Host Factors Affect the Clinical Presentation and Biomarker Sensitivity in Patients with Invasive Pulmonary Aspergillosis

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Background: Early treatment of invasive pulmonary aspergillosis (IPA) is essential, but the clinical cues that trigger treatment are non-specific. Here, we asked whether patient characteristics affect the clinical presentation and performance of diagnostic assays of IPA.

Methods: We reviewed adult patients with hematological malignancies who met the EORTC/MSG criteria for probable or proven IPA (2007-2015). The radiographic pattern was defined according to established CT criteria as angioinvasive, airway-invasive or atypical infiltrates. Serum galactomannan was monitored weekly in susceptible patients. Patients with new pulmonary infiltrates underwent flexible bronchoscopy. Bronchoalveolar lavage fluid (BALF) was analyzed using standard mycological culture and galactomannan testing.

Results: 46 patients met criteria for IPA. Respiratory symptoms were significantly more frequent in patients with lymphoma (71% vs 8%). Radiographic patterns were angioinvasive (n=27), airway-invasive (n=15) and atypical infiltrates (n=7). The predominant radiographic pattern differed among patient groups: patients with AML presented with angioinvasive disease (100%, *P*<0.001) whereas stem cell transplant recipients often had airway-invasive disease (43%, *P*=0.011). Serum galactomannan was elevated in 47% and BALF galactomannan was detected in 58%. Serum galactomannan positivity was associated with the number of nodules on chest CT. The sensitivity of BAL galactomannan was highest in patients with airway-invasive disease.

Conclusion: Patient characteristics predispose to different patterns of lung involvement and affect the yield of biomarker testing. This information should be useful in designing a rational diagnostic strategy for high-risk patient populations.

Introduction

- Early diagnosis of invasive pulmonary aspergillosis (IPA) is essential.
- Diagnosis relies on chest CT and galactomannan (GM) measured in serum or bronchoalveolar lavage fluid (BALF).
- Patient factors affecting chest CT findings and biomarker performance are poorly defined.
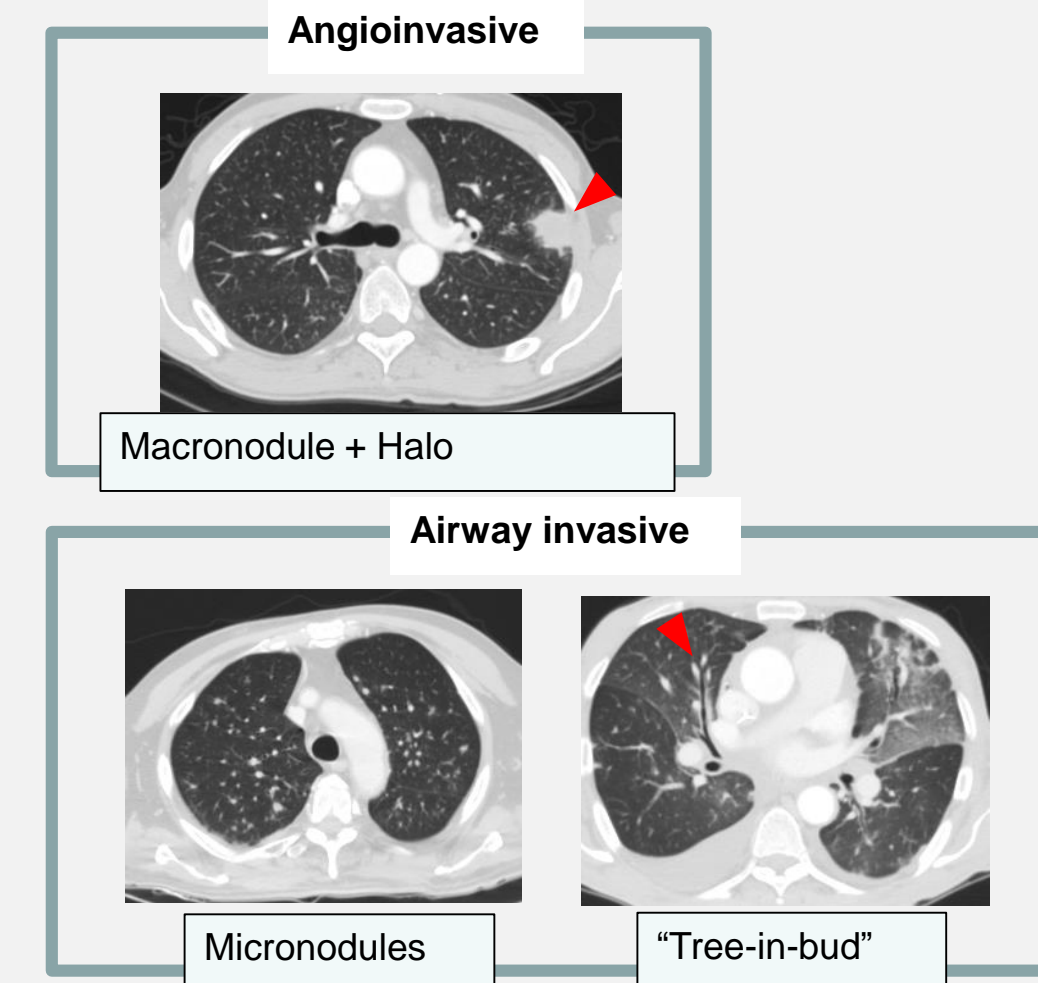
Objectives

To characterize radiographic patterns and biomarker sensitivity among patients with different underlying malignancies and other host factors.

