (CT) of the chest with chest radiology (CXR) in the assessment of febrile neutropenic patients with hematologic malignancy.

Patients and methods: A prospective study, carried out in the hematological ward, Baghdad teaching hospital, for the period from 1stApril 2011to 30thApril 2012.It included 46 neutropenic febrile patients .All had chest X-ray (CXR) and computerized tomography (CT) of the chest.

Results: Male were 21, and female were 25. Mean age was 47.89 ± 15.32 years. Mean absolute neutrophil count (ANC) was 0.25X109/L. 29 (63%) patients had normal CXR in which CT was abnormal in 3 of them. 17 (37%) had the same abnormalities on CXR and CT.

Conclusion: Computerized tomography is superior to CXR in patients with neutropenic fever, and it should be included in the investigations, especially in patients with respiratory symptoms.

Key words: Chest radiography, Computerized tomography, Neutropenic fever.

Introduction:

Patients with hematologic malignancy are at increased risk of potentially fatal infection as a consequence of treatment induced neutropenia. Currently the common approach to immunosuppressed patients with fever or respiratory symptoms is to assess pulmonary involvement by CXR, start empirical broad–spectrum antibiotics early, and add antifungal agents if fever or symptoms persist (1), as aggressive opportunistic fungal infections can develop in patients with neutropenia presented beyond one week(2).The risk of infection correlate closely with the degree as well as duration of neutropenia. It is highest when neutropenia is prolonged (>10-14days) and profound (ANC<0.1x 109/L), and when the ANC fall sharply(3,4).In patients with persistent fever, reaction to drugs (including hemopoietic growth factors and antibiotics) or blood products, underlying malignancy, graft versus host disease and severe mucositis caused by chemotherapy should be considered as non-infectious causes of fever(5). However in the face of severe immunodeficiency, the systemic and pulmonary inflammatory response to infectious and non-infectious processes may be poor and occasionally virtually absent. Thus, due to its low sensitivity, plain CXR of the chest may be normal or shows only minimal non-specific abnormalities (6). This may delay further diagnostic and therapeutic measures in potentially fatal

condition(7).Computerized tomography of the chest has greater sensitivity and has been proposed to replace the plain CXR in the primary evaluation of immuncompromised patients(8).It has been shown to be superior for identifying localization and spread of lesions as well as assessment of etiology(9). About 50% of patients with hematologic malignancy will present with pulmonary infections during their management (10), which are the direct cause of almost 40% of death in these populations, and the prognosis correlate to how early diagnosis is made, meaning that quick access to cross sectional imaging is required: a key factor in the management of lung disorders (11). The purpose of this study was to compare thoracic CT to conventional CXR in the initial assessment of ill neutropenic patients with hematological malignancy, and their effect on mortality.

Patients and methods:

Between April 2011 and April 2012, 46 adult patients, aged 20-69 years were recruited from the hematology ward in Baghdad teaching hospital. All had received chemotherapy for different hematologic malignancies, their ANC < 0.5x109/L, and all were febrile with body temperature of ≥ 38.8oC for single reading or ≥ 380C, twice over one hour. Full history and type of hematologic malignancy were documented. Demographic information including age, gender were obtained, followed by medical examination, then patient's consent was taken. All were sent for plain CXR (Shimadzu), then to conventional CT

College of medicine-Baghdad University. Assistant professor in General. Email:dr_Khuder@yahoo.com
*** Azadi Teaching Hospital (Kirkuk). Specialist in Hematology*
****Baghdad Teaching Hospital. Consultant in General medicine and Hematology.*

of the chest on the same day or the day afterward (Philips / 120 KV, using 64 slides technique with slice thickness of 3 mm). Results were interpreted by one consultant radiologist, and sometimes by two. Patients were classified into 4 groups according to the presence or absence of respiratory signs and symptoms, and results of their CXRs and CTs.

Statistical analysis : A cross sectional study. All data were coded and tabulated by using number, percentage. Using SPSS and Microsoft excel software to calculate association of different variables.

