Fungal infections are definitely increasing in neutropenic patients with hematologic malignancies. In view of a previous report on a likely correlation between nose cultures positive for *Aspergillus* spp. and pulmonary aspergillosis, a retrospective study on 306 consecutive neutropenic patients was performed. Twenty-six patients had one or more nose cultures positive for *Aspergillus*: thirteen of them developed pulmonary aspergillosis. On the other hand, only twenty out of the remaining 280 patients with negative nose cultures developed this fungal pneumonia (p < 0.00001). Even if negative results do not obviously exclude the possibility of invasive aspergillosis, nose cultures positive for *Aspergillus* might prove helpful in predicting this fungal infection in febrile neutropenic patients.

**Key words:** Pulmonary aspergillosis, neutropenia, Aspergillus colonization.

Recent reports have suggested a likely correlation between nose cultures positive for *Aspergillus* spp. and pulmonary aspergillosis in neutropenic patients with hematologic malignancies. Because these infections are frequently fatal and since non-invasive predictive methods that might help identify potentially infected patients are much needed, we have conducted a retrospective study to evaluate the consistency of our data regarding this emerging pathogen and its presumed correlation with nose cultures.

**Materials and methods**

Results of surveillance nose cultures from 306 patients with hematologic malignancies (62 chronic myeloid leukemias, 73 acute lymphoid leukemias, 2 leukemic lymphomas and 169 acute non-lymphoid leukemias) admitted between March, 1983 and March, 1987 were reviewed. Nose cultures were obtained by swabbing the anterior nares and then plating the calls onto multiple media, including Sabouraud-Agar to favour the growth of fungal isolates. *Aspergillus* organisms were identified as *A. fumigatus*, *A. flavus* and *A. niger* according to the morphological features seen at light microscopy. Diagnosis of pulmonary aspergillosis was divided into «presumed», in cases having chest X-ray evidence of mycetoma or lung ball lesion (Fig. 1), and «proven», in cases with histologic and cultural evidence of infection. Neutropenia was defined as a neutrophil count below 0.5 x 10^9/l. The control group consisted of 280 patients with underlying diseases and clinical characteristics comparable with those of the study group. Statistical analysis of the data was carried out by means of the chi-square method.

**Results**

Nasal swabs yielded pathogenic *Aspergillus* spp. in 26 out of 306 consecutive neutropenic patients with hematologic malignancies which included 14 acute

![Fig. 1. - Chest tomogram of a patient with acute non lymphoid leukemia who developed a cavitating infiltrate in the right middle lobe after prolonged antibacterial therapy.](image)
non lymphoid leukemias, 6 chronic myeloid leukemias undergoing bone marrow transplantation, 5 acute lymphoid leukemias and 1 leukemic lymphoma. As shown in Table 1, proven or presumed pulmonary aspergillosis developed in 13 of these 26 patients and in 20 (7.1%) of the remaining 280 with no Aspergillus growth in the nasal swabs (p<0.00001).

The correlation between nose colonization by Aspergillus spp. and proven or presumed fungal infection in 306 neutropenic patients is shown on Table 2. The pulmonary infiltrates appeared on chest X-rays after 6 to 28 days of cytotoxic-induced neutropenia (median 13 days). Median polymorphonucleates per microliter at the onset of pulmonary infiltrate were 150 (range 20 to 700), and rose to 660 (range 20 to 6000) when lung ball cavitation became apparent on chest X-rays (Fig. 1). Nose colonization with Aspergillus spp. always preceded the clinical onset of proven or presumed pulmonary aspergillosis. In particular, the median time from positive nose cultures to typical pulmonary cavitation was 15 days (range 1 to 150).

**Discussion**

Invasive pulmonary aspergillosis represents one of the most dreaded infectious complications in patients with hematologic malignancies undergoing intensive cytoreductive chemotherapy. Under these circumstances, early diagnosis and prompt antifungal therapy with systemic amphotericin B may prove life saving. Definite diagnosis requires histologic demonstration of fungal infiltrates as well as tissue culture confirmation. However, in the setting of bone marrow aplasia, invasive tools such as percutaneous, transbronchial or open lung biopsy are contraindicated by bleeding complications.

Our results, even though based on a retrospective study, are consistent with a previous report and seem to confirm the epidemiologic trend of Aspergillus colonization and Aspergillus pneumonia in our hemisphere also. We outline here that Aspergillus nose colonization always preceded not only the clinical onset of invasive fungal pulmonary disease but also the radiologic appearance of the typical ball lesions highly suggestive of Aspergillus infection. However, in neutropenic patients with fever unresponsive to broad spectrum antibiotics, positive nose cultures may be associated not only with pneumonia but also with Aspergillus sinusitis, which ought to be considered further as the cause of fever in cases with a negative chest X-ray. In this situation X-ray or biopsy of the paranasal sinuses should be seriously considered for diagnosis.

To conclude, nose cultures even though non-specific, may be considered as a non-invasive tool that can prove helpful in cases of suspected fungal infections, when used together with CT scan, bronchoalveolar lavage, and serial monitoring of serum C reactive protein.

**Table 1.** Relationship between nose colonization by Aspergillus spp. and proven or presumed fungal infection in 306 neutropenic patients.

<table>
<thead>
<tr>
<th>Pulmonary Aspergillosis</th>
<th>YES</th>
<th>NO</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colonization YES</td>
<td>* 13 (4)</td>
<td>13</td>
<td>26</td>
</tr>
<tr>
<td>Colonization NO</td>
<td>* 20 (10)</td>
<td>260</td>
<td>280</td>
</tr>
<tr>
<td>Total</td>
<td>33 (14)</td>
<td>273</td>
<td>306</td>
</tr>
</tbody>
</table>

( ) = proven aspergillosis; * Chi-square = 45.4; p < 0.00001.

**Table 2.** Correlation between positive nose cultures, neutropenia and evolution of abnormalities on chest X-ray in 13 patients with hematologic malignancies and proven or presumed aspergillosis.

<table>
<thead>
<tr>
<th>Median days of neutropenia before pulmonary infiltrate (range)</th>
<th>13 (6 to 28)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median PMN per al at pulmonary infiltrate (range)</td>
<td>150 (20 to 700)</td>
</tr>
<tr>
<td>Median PMN per al at pulmonary cavitation (range)</td>
<td>660 (20 to 3000)</td>
</tr>
<tr>
<td>Median days from positive nose culture to pulmonary infiltrate (range)</td>
<td>10 (1 to 150)</td>
</tr>
<tr>
<td>Median days from positive nose culture to pulmonary cavitation (range)</td>
<td>15 (1 to 150)</td>
</tr>
</tbody>
</table>

PMN = Polymorphonucleates.
Aspergillus colonization and infection in neutropenic patients

zienti ebbero uno o più tamponi nasali positivi per Aspergillus spp.; tredici di loro svilupparono una aspergillosi polmonare. Dei rimanenti 280 pazienti con tampone nasale negativo solo 20 svilupparono questa infezione fungina (p<0.00001). Anche se le colture negative non escludono la possibilità di una aspergillosi invasiva, la colonizzazione nasale da Aspergillus spp. può dimostrarsi utile nel riconoscere precocemente questa infezione nei pazienti neutropenici con febbre.

REFERENCES