Methods

- Review of adult patients with hematological malignancy meeting EORTC/MSG criteria for proven or probable IPA.
- Chest CT radiographic pattern defined as angio-invasive or airway-invasive (Figure 1).
- Serum GM monitored weekly in susceptible patients.
- Patients with new infiltrates on chest CT underwent bronchoscopy with BAL and GM measurement in BALF.

Fig. 1: Radiographic patterns of IPA

Angioinvasive

Macronodule + Halo

Airway invasive

Micronodules

"Tree-in-bud"

Table 1: Host factors and clinical presentation of IPA

	Angio-invasive	Airway-invasive	Consolidation	P	Respiratory symptoms
AML (n=13)	13 (100)	0 (0)	0 (0)	<0.001	1 (8)
Stem-cell transplant (n=21)	7 (33)	9 (43)	5 (24)	0.011	4 (19)
Lymphatic malignancy (n=7)	3 (43)	3 (43)	1 (14)	0.9	4 (57)
Total	23	12	6		

Fig. 2: Effect of host factors on Galactomannan sensitivity

Serum GM ≥0.5 — Yes / No — * *P* <0.05

Percent vs: Neutropenia, AML, SCT, Induction, Relapse, CMV, Angioinvasive, No. Nodules (1, >1) #

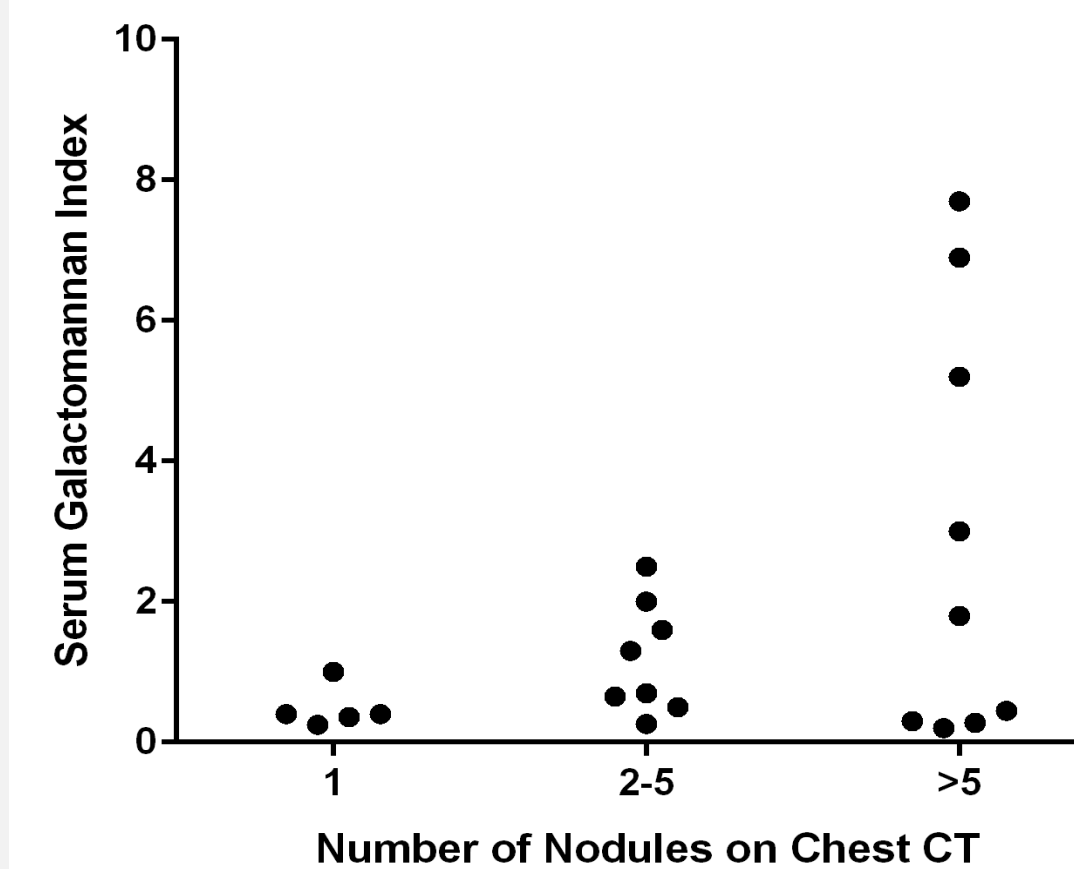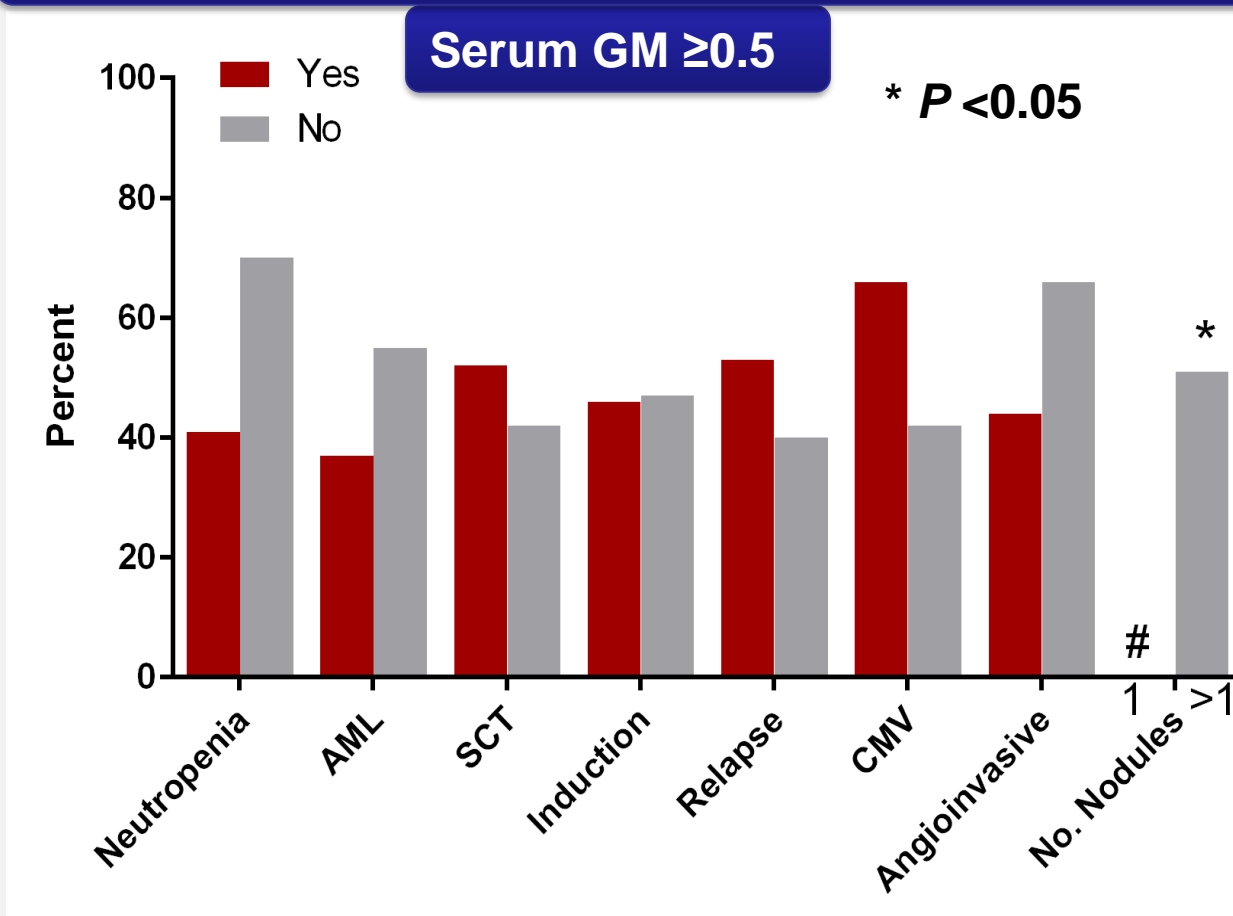Serum Galactomannan Index vs Number of Nodules on Chest CT (1, 2-5, >5)

Results

- Forty-six patients with IPA were included.
- Radiographic patterns of lung involvement were: angio-invasive (n=27), airway-invasive (n=15), and atypical consolidation (n=7); Table 1.
- An angio-invasive chest CT pattern was significantly associated with AML.
- Patients who received stem cell transplantation were most likely to develop airway-invasive disease.
- Atypical pulmonary infiltrates were associated with non-neutropenic status (*P*=0.06), disease other than acute leukemia (*P*=0.06), GVHD (*P*=0.06), and treatment with corticosteroids (*P*=0.02).
- Respiratory symptoms were uncommon in patients with AML and SCT recipients, and frequent in patients with lymphatic malignancy.
- The overall sensitivity of serum galactomannan was 47%.
- The only patient factor associated with serum galactomannan positivity was the presence of multiple nodules on chest CT (Figure 2).
- Detection of galactomannan in BALF was non-significantly more frequent in patients with an airway-invasive CT pattern (83% vs 46%, *P*=0.3).

Conclusions

- Patient characteristics predispose to different patterns of lung involvement and affect the yield of biomarker testing.
- This information should be useful in designing a rational diagnostic strategy for high-risk patient populations.