

"Crazy-Paving" Patterns on High-Resolution CT Scans in Patients with Pulmonary Complications after Hematopoietic Stem Cell Transplantation

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Objective: To describe the pulmonary complications following hematopoietic stem cell transplantation (HSCT) that can present with a "crazy-paving" pattern in high-resolution CT scans.

Materials and Methods: Retrospective review of medical records from 2,537 patients who underwent HSCT. The "crazy-paving" pattern consists of interlobular and intralobular septal thickening superimposed on an area of ground-glass attenuation on high-resolution CT scans. The CT scans were retrospectively reviewed by two radiologists, who reached final decisions by consensus.

Results: We identified 10 cases (2.02%), seven male and three female, with pulmonary complications following HSCT that presented with the "crazy-paving" pattern. Seven (70%) patients had infectious pneumonia (adenovirus, herpes simplex, influenza virus, cytomegalovirus, respiratory syncytial virus, and toxoplasmosis), and three patients presented with non-infectious complications (idiopathic pneumonia syndrome and acute pulmonary edema). The "crazy-paving" pattern was bilateral in all cases, with diffuse distribution in nine patients (90%), predominantly in the middle and inferior lung regions in seven patients (70%), and involving the anterior and posterior regions of the lungs in nine patients (90%).

Conclusion: The "crazy-paving" pattern is rare in HSCT recipients with pulmonary complications and is associated with infectious complications more commonly than non-infectious conditions.

Hematopoietic stem cell transplantation (HSCT) is frequently associated with pulmonary complications, which usually result in increased morbidity and mortality in these patients (1, 2). Early and accurate diagnosis of pulmonary complications following HSCT is important because of this high mortality and morbidity, as well as the severe complications associated with the treatment of those diseases (3, 4).

The importance of the high-resolution CT scan in diagnosing pulmonary complications after HSCT has been emphasized in several studies (4–9). CT scans may show pulmonary abnormalities in patients with normal radiographs, and it is superior to conventional radiographs in visualizing the patterns of abnormality and their extent (4, 6).

The "crazy-paving" pattern consists of interlobular septal and intralobular interstitial thickening superimposed on an area of ground-glass attenuation on high-resolution CT scans. This finding was initially seen in patients with pulmonary alveolar proteinosis, but occurs in several diseases, including *Pneumocystis carinii* pneumonia, bronchioloalveolar carcinoma, sarcoidosis, non-specific interstitial pneumonia, cryptogenic

organizing pneumonia, lipoid pneumonia, adult respiratory distress syndrome, and pulmonary hemorrhage syndromes (10, 11). The “crazy-paving” pattern was also described in pulmonary complications after HSCT, i.e., pulmonary toxoplasmosis or diffuse pulmonary hemorrhage (12, 13). To our knowledge, the type and incidence of pulmonary diseases with the “crazy-paving” pattern following HSCT have not been described.

We present 10 patients with pulmonary complications following HSCT who presented with the “crazy-paving” pattern in high-resolution CT scans.

MATERIALS AND METHODS

This retrospective study was based on the review of medical records from 2,537 patients who underwent HSCT between January 1993, and July 2006. Of these cases, 912 had clinically-suspected pulmonary disease, and 495 had proven pulmonary complications, with a high-resolution CT performed within 24 hour of symptom onset.

The high-resolution CT scans were performed on a Somatom ART scanner (Siemens, Erlangen, Germany) or a Toshiba Asteion CT scanner (Toshiba Medical Systems, Tokyo, Japan). The scans were obtained at end inspiration using 1.0 or 2.0 mm collimation and performed at 10- or 20-mm intervals from the apex of the lung to the diaphragm. Images were photographed at mediastinal (width, 400 H; level, 20 H) and lung (width, 1,500 H; level, -700 H) window settings.

Patients with “crazy-paving” patterns detailed in the radiologic report were retrospectively reviewed by two radiologists who were aware that all patients had pulmonary complications; the final decision on the findings was reached by consensus. The “crazy-paving” pattern

was defined as an area of ground-glass attenuation with superimposed reticular opacities (interlobular septal and intralobular interstitial thickening) (14). The distribution of this pattern (central and/or peripheral, unilateral or bilateral, anterior and/or posterior, and upper/middle/lower zones distribution) and ancillary findings were also noted. Criteria for these findings were those defined in the Fleischner Society’s Glossary of Terms (14).

The pathogens responsible for the infectious episodes were documented by the following methods: bronchoalveolar lavage, sputum culture, and/or autopsy. Diagnosis of virus infection was documented by fluorescence antibody testing or polymerase chain reaction specimens obtained from bronchoalveolar lavage. The diagnosis of toxoplasma pneumonia was defined in the autopsy.

