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Diagnosis of *Pneumocystis jirovecii* pneumonia in an Intensive Care Unit: a 3-year prospective study

Nahéma ISSA[1,2], Gildas BAULIER[3], Fréderic GABRIEL[4], Isabelle ACCOCEBERRY[4], Gaëlle MOURISSOUX[1], Olivier GUISSET[1], Fabrice CAMOU[1,2]

[1]Intensive Care Unit, [2]Infectious Disease Unit, [3]Internal Medicine, [4]Mycology, Bordeaux University Hospital, FRANCE

Fabrice CAMOU, MD
fabrice.camou@chu-bordeaux.fr
www.endocardites-aquitaine.fr

CHU Hôpitaux de Bordeaux

Introduction

Pneumocystis jirovecii is a ubiquitous fungus that is specific for humans and responsible for *P. jirovecii* pneumonia (PCP). It mainly occurs in immunocompromised patients, including HIV-positive patients and those receiving chemotherapy, long-term corticosteroid therapy and/or biotherapy. As a life-threatening infection, secondary to acute respiratory failure, up to 50% of patients require an intensive care unit (ICU) admission. Direct microbiological exam (DME) of respiratory samples remains the gold standard for the diagnosis of PCP. However, with the advent of new diagnostic tools like quantitative real time PCR (qPCR), early detection of low fungal burden of *P. jirovecii* in respiratory samples is possible. The clinical utility of such tool in ICU is not yet well defined.

Methods

The aim of this 3 year prospective study was to evaluate the diagnostic contribution of positive *P. jirovecii* qPCR (commercial kit targeting the major surface glycoprotein gene) in patients admitted in the ICU for acute respiratory failure. Microbiological exams (DME and qPCR) were performed in the mycology laboratory of Bordeaux University Hospital. The clinical, microbiological (from respiratory samples) and radiological data for each patient were recorded. Treatment (curative and prophylactic) and outcome were also analyzed. Retrospectively, all cases were reviewed by a collegial multidisciplinary team and classified according to clinical, radiological and microbiological data as having retained PCP (positive DME), possible PCP or colonization (negative DME and favorable clinical outcome in the absence of curative PCP treatment). Categorical variables are presented as percentages and were compared using the chi-squared test or Fisher's exact test, as appropriate.

Results

Seventy five patients were included and 68% were men. The mean age was 61 years. Risk factors and/or underlying disease were identified in 96% of patients : 21% were HIV positive and 79% were HIV negative. Among HIV-negative patients, 53% were receiving corticosteroid therapy, 28% had onco or hematological malignancy and 19% had undergone an organ transplantation (Figure 1). Overall, 97% of patients were not receiving PCP prophylaxis. Dyspnea, fever and cough were present in 96%, 88% and 89% respectively. The triad was identified in 77% of cases. Chest computed tomography showed an interstitial pneumonia in 83% of patients. DME of the respiratory samples (BAL for 63% of patients) was positive in 88% of HIV patients and 27% of non-HIV patients. Cotrimoxazole was the first-line treatment in 85% of patients. Steroid therapy was used in 69% of patients and 45% of the patients needed mechanical ventilation. The in-hospital mortality was 39% and attributable PCP mortality was 52%. Retrospectively, 30 patients had a retained PCP, 34 had a possible PCP and 11 were colonized. The qPCR value was significantly higher in infected patients than in colonized patients (Figure 2). When considering a qPCR cut-off at 10 100 copies/mL, the overall sensitivity would be 77% (Figure 3).

Conclusion

This study confirms that the combination of clinical, radiological parameters and qPCR on respiratory samples allows to discriminate between *P. jirovecii* colonization and PCP in ICU patients when DME is negative. In case of colonization (qPCR < 10 100 copies/mL), diagnosis of PCP is uncertain. However clinicians should be encouraged to prescribe a prophylactic PCP treatment.

References : Robert-Gangneux, *J Clin Microbiol* 2014 ; 52(9) : 3370-6. Fauchier *et al*, *J Clin Microbiol* 2016 ; 54(6) : 1487-95

