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Discrimination between invasive pulmonary aspergillosis and pulmonary lymphoma using CT

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ABSTRACT

Objective: The purpose was to assess the characteristic CT features of invasive pulmonary aspergillosis (IPA) and pulmonary lymphoma (PL) and to analyze the potential to distinguish the two entities using CT.

Methods: The CT images of 70 patients with either proven IPA ($n = 35$) or PL ($n = 35$) were evaluated retrospectively and independently by two radiologists (reader 1 [R1] and reader 2 [R2]), analyzing images for presence, number and characteristics of pulmonary nodules and masses, ground-glass opacities, consolidations and other interstitial changes.

Results: Interreader agreement was moderate (4/33 CT features), good (9/33) or excellent (20/33). Pulmonary nodules ($P = 0.045$ [R1], $P = 0.001$ [R2]), nodules with spiculated outer contours ($P < 0.001$ [R1], $P = 0.001$ [R2]), nodules with a halo sign ($P < 0.001$ [R1+R2]), nodules with homogeneous ($P = 0.030$ [R1], $P = 0.006$ [R2]) and inhomogeneous ($P = 0.001$ [R1], $P < 0.001$ [R2]) attenuation patterns, nodules with cavitation ($P = 0.006$ [R1], $P = 0.003$ [R2]) and wedge-shaped, pleural-based consolidations ($P < 0.001$ [R1 + R2]) occurred significantly more often in patients with IPA, while masses without a halo sign ($P = 0.03$ [R1], $P = 0.01$ [R2]), lobar consolidations with bronchogram ($P = 0.02$ [R1 + R2]) and consolidations with homogeneous attenuation patterns ($P < 0.001$ [R1 + R2]) were found significantly more frequent in PL-patients.

Conclusions: Those CT features can therefore be considered suggestive for either IPA or PL. However, in most cases the diagnosis cannot be made based on CT findings solely because no single feature gained a high sensitivity and specificity concomitantly. Furthermore, the logistic regression did not show a combination that was significantly better than the best univariate predictor.

1. Introduction

Invasive pulmonary aspergillosis (IPA) is a fungal infection still associated with a high mortality rate reaching up to 100% in some series [1,2]. Early diagnosis may reduce mortality rate by facilitating an early initiation of therapy [3].

Non-Hodgkin's Lymphoma (NHL) and Hodgkin's disease (HD) are malignant neoplasms typically originating from lymph node tissue, however may also involve or be found solely in extra nodal sites such as the lung [4].

IPA and PL may occur in patients with immunodeficiency of different origins and differential diagnoses have to be made within the context of the clinical constellations [4–8].

Immunocompromised patients due to AIDS may develop AIDS related lymphoma (ARL) as well as IPA [5,7]. Posttransplantation lymphoproliferative disease (PTLD) as well as IPA are known complications of posstransplantation iatrogenically induced immunosuppression. Patients suffering from lymphoma with a poor response to chemotherapy may show a subsequent pulmonary lymphoma involvement as well as an IPA due to chemotherapy induced immunocompromise. Finally both diseases can occur in non-immunocompromised patients, but with regard to IPA this is very rare.

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Because of the differences in their therapies, the ability to reliably distinguish between IPA and PL is essential. Most chemotherapeutic regimes including corticosteroids used to treat lymphoma accelerate the growth of aspergilli and additionally weaken the defense mechanisms of the host [6]. By contrast, antifungal drugs are usually not administered until a definite diagnose of IPA is made because of the severity of side effects [9].

Due to their similar clinical presentations with symptoms such as cough, fever and dyspnea, clinical evaluation alone is not appropriate to distinguish reliably between both entities [2,6].

Several histological and laboratory methods using tissue biopsies, resection material, or broncho-alveolar lavage (BAL) have been established to verify the diagnosis of IPA [10]. Notably the sensitivities of some tests are still not very high, e.g. in most series the sensitivity of BAL is only about 50% [10]. The risk of developing complications as a result of invasive diagnostic methods is substantial by diminished respiratory status and coagulation deficiencies.

Several studies had been conducted to develop characteristic CT patterns for either IPA or PL [1,3–6,11–14] , but to our knowledge CT characteristics of IPA versus PL have not to date been assessed. The purpose of this study was to conduct a broad analysis of the CT appearance of invasive pulmonary aspergillosis in contrast to pulmonary lymphoma and to assess the possibility to distinguish the two entities based on their CT features.

2. Materials and methods

2.1.1. Patient population

A retrospective search of the electronic databases at the Institute of Pathology and Microbiology, including the years 1999–2006, resulted in 39 patients with IPA and 38 patients with PL. Medical records of all 77 patients were retrieved. 70 patients (43 male [61%] and 27 female [39%], mean age: 55.5 years, age range: 15–80 years) with available CT examinations were included in the present study. According to the regulations of the Institutional Ethics Committee informed consent was not necessary for this retrospective study.