The diagnosis of idiopathic pneumonia was made following the criteria proposed by Clark et al. (4): symptoms and signs of pneumonia, evidence of abnormal pulmonary physiology, evidence of widespread alveolar injury suggested by chest X-ray or CT, and absence of active lower respiratory tract infection. The diagnosis of pulmonary edema was defined based on clinical and laboratory data, as well as on the imaging findings at presentation and follow-up.

RESULTS

From these 495 patients, we identified 10 cases (2.02%) presenting with a “crazy-paving” pattern, seven males and three females, with ages ranging from 16 to 62 years (median 40.5 years, standard deviation 16.19). The patients underwent HSCT because of acute myeloid

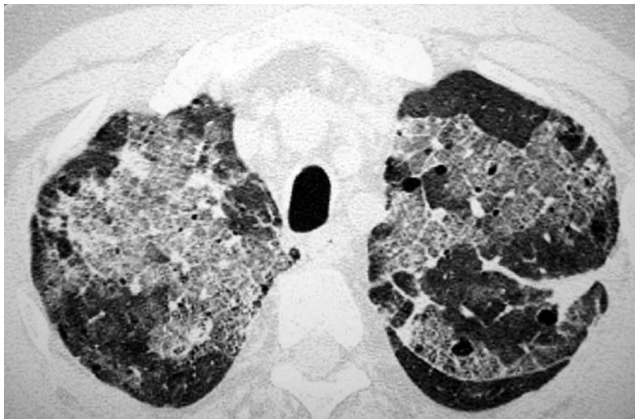


Fig. 1. 38-year-old man with adenovirus pneumonia high-resolution CT scan at level of upper lobes shows bilateral areas of ground-glass attenuation with superimposed interlobular septal thickening (“crazy-paving” pattern).

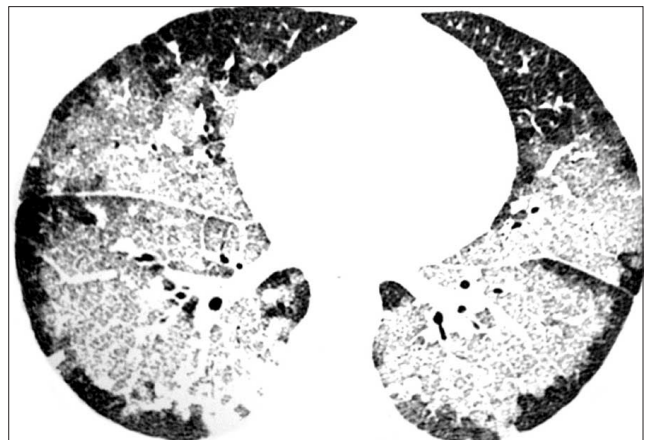


Fig. 2. 16-year-old woman with toxoplasmosis. High-resolution CT scan at level of lower lung zones demonstrates bilateral ground-glass opacities with interlobular septal and intralobular interstitial thickening, “crazy-paving” pattern, associated with air-space consolidation areas.



Fig. 3. 56-year-old man with idiopathic pneumonia syndrome. High-resolution CT scan at level of lower lung zones shows extensive "crazy-paving" pattern involving both lower lobes, lingula and middle lobe, in association with areas of air-space consolidation.

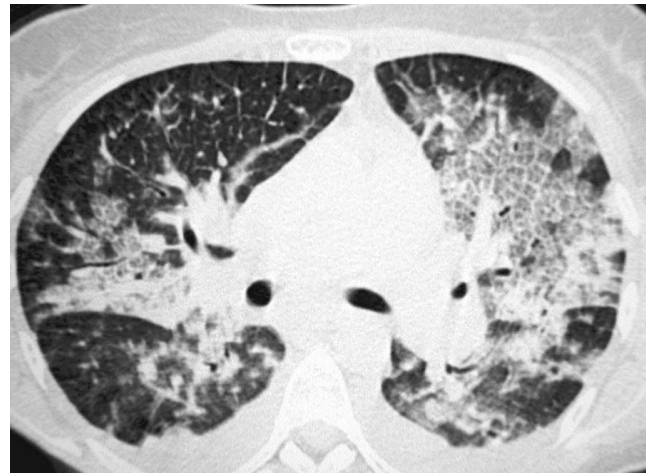


Fig. 4. 28-year-old man with acute pulmonary edema. High-resolution CT scan at level of main bronchi demonstrates areas of consolidation and ground-glass attenuation with superimposed interlobular septal thickening defining "crazy-paving" pattern. Lesions predominated on left upper lobe. Bilateral pleural effusion is also observed.

leukemia (n = 4), myelodysplastic syndrome (n = 4), and multiple myeloma (n = 2). Pulmonary complications occurred between 12 and 500 days after the transplantation (mean 85 days, standard deviation 147.1).

