Pneumocystis jirovecii pneumonia: still a concern in patients with haematological malignancies and stem cell transplant recipients—authors’ response

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Sirs,

We would like to thank Antorini et al.1 for their comments on the European Conference on Infections in Leukemia (ECIL) guidelines for the management of Pneumocystis jirovecii pneumonia (PCP).2 Antorini et al.1 listed four points, which we would like to address one by one.

Mode of acquisition of PCP in haematology patients

The mode of acquisition of PCP in haematology patients is uncertain, but there is no reason to think that it is different from that in other immunocompromised patients. Exposure to P. jiroveci through inhalation begins early in life, as shown by autopsy series, and PCR and serological screenings.1,4 The high rate of mixtures of genotypes during PCP (up to 90%) also supports continuous exposure to P. jiroveci from the environment via other humans.7 When investigating outbreaks in solid organ transplant units using genotyping, only some of the cases were shown to be due to inter-human or environmental transmission.5,6 To our knowledge, only two outbreaks have been reported in haematology wards. The first one included five cases in 6 months in the same haematology unit, but without any molecular investigation.10 The second study established a genetic link using internal transcribed spacer (ITS) sequencing between the strains for two out of eight haematology patients (and two out of six HIV-positive patients), suggesting that person-to-person transmission was relatively infrequent.11 Recently, transmission between patients from different wards was reported with the help of six new short tandem repeat markers located in the nuclear genome.12 However, even with this highly discriminant genotyping method, we could not differentiate between reactivation and a new infection.12 Despite the lack of solid data reflected by a grading of only C-III, ECIL proposed that patients in haematology should, nonetheless, avoid contact with those infected with PCP.13

Differences in clinical presentation and hypoxaemia between patients with and without HIV infection

Antorini et al.1 show that two-thirds of their patients with HIV infection had a PaO2 < 70 mmHg. However, the PaO2 of patients with PCP, but without HIV infection, was not presented. This makes any conclusion about PaO2 at diagnosis difficult. We agree with Antorini et al.7 that PaO2 at presentation can be

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highly dependent on the quality of local care, especially rapid access to bronchoalveolar lavage. Indeed, the delay from the onset of symptoms to establishing a diagnosis of PCP was variable according to the year of diagnosis and the centres involved and may well have had an impact on the severity at presentation.14-18 Nevertheless, apart from open studies reporting high rates of hypoxaemia in patients with PCP and underlying haematological conditions, parallel comparisons of those with and without HIV infection showed that the degree of respiratory failure at presentation (often before admission to the ICU), whether assessed by PaO₂, SaO₂ or PaO₂/FiO₂, was significantly higher in those without HIV infection.19-22,26 and the need for ventilation was significantly more frequent in three series,1,4,17,19 but not in a fourth one.18 A recent French series, which was not available at the ECIL-5 meeting, confirms this pattern since only 25 (11%) of 223 patients with AIDS required invasive mechanical ventilation, compared with 98 (30.5%) of 321 with another underlying condition, including 111 with haematological diseases.19 Moreover, a diagnosis of AIDS was associated with lower mortality, whereas the converse was true for receipt of an allogeneic HSCT and the need for mechanical ventilation.19

**Lactate dehydrogenase (LDH) levels at presentation**

LDH levels at diagnosis were 39%–46% higher among patients with HIV infection than among those without.14-16,18,19 However, the ECIL-5 laboratory diagnosis group concluded that this discussion had been superseded by the ready availability of more specific laboratory tools, such as PCR or β-D-glucan detection, making further mention of LDH elevation for the diagnosis of PCP redundant.22 We consider, however, that an unexplained serum LDH elevation in the presence of a suggestive clinical presentation could be taken into account when deciding upon initiation of PCP treatment, providing quick, direct investigations.23

**Mortality rates in HIV-positive patients**

The mortality due to PCP is usually assessed at day 90 after onset. In series of patients with HIV infection reported from 2000s, it was reported to vary from 9.6%17 to 30%.18,20 By contrast, a recent French survey reported an of patients with HIV infection reported from 2000s, it was reported to vary lower than the 27% rate found for those with other underlying conditions.19 Besides the higher mortality, PCP in those not infected with HIV tends to occur very abruptly and carries a high risk of ICU transfer. Hence, the haematology community should be alerted to this possibility and needs to ensure adequate and timely diagnostic and prevention strategies are developed and implemented to offer the best outcomes.

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