Figure 1. No. of patients with the following underlying disease or condition

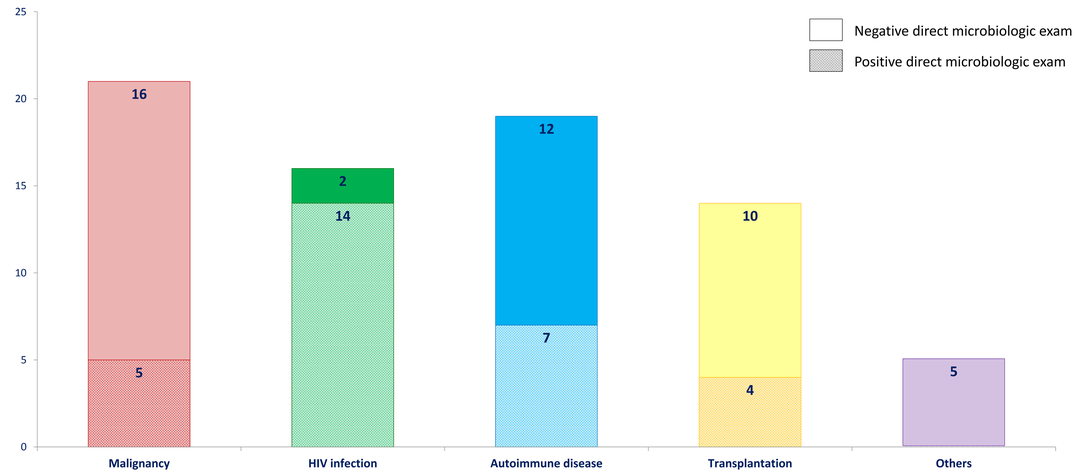


Figure 2. Values of qPCR

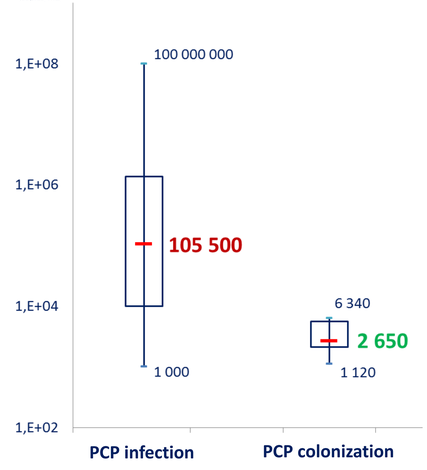
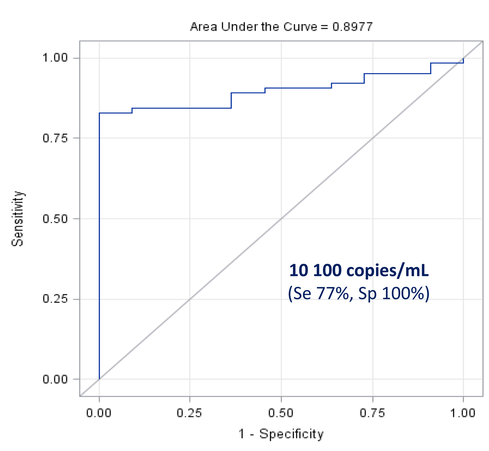


Figure 3. Receiver operator characteristic (ROC) curve for the diagnosis of PCP



Abstract (revised)

Background

Pneumocystis jirovecii pneumonia (PCP) is a life-threatening infection. The increasing use of corticosteroids, chemotherapy and immunosuppressive drugs may lead to an outbreak of PCP in patients not affected by HIV and sometimes their admission to an intensive care unit (ICU) for acute respiratory distress.

Methods

The aim of this 3 year prospective study was to evaluate the diagnostic contribution of positive *P. jirovecii* qPCR in patients admitted in the ICU for acute respiratory failure. Patients were classified as having retained PCP (positive direct microscopic examination), possible PCP or colonization according to clinical, radiological and microbiological data. Treatment and outcome of patients were also analyzed.

Results

Seventy-five patients were included and 68% were men. The median age was 61 years. Risk factors were identified in 96% of patients: 53% had corticosteroid therapy, 28% onco-hematological malignancy, 19% transplantation and 21% HIV. Dyspnea, cough and fever were the most frequent clinical manifestations. Overall, 97% of patients were not receiving PCP prophylaxis. Typical radiological results were found in 83% of patients. Direct microscopic examination (DME) of the respiratory secretions (BAL and or sputum) was positive in 88% of HIV patients and 27% of non-HIV patients. Among the 45 patients with negative DME, 34 (75%) had a possible PCP and 11 were colonized. Cotrimoxazole was the first-line treatment in 85% of patients. Steroid therapy was used in 69% of patients and 45% of the patients needed mechanical ventilation. The in-hospital mortality was 39% and attributable PCP mortality was 52%.

Conclusions

This study confirms that quantitative rtPCR is a useful tool to diagnose PCP in the ICU, especially in non-HIV patients of whom 73% had a negative direct microbiologic examination.