Results:

Total patients number was 46, including 25 (54.3%) female and 21 (45.7%) male. Mean age was 47.89 ± 15.32 years (range 20-69). (Table1). Forty three (74%) patients had acute leukemia. Absolute neutrophil count was < 0.2 x 109/L in 35 (76.1%). Thirty patients (62.5%) had received chemotherapy before > 1 week.(Table 2). Seventeen (37%) patients had abnormal CXR, and all of them had abnormal CT.(P = 0.000), while 29 (63%) patients who had normal CXR, 3(10%) of them had abnormal CT.(Table 3). Twenty (43.5%) of patients (Group 1) had signs and symptoms of respiratory disease but a normal CXR, CT was abnormal in 3(10%) 0f them, while those who had respiratory signs and symptoms and abnormal CXR (Group 2) all had abnormal CT. Patients without signs and symptoms of respiratory disease included Group 3 (4, 8.7%) who had abnormal CXR, CT was abnormal in all of them, and Group 4 with no respiratory signs or symptoms (9, (19.5%)) with normal CXR, all their CTs were normal.(Table 4).Radiological diagnoses after CTs in 20 patients were: Pneumonic consolidations in 12(26.1%), malignant infiltration in 4(8.7%), invasive aspergillosis 3(6.5%), tuberculosis ? in 1(2.2%). Diagnosis in patients with normal CXRs and abnormal CTs included 2 with pneumonic consolidation and I patient with aspergillosis. Compatibility between CXR and CT diagnoses were positive in 13 patients, while they were different in 4 patients after CT. Regarding mortality and survival; only twenty two (76%) out of 29 with normal CXR survived, and 11(65%) out of 17 with abnormal CXR survived (P = 0.225). Twenty two (84.6%) out of 26 with normal CT survived, and 11 (55%) out of 20 with abnormal CT survived (P = 0.03).(Table 5).

Table1: Demographic distribution of 50 patients with neutropenic fever

Demographic character	No	%
Age (years)		
20-29	8	17.4
30-39	7	15.2
40-49	7	15.2
50-59	9	19.6
≥ 60	15	32.6
Gender		
Female	25	54.3
Male	21	45.7

Table 2: Variables in 46 patients with neutropenic fever

Variables	No	%
Diagnosis		
Acute myelogenous leukemia	21	45.75
Acute lymohocytic leukemia	13	28.30
Non Hodgkin,s lymphoma	8	17.40
Hairy cell leukemia	1	2. 13
Hodgkin,s lymphoma	2	4.39
Chronic lymphatic leukemia	1	2.13
Absolute neutrophil count x 109/L		
< 0.2	35	76.1
0.2-0.5	11	23.9
Last dose of chemotherapy		
< 1 week	16	34.8
≥ 1 week	30	65.2

Table 3: Relation between CXR and CT in 46 patients with neutropenic fever

CXR	CT chest					
	Abnormal		Normal		Total	
	No	%	No	%	No	%
Abnormal	17	100	0	0	17	100
Normal	3	10	26	90	29	100

Table 4: Relation between patient's group and abnormal CT in 46 patients with neutropenic fever

Patient group	No	Abnormal CT No	%
1.Resp*S&S** +normal CXR	20	3	15
2.Resp S&S + abnormal CXR	13	13	100
3.NO Resp S&S + abnormal CXR	4	4	100
4.NO Resp S&S +normal CXR	9	0	0

* Respiratory, ** Signs and symptoms

Table5: Relation between CXR and CT with mortality in 46 patients with neutropenic fever

Radiological investigation	Outcome Dead Survived No (%) No (%)		Total	P value
CXR Normal	7 (24)	22 (76)	29	P 0.225
Abnormal	6 (35)	11 (65)	17	
CT chest Normal	4 (13)	22 (84.6)	26	P 0.03
Abnormal	9 (45)	11 (55)	20	

Discussion:

Chest radiography has an important role in detection of pulmonary infiltration and in follow up the response to treatment, however, chest radiography has lower sensitivity for detection of early infection, and finding are often non specific. (12) Computerized tomography overcomes some limitations of CXR: as CT can detects 20% more pneumonias in patients with pulmonary infection 5 days earlier than CXR.(13) Ten percent of symptomatic patients with normal CXR had abnormal CT (P 0.225). This is comparable to what was obtained by Primack,(14)and McLoud(15)in north America. This can be explained by either early pulmonary infection, or the infection is mild and could not be visualized by CXR. All patients with abnormal CXR had abnormal CT. This is expected, as CT is more sensitive than CXR. Nine patients with no respiratory signs or symptoms had normal CXRs, all had normal CT, Elena(16) had recommended that high resolution CT (HRCT) may benefit such patients. Pneumonic consolidation Invasive aspergillosis almost always occurs in immunocompromised host, and causes significant hemorrhagic infarction. Early in the course of infection, CT may reveals single or multiple nodules, often with surrounding ground – glass opacity, the so called "hallo sign".(18,19)Invasive aspergillosis was highly suggested in 3 (6.5%)patients after CT examination, which was not clear on CXR, 2 with nodular lesions and 1with hallo sign.

