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ORIGINAL

Prevalence of invasive fungal infections detected at necropsy in a medium-sized hospital: A 15-year review of autopsy findings

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KEYWORDS
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Abstract Invasive fungal infections (IFIs) have an increasing importance as a cause of morbidity and mortality in hospital patients, especially long stay patients in critical care units.
Methods: We reviewed all necropsy records from the years 1999–2013 in the Hospital Universitario Fundación Alcorcón (HUFA), Madrid, and screened retrospectively for the presence of IFIs and underlying, predisposing factors.
Results: The analysis of 171 autopsies identified 22 patients with IFIs. The prevalence of IFIs slightly increased over time (from 6.3% in 1999 to 20% in 2013) and this increasing prevalence of IFIs was mainly caused by the *Aspergillus* species. Patients with invasive mechanical ventilation have the highest frequency of IFIs.
Conclusion: IFIs remain an important cause of mortality difficult to diagnose, thus post-mortem data are indispensable to evaluate its epidemiology.

PALABRAS CLAVE
Autopsia;
Micosis invasiva;
Epidemiología

Prevalencia de micosis invasivas detectadas en autopsia en 15 años, en un hospital medio

Resumen Las micosis invasivas son una causa importante de morbimortalidad en pacientes hospitalizados.
Metodología: Se hizo una revisión retrospectiva de todos los informes de autopsia del Hospital Universitario Fundación Alcorcón, Madrid, desde 1999 a 2013, evaluando la presencia de micosis invasivas y factores predisponentes.

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Resultados: Se identificaron 22 pacientes con micosis invasivas de un total de 171 autopsias. La prevalencia ha ido aumentando en el tiempo (del 6,3% en 1999 al 20% en 2013), siendo *Aspergillus* especies el agente más frecuentemente aislado.
Conclusión: Las micosis invasivas son difíciles de diagnosticar ante mórtem, por lo que las necropsias siguen siendo una fuente indispensable para evaluar su epidemiología.

Introduction

Invasive fungal infections (IFIs) are serious complications, both of diseases which impair normal immunity and of immunosuppressive treatment. Recent data suggest that IFIs appear to have increased, compared with observations in the 1990s.[1] Given the limited utility of current diagnostic approaches and due to the continuing lack of sensitive and specific diagnostic tools, opportunistic IFIs remain difficult to recognize. Therefore, patients with IFIs continue to die and autopsy series provide indispensable information for the understanding and monitoring of trends in frequency, disease patterns and organ involvement.

Indeed, in recent years several reports have underlined the increasing importance of IFIs as a cause of morbidity and mortality in immunocompromised and severely ill patients. Two multicentre Spanish studies (EPI-FOCI and ENVIN-UCI)[2,3] and one Italian study[4] of critically ill patients reported an incidence of aspergillosis (the most frequent fungal infection) of 6.3 per 1000 admissions. One of those reports summarized the conclusions from a meeting held in Spain in 2012 with participating experts from two scientific societies (The Spanish Society for Chemotherapy and The Spanish Society of Intensive Care and Coronary Units). The epidemiological issues and the risk factors of fungal respiratory infections in the critically ill patient were reviewed. The principal risk factors for development of invasive pulmonary aspergillosis were found to be neutropenia in those with haematological malignancies and patients undergoin prolonged steroid treatment, especially in severe chronic obstructive pulmonary disease (COPD).[5] In 2014, one report analyzed the epidemiology of IFIs obtained from autopsy series published during the previous 6 years,[6] concluding that the median prevalence of IFIs was 8.7 per 100 autopsies, aspergillosis being the most prevalent; the pre-mortem diagnosis was 46 patients per 100 necropsies, and the median autopsy rate was 15 per 100 deceased patients (most reports come from the general population of Japan, because all necropsies throughout the country are reported through the Japanese Society of Pathology).[7]

The objective of our study was to review all necropsy records from one centre during the years 1999–2013 inclusive, in order to document the prevalence of invasive fungal infections together with underlying predisposing factors and pathological findings.

Materials and methods

This was a descriptive retrospective study carried out in the Hospital Universitario Fundación Alcorcón (HUFA), Madrid, a 448-bed facility with all major medical subspecialties except transplant and burns department.

We collected all the patient data from a retrospective review of electronic medical record files and autopsy reports.

The review included all 1075 necropsies carried out by the pathology department between January 1st, 1999 and December 31st, 2013 and the cases with fungal infections were analyzed. Autopsies are not carried out on all hospital deaths, only those where clinicians felt a need for definitive diagnosis and after obtaining familiar consent. This policy limits the number of autopsies. Study variables included basic demographics and clinical and laboratory characteristics, obtained from medical records: age and gender; predisposing risk factors such an underlying conditions (diabetes mellitus, COPD, lupus); neutropenia (defined as <500 neutrophils/μL); corticosteroid treatment (defined as intake of >10 mg of prednisone equivalent per day); type and status of oncohaematological disorder; solid tumour malignancy; human immunodeficiency virus infection; presence of intercurrent bacterial or viral infections; ante mortem suspicion; length of hospital stay; use of invasive mechanical ventilation (IMV); type of antifungal prophylaxis administered, and organ involved, were noted in every case.

The fungus was identified morphologically: thin septate hyphae with acute angle branching and with unequivocal evidence of tissue infiltration were diagnosed as *Aspergillus* species. Broad, aseptate, irregularly branching hyphae as *Zygomycetes* species. *Candida* species were identified by pseudohyphae and budding yeast forms and Cryptococcus was identified by capsulated yeast forms. *Pneumocystis jirovecci* was identified by the cup-shaped form of the fungus. When fungal infection was mentioned in the histology description, slides were stained with Grocott method.

Statistical analysis was made with STATA 12.0. Data are presented as count and percentages in qualitative variables and mean and standard deviation in quantitative variables. To analyze trends over time in rate of autopsies and in prevalence of invasive fungal infection, incidence rate ratio (IRR) was estimated with Poisson regression models or Negative Binomial models in case of over-dispersion. A multivariate Poisson regression model was applied to estimate the trends in prevalence adjusted by the risk factors studied.

In the autopsy samples, an exploratory univariate analysis was performed to study IFI associated factors. Chi-squared test or Fisher exact test and *U* Mann Whitney test was used to compare autopsies with IFI and without IFI.

All tests were two-tailed, and p values of less than 0.05 were considered to be statistically significant.