According to the international consensus of the European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/MSG) the diagnosis IPA was considered proven on the basis of histopathology and microscopy findings [15]. Additionally, proof of aspergillus in immunosuppressed patients, according to other studies [16], was a positive culture of broncho-alveolar-lavage fluid and associated radiologic findings. Of 35 patients with proven IPA, histopathologic confirmation was found in 17 cases (biopsy $n = 15$, autopsy $n = 2$), while positive BAL cultures were found in 18 cases (Fig. 1). In the 18 BAL cultures, the exact Aspergillus species was diagnosed. Amongst the histologically confirmed group ($n = 17$), the diagnosis was established microscopically and therefore the aspergillus species was not classified. PL was histopathologically proven in 35 patients (biopsy $n = 31$, autopsy $n = 4$). Lymphomas were diagnosed as Hodgkin's disease (HD) in 8 cases (23%) and Non-Hodgkin lymphoma (NHL) in 27 cases (77%) (Fig. 1). NHL-cases were further classified in primary lymphoma of the lung ($n = 7$), recurrent ($n = 14$) or secondary ($n = 2$) lymphoma of the lung, PTLD ($n = 2$) and ARL ($n = 2$).

Time delay between CT-acquisition and definite confirmation of diagnosis was 10 days on average in the IPA-group (range: 0–28 days) as well as in the PL-group (range: 0–26 days).

2.1.2. CT image acquisition and reconstruction

CT examinations were acquired between January 1999 and November 2006. A single slice spiral CT scanner (Somatom Plus 4, Siemens Medical Solutions, Forchheim, Germany) was used for all CT datasets that were acquired before February 2000 ($n = 23$). For all CT examinations after February 2000 ($n = 47$), multidetector row CT scanners were used (Siemens 4-, 16- or 64-channel scanners).

Tube voltage was either 120 kV or 140 kV, tube current–time product varied between 100 mAs and 172 mAs. Chest CT was performed after i.v.-administration of 100–120 ml non-ionic contrast media (different brands and vendors) with a delay varying from 25 s to 35 s. Slice thickness ranged from 8 mm for the single-row CT scanner to 1.25 mm for the 4-row scanner and 1 mm for the 16- and 64-row scanners.

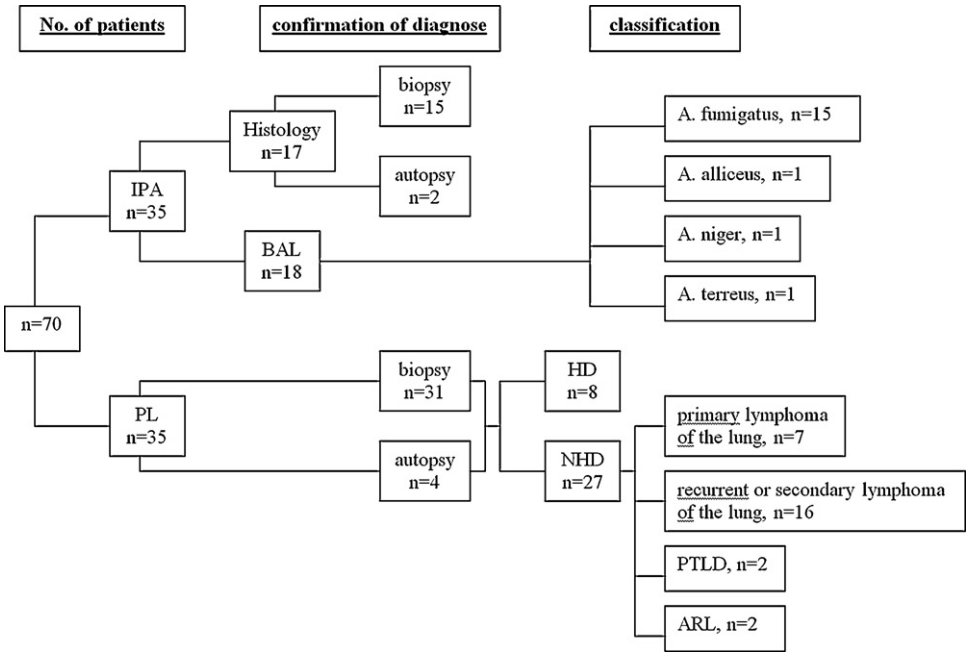

Fig. 1. Flowchart of patient distribution (IPA, invasive pulmonary aspergillosis; PL, pulmonary lymphoma; NHL, Non-Hodgkin's Lymphoma; HD, Hodgkin's disease; ARL, AIDS related lymphoma; PTLD, posttransplantation lymphoproliferative disease; BAL, broncho-alveolar lavage).