Accepted Manuscript

Mycobacterial blood cultures in the diagnosis of tuberculosis in HIV-infected patients: are they useful?

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21   **Word count:** 756

22

23   **Reference count:** 5

24   To the Editor

25   The use of mycobacterial blood cultures (MBC) for the diagnosis of tuberculosis (TB) is advised

26   in immunosuppressed patients to increase the diagnostic recovery (1). In HIV-infected

27   patients, it is not clear if MBC provide additional value over a well-directed study and other

28   properly collected samples for microbiological investigation. Also, the number of MBC that

29   should be processed is not defined. We performed an assessment of the overall sensitivity of

30   MBC for the diagnosis of TB in HIV-infected adult patients requiring acute hospital admission,

31   at Centro Hospitalar São João, Porto/Portugal, between 2008 and 2014. TB was classified as

32   probable [clinical criteria and one positive acid-fast bacilli (AFB) smear or granuloma in biopsy

33   or positive nucleic acid amplification test (NAAT)] and definitive (clinical criteria and positive

34   culture or two positive AFB smears or a positive AFB smear and positive NAAT). Disseminated

35   TB was defined as TB in 2 non-contiguous locations.

36

37   We included 139 HIV-infected patients. In our sample, 111 (79.9%) were male, mean age was

38   44.8 years (±12.7). Median CD4+ count at the time of TB diagnosis was 86/mm^3 (IQR 30-177).

39   In 51 (37%) patients, TB and HIV were diagnosed simultaneously.

40   The majority of patients had lung disease (N=115; 82.7%), of which 52 (45.2%) had also

41   extrapulmonary manifestations. Forty-six patients (33.1%) had disseminated disease.

42   A total of 218 MBC were drawn to 121 patients (87.1%), with 56 patients (46.2%) having

43   collected at least 2 MBC, and 25 (20.7%) at least 3. Eleven patients (9.1%) had more than 3

44   MBC collected. All samples were collected in separate days. From the 81 patients with a

45   definitive or probable diagnosis, a total of 144 MBC was collected. Of those, 15 (12.4%)

46   patients had a positive MBC result, of which 12 (80%) were positive in the first MBC drawn.

47   Thus, the overall sensitivity of one MBC in the diagnosis of TB was 14.8%. Other 3 out of 56

48   patients had a second positive MBC sample, which increased the sensitivity to 27.5%. Adding a

49   third MBC sample did not increase the overall sensitivity of the test.

50 The sensitivity of MBC was higher in patients with CD4+ <50/mm^3 (the estimated sensitivity of

51 MBC was 27.3% and 33.3%, for one or two samples, respectively) and patients with

52 extrapulmonary commitment had a significantly higher proportion of positive MBC samples

53 (80% vs. 20%; p=0.006).

54 Of the 15 patients with a positive MBC, 3 had only pulmonary manifestations (20%), 10 had

55 pulmonary and extrapulmonary disease (66.7%) and 2 had strictly extrapulmonary

56 commitment, with lymphatic disease.

57 Of notice, all patients with a positive MBC for *Mycobacterium tuberculosis complex* had a

58 positive culture in at least one other biological sample, and all but one had either a positive

59 AFB smear or NAAT. Indeed, eighty percent of MBC-positive cases had a positive AFB smear. In

60 our analysis, we included respiratory specimens collected from invasive procedures (e.g.,

61 bronchoscopy) and auramin staining was performed in all samples.

62

63 As some previous studies (2-5) MBC showed low sensitivity and overall low diagnostic yield in

64 the diagnosis of TB, namely among HIV-infected patients. In our study, we included severely

65 immunosuppressed patients requiring acute hospital admission. We found that the overall

66 sensitivity of one MBC was 14.8%. Having two blood samples for culture increased sensitivity

67 to a maximum of 33.3% in those below 50/mm^3. A third sample had no additional value in any

68 strata.

69 When comparing patients with positive and negative MBC, patients with positive MBC had

70 more advanced HIV disease, as shown by a higher mean viral load and lower CD4+ count, and a

71 higher rate of extrapulmonary reflecting failure of the severely impaired immune system at

72 controlling TB infection.

73 In all MBC-positive cases, *M. tuberculosis* was also isolated in samples collected from other

74 sites and all but one patient had either a positive AFB smear or NAAT.

75 The mean time to positivity of MBC, when using standard media, is between 2-6 weeks,

76 considerably longer than both AFB smear and NAAT. Moreover, only a small percentage of

77 patients with evidence of TB had a positive MBC.

78 Although current guidelines and standards recommend performing MBC in HIV-infected

79 patients with suspected TB, we found no added value of MBC in the diagnosis of TB in a setting

80 where invasive biological samples and microbiological tests (including molecular studies and

81 culture with automated techniques) are done.

82 We do not know if the results are different for mycobacterial infections other than *M.*

83 *tuberculosis* that often are considered in the differential diagnosis. More studies, including cost

84 analysis are needed to better define the role of MBC in the diagnosis of mycobacterial

85 infections.

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88 **Conflicts of interest**

89 The authors have none to declare.

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