Malignant infiltration was found in 4(8.7%), and cavitory lesion suggestive of pulmonary tuberculosis in 1(2.2%).

Out of 17 patients with abnormal CXR, diagnoses were similar in 4 after CT (2 pneumonia, 1 malignant infiltration and 1 with cavity), while 13 had different diagnosis. Mortality were significantly (P = 0.03) associated with abnormal CT, but not with abnormal CXR (P = 0.225). (Table 5).

Conclusion:

Computerized tomography has a superior role over CT in patients with respiratory signs and symptoms even with normal CXR, but it is not recommended in those without signs and symptoms and normal CXR.

References:
1. Patsios D, Maimon N, Chung TB et al. Chest low – dose computed tomography in neutropenic acute myeloid leukemia. Respir Med 2010; vol 104 (4): 600-05.
2. Bergeron A, Porcher R, Sulahian A et al. The strategy for the diagnosis of invasive aspergillosis should depend on the underlying condition and the leucocyte count of the patient with hematolohical malignancy. Blood 2012; 119: 1831-37.
3. Dale DC, Cuerry DV, Wewerka JR et al. Chronic neutropenia. Medicine 1997; 58: 128-44.
4. Pizzo PA, Robichard KJ, Wesley R et al. Fever in the pediatric and young adult patients with cancer: A prospective study of 1001episodes. Medicine 1982; 61:153-65.
5. Pizzo PA. Fever in immunocompramised patients. N Eng J Med 1999; 341: 883-90.
6. Krowka MJ, Rosenaw EC, Hoagland HC et al. Pulmonary complications of bone marrow transplantation. Chest 1985; 87: 237-45.
7. Harori S. Current strategy in the treatment of invasive aspergillous infection in immunocompramised patients. Drugs 1999; 58: 621-31.
8. Kang EY, Staples CA, McGuiness G et al. Detection and differential diagnosis of pulmonary infections and tumors in patients with AIDS.: Value of chest radiology versus CT. AMJ Roentgenol 1966; 166(1): 15-19.
9. Oh YM, Effman EL, Godwin JD. Pulmonary infections in immunocompramised hosts: the
importance of correlating the conventional radiological appearance with the clinical settings. Radiology 2000; 217: 647-56.
10. Morrison VA. Infectious complications in patients with chronic lymphocytic leukemia: pathogenesis, spectrum of infection and approach to prophylaxis. Clin Lymphoma Myeloma 2009; 9: 365-70. (ivsl)
11. Hicheri Y, Toma A, Muray S et al. Updating guidelines for managing fungal diseases in hematology patients. Expert Rev Anti infection Ther 2010; 8: 10: 49-60.
12. Lyman GL. Risk assessment in oncology clinical practice, from risk factors to risk models. Oncology (Williston Park) 2003; 17(Suppl 11): 8-13.
13. Klastersky J, Paesmans M, Robenstein E et al. The MASCC Risk index: a multinational scoring system to predict low risk febrile neutropenenic cancer patients. J Clin Oncol 2000; 18: 3038-51.
14. Primach SL, Muller NL. High – resolution computed tomographyinacutediffuselungdiseaseinimmunocompromised

patients. Radiol Clin North AM 1994;32:731-44.

15. McLoud TC, Naidich DP. Thoracic diseases in immunocompramised patients. Radiol Clin North Am 1992;30:525-54.

16. Elena R, Anna S. Bronchoscopy guided by high resolution computed tomography for the diagnosis of pulmonary infections in patients with hematological malignancies and normal chest-X-rays. Haematologica 2000; 85:961-66.

17. Figen B, Aylin A. CT findings in immunocompramised patients with pulmonary infections. Diagn Inter Radiol 2008;14: 75-82.

18. Gotway MB, Dann SK, Caoili EM et al. Radiological spectrum of pulmonary aspergillous infection. J Comput Assist Tomogr 2002;26:159-73.

19. Hussel CP, Kauczor HU, Hyssel GE et al.Pneumonia in febrile neutropenic patients and in bone marrow and blood stem cell transplant recipients: Use of high resolution computed tomography. J Clin Oncol 1999;17:796-05.