The pulmonary infection was diagnosed in seven (70%) out of 10 patients: adenovirus pneumonia (n = 2) (Fig. 1), herpes simplex pneumonia (n = 1), influenza virus pneumonia (n = 1), cytomegalovirus pneumonia (n = 1), respiratory syncytial virus (RSV) pneumonia (n = 1), or toxoplasmosis pneumonia (n = 1) (Fig. 2). Non-infectious complications were diagnosed in the three remaining patients, which included idiopathic pneumonia syndrome (n = 2) (Fig. 3) or acute pulmonary edema (n = 1) (Fig. 4).

The "crazy-paving" pattern was bilateral in all cases. Diffuse distributions of the pattern throughout lungs were seen in nine patients (90%), with peripheral predominance in one patient who had an adenoviral infection (10%). The "crazy-paving" pattern was seen predominantly in the middle and inferior lung regions in seven patients (70%), and in the superior lung areas in three patients (30%). The "crazy-paving" pattern was distributed in the anterior and posterior regions of the lungs in nine patients (90%) and in the anterior areas in only one patient with adenoviral infection (10%).

Ancillary findings included focal areas of air-space consolidation (n = 6), areas of small centrilobular nodules (n = 6), pleural effusion (n = 2), and pneumomediastinum (n = 1). Pleural effusion was unilateral in one patient with herpes virus infection, and bilateral in a patient with pulmonary edema. Three patients (30%) had no ancillary findings.

DISCUSSION

Hematopoietic stem cell transplantation is a well-established form of treatment for various hematological disorders. Respiratory complications occur in 40% to 60% of patients after HSCT and are major causes of morbidity and mortality. These complications are associated with the immunologic status of the patients and occur in three phases: i) neutropenic phase: characterized by a period of severe neutropenia lasting 2–3 weeks. Pulmonary complications in the neutropenic phase include fungal infections, invasive aspergillosis, RSV infection, diffuse alveolar hemorrhage, pulmonary edema, and drug toxicity. ii) Early phase: occurs up to 100 days after HSCT, during which time there is a gradual recovery of neutrophils and immune impairment. The two most common pathogens to cause pulmonary complications during this phase are cytomegalovirus and RSV. iii) Late phase: occurs at least 100 days after HSCT when immune status has recovered. Pulmonary complications typically encountered in the late phase include obliterative bronchiolitis, organizing pneumonia, and chronic graft-versus-host disease (1–3, 10).

High-resolution CT scans are important in the early diagnosis of pulmonary diseases following HSCT, as the progression of those complications is usually quick and associated with high morbidity and mortality (4, 6–9). Although several high-resolution CT patterns have been described in these patients, those findings are frequently non-specific, and correlation with clinical and laboratory data is essential for an accurate diagnosis (4, 6).

The “crazy-paving” pattern consists of scattered or diffuse ground-glass attenuation with superimposed interlobular septal and intralobular interstitial thickening. Initially described in cases of alveolar proteinosis, this pattern also occurs in a variety of infectious, neoplastic, idiopathic, inhalational, and sanguineous disorders of the lung. Specific disorders that can cause the “crazy-paving” pattern include *Pneumocystis carinii* pneumonia, mucinous bronchioloalveolar carcinoma, pulmonary alveolar proteinosis, sarcoidosis, nonspecific interstitial pneumonia, organizing pneumonia, exogenous lipoid pneumonia, adult respiratory distress syndrome, and pulmonary hemorrhage syndromes (10, 11).

There are sporadic reports of “crazy-paving” patterns on the high-resolution CT of patients who underwent HSCT and presented with pulmonary complications (12, 13). For example, Escuissato et al. (12) reported a case of pulmonary toxoplasmosis following HSCT that presented on high-resolution CT scan. Also, Franquet et al. (13), in a review of the high-resolution CT and pathologic findings of noninfectious pulmonary complications after HSCT, showed a case of diffuse pulmonary hemorrhage presenting with “crazy-paving” patterns in CT scans. Similar patterns occurred during pulmonary complications following HSCT, including bacterial pneumonia, pulmonary edema, drug-induced pneumonitis or cryptogenic organizing pneumonia (10, 11). In our series, the “crazy-paving” pattern occurred in 2% of the patients who had high-resolution CT following HSCT. Most (70%) of those patients had infectious pulmonary complications.

The “crazy-paving” pattern was most commonly distributed in the central and peripheral areas, predominantly in the middle and inferior lung regions, involving both the anterior and posterior areas. Patchy areas of ground-glass opacity were seen as a part of a mixed pattern in seven cases (70%), and consolidations in six (60%). The “crazy-paving” pattern was the only HRCT finding in three patients (30%).

Our retrospective study includes a relatively small number of patients with each type of pulmonary complication. Future studies, with a larger series, may have a different pattern incidence in pulmonary complications following HSCT.

In conclusion, the “crazy-paving” pattern is rare in

HSCT patients with pulmonary complications, and was associated with infectious complications more commonly than with non-infectious conditions.

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