Yield of Bone Marrow Culture in the Diagnosis of Infectious Diseases in Patients with Acquired Immunodeficiency Syndrome

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The yield in cultures of bone marrow aspirations or biopsies was determined in 50 patients with acquired immunodeficiency syndrome. Most patients were febrile and had no identifiable source of infection. Concurrent stool, urine, and blood samples were also cultured. The bone marrow aspiration and biopsy procedures produced no complications and enabled a microbiological diagnosis to be made in 42% of the cases. Granuloma formation was not seen in any of the infected bone marrow specimens despite the fact that mycobacteria were seen in abundance in some. Bone marrow culture is a valuable low-morbidity invasive procedure in the evaluation of febrile patients with acquired immunodeficiency syndrome.

Patients with acquired immunodeficiency syndrome (AIDS) are more susceptible to opportunistic pathogens, which include Pneumocystis carinii (4), Salmonella spp. (7, 15), Toxoplasma gondii (L. R. Sharer and R. Kapila, Acta Neuropathol., in press), Mycobacterium tuberculosis (10), Mycobacterium avium-Mycobacterium intracellulare complex (MAI) (10), Mycobacterium xenopi (5), and Cryptococcus neoformans (R. H. K. Eng, E. Bishburg, S. M. Smith, and R. Kapila, Am. J. Med., in press). These infections can present with an insidious onset, and the diagnosis can often be difficult. Therefore, it is important to know the diagnostic yields of the procedures used to recover these pathogens. Hence, the medical records of AIDS patients were retrospectively reviewed to determine the yield of bone marrow aspirations and cultures for the diagnosis of these infectious diseases.

The medical records of patients diagnosed as having AIDS from June 1981 to June 1985 at the Veterans Administration Medical Center, East Orange, N.J., and University Hospital, Newark, N.J., were reviewed. These two institutions have a total of 1,200 acute-care beds and serve the Newark and Northern New Jersey area. Only patients who met the criteria for AIDS as determined by the Centers for Disease Control were included in the study (3).

Specimens of bone marrow and other deep body sites were cultured on blood, chocolate, and Sabouraud dextrose agars and into brain heart infusion and chopped meat glucose broths. The specimens were inoculated into Dubos broth with subcultures onto Lowenstein-Jensen agar. All cultures were incubated in 5 to 8% CO2 at 35°C. When requested, specimens from other sites (spuata, urine, and stools) were also cultured on Lowenstein-Jensen agar for mycobacteria (16).

Blood was cultured for bacteria and fungi in BACTEC 6B and 7D bottles and monitored radiometrically. A limited number of blood specimens were processed for mycobacteria in the Du Pont Isolator (Du Pont Co., Wilmington, Del.) with inoculation onto blood, chocolate, Lowenstein-Jensen, and Sabouraud dextrose agars (11). Only data obtained from specimens submitted in Du Pont Isolators were included in the analysis of mycobacterium yields.

Acid-fast bacilli were referred to the New Jersey State Department of Health, Trenton, N.J., or to the Veterans Administration Reference Laboratory for Tuberculosis and Other Mycobacterial Diseases, West Haven, Conn., for identification. Yeasts were identified by microscopic morphology and the Uni-Yeast-Tek (Flow Laboratories, Inc., McLean, Va.) or Minitek Yeast Assimilation system (BBL Microbiology Systems, Cockeysville, Md.) and by pigment production on birdseed agar. Filamentous fungi were identified by microscopic morphology.

During the 4-year period, 200 patients with AIDS were diagnosed, with 50 (25%) having had bone marrow aspirations or bone marrow biopsies performed. This group consisted primarily of patients with a history of parenteral drug abuse (90%). Of these 50 patients, 37 had the marrow examined for evaluation of unexplained fever, 10 had it examined for suspected granulomatous infections, and 3 had it examined for evaluation of a deficiency in peripheral blood elements. These 50 patients had been diagnosed for less than 12 months or were pre-AIDS at the time of examination and subsequently met the criteria for AIDS. Twenty-five patients (50%) had one prior hospital admission for AIDS-related diseases, 16 (32%) had two prior admissions, and 9 (18%) had three or more prior admissions. Half the patients had prior opportunistic infections, of which 64% were caused by P. carinii.

A comparison of AIDS patients in whom marrow cultures were positive (42%) with those whose cultures were negative (58%) indicated that all patients had normal to mildly elevated serum alkaline phosphatase levels, the same incidence of granulocytopenia and thrombocytopenia, and the same degree of pyrexia. All patients had additional suspected sites of infection, including the lungs and meninges. Neither group had evidence of bone pain, and there were no predictive clinical parameters to distinguish patients with positive bone marrow cultures.

For 14 patients in whom the bone marrow was aspirated as well as biopsied, organisms were seen microscopically on histologic examination on all specimens. Mycobacteria were seen in abundance without accompanying formation of granuloma, or cryptococci were seen without accompanying evidence of marrow necrosis. Of the three bone marrow aspirations performed because of abnormal peripheral blood
counts, only one was culture positive. For the 47 bone marrows obtained because of unexplained fever or suspected granulomas, the pathogen yield was 42.5% (20 of 47). The concurrent culture results from the different body sites are shown in Table 1. Four of 13 patients with *C. neoformans* infections had positive bone marrow cultures. All four patients also had the organism recovered from blood cultures. The remaining nine patients with cryptococcal infections had the organism isolated from only the cerebrospinal fluid. In cryptococcal infections, the most sensitive test was a serum cryptococcal antigen determination (Eng et al., in press). For the 17 patients with MAI infections, the bone marrow aspirate was a sensitive test, with 16 of 17 patients being positive. Additional specimens which gave significant yields included liver (4 of 6) and sputum (5 of 12) specimens. Of the six patients who had blood processed by the Du Pont Isolator, only one was positive for MAI. Also, 3 of 10 patients had MAI isolated from the stool. For *M. tuberculosis* infections, sputum had the highest yield (10 of 20). The overall pathogen yield of bone marrow cultures in all AIDS patients was 21 of 50 or 42%.

For comparison, results for 161 bone marrow aspirations or biopsies from non-AIDS patients from 1976 to 1985 were reviewed. Some of these specimens could have been from undiagnosed AIDS patients. Four of the 161 specimens were culture positive, one each for MAI, *M. tuberculosis*, *Escherichia coli*, and *Basidiobolus* spp. The latter was considered a laboratory contaminant, and the patient improved without therapy. The patient with MAI was a drug addict lost to follow-up and could have had AIDS. The diagnostic yield in this group was 2.1% (3 of 161), a value much lower than that of confirmed AIDS patients.

Bone marrow culture was previously reported to be a valuable diagnostic procedure (8, 13, 14). In this study, the yield was 42%, similar to that reported by Horsburgh et al. (8), 41%. In the present study, marrow examination had a yield of 94.1% for MAI, 30.8% for *C. neoformans*, and 5% for *M. tuberculosis*.

Bone marrow examination has been shown to be useful for the diagnosis of infections by intracellular organisms in non-AIDS patients (1, 2, 6, 9, 12, 17), and its usefulness was also affirmed in this study of AIDS patients. Our patients had a conglomeration of indications for marrow examination, and the many factors which contributed to the arguments for the procedure cannot be retrieved, but the overall results were rewarding because the pathogens isolated were treatable. The number of Du Pont Isolator blood cultures obtained from patients with MAI was small, and a comparison of this method of culture and bone marrow culture was not possible. Enthusiasm for bone marrow culture should be tempered, because it is still considered an invasive procedure. In view of the wide availability of the Du Pont Isolator, blood cultures by this noninvasive procedure should always be performed first. Our data with the Du Pont Isolator did not indicate a high yield, but the data are limited and the blood samples were split among four types of culture media, of which only one can support mycobacterial growth. When no organisms are isolated from the blood, perhaps bone marrow cultures may be considered as a low-morbidity adjunctive procedure for diagnosis in the febrile AIDS patient.

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LITERATURE CITED


