NOTE

Routine Cultures of Bone Marrow and Peripheral Stem Cell Harvests: Clinical Impact, Cost Analysis, and Review

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The American Association of Blood Banks requires routine culture of hematopoietic progenitor cells prior to bone marrow transplantation. We sought to evaluate the cost of that requirement and the incidence and clinical significance of positive cultures. We performed a retrospective analysis of transplant recipients at our institution. Of the 605 patients for whom 1,934 consecutive cultures of harvests were done between December 1992 and February 1996, 11 had positive cultures. Six patients received a culture-positive harvest with no adverse effects. The total cost of cultures was $35,660 (U.S. $). In North America and worldwide in 1995, routine culture of harvests would have prevented 7.9 and 18.9 cases of bacteremia, respectively, at a cost of $95,000 per bacteremia prevented. We conclude that routine culture of hematopoietic progenitor cells yields low rates of positivity and that infusion of contaminated harvests rarely results in clinically adverse outcomes.

Hematopoietic progenitor cell transplantation has become standard therapy for many conditions [1]. The number of such transplantations has increased markedly since the 1980s. Complex steps in the collection, processing, cryopreservation, and infusion of bone marrow and peripheral stem cells involve ex vivo manipulation of these products, processes that are prone to microbial contamination. There is concern about ensuring the sterility of these preparations because patients receiving them are immunocompromised.

In 1991 the American Association of Blood Banks (AABB) established the standard of requiring microbiological culture of all hematopoietic progenitor cell components [2]. Several studies have investigated the incidence and clinical significance of positive cultures [3–16], but conclusions and clinical recommendations vary. Several questions remain unanswered, which prompted us to review our experience.

Methods

In compliance with AABB standards, The Cleveland Clinic Foundation blood bank submits a sample of every progenitor cell harvest for bacterial and fungal cultures. We reviewed the microbiology reports of all positive cultures from the period between December 1992 and February 1996, noting the microbial isolate, amount of growth, and time to growth. We reviewed medical records of all patients with positive cultures and collected data on demographics, underlying disease, and outcomes if the unit with positive growth was infused.

Results

During the 39-month period, 1,660 cultures of peripheral stem cell harvests were performed for 417 patients (mean, 3.98 harvests per patient), yielding 11 positive cultures (0.66%). Three of these were recultured and showed no growth. All 274 cultures of bone marrow harvests from 188 patients (mean, 1.46 harvests per patient) were negative.

Table 1 summarizes results of the 11 positive cultures. For eight (67%) of the 12 isolates, growth was reported as rare or as a single colony. The mean time to growth was 2.67 days (range, 1–6 days). Eight (67%) of the 12 isolates were fungal. No gram-negative bacilli were isolated. The mean age of the patients was 45 years (range, 30–60 years).

Seven patients had lymphoma and four had breast cancer. One patient died of metastatic disease before transplantation. Six (60%) of the remaining 10 patients received the culture-positive harvest. No adverse clinical sequelae resulting from infusion were noted. None developed fever or chills during the infusion. Two of the six patients developed bloodstream infections with organisms other than the ones isolated from the harvests.

Discussion

The AABB requires that a sample of each bone marrow and peripheral stem cell harvest be screened for bacterial and fungal...
Our study likely reflects that fungal cultures were performed covered [8, 9, 15]. The greater number of fungal isolates in skin flora and occasionally water-borne gram-negative bacilli preparation need not be performed routinely. We suggest that zero rate of positivity of cultures of bone marrow harvests expensive procedure.

The overall contamination rate for bone marrow preparations ranged from zero to 36% (average, 4.4%). The contamination rate for peripheral stem cell preparations was lower, ranging from 0.2%–18% (average, 1.1%). In our study, we found a low rate of positive cultures (0.66%) of stem cell harvests, comparable to that reported in other studies [10, 12–15]. Our zero rate of positivity of cultures of bone marrow harvests compared favorably with other reports [3–7, 10–13, 15].

The microbiology of isolates in our study was different from descriptions in the literature. Most investigators reported usual skin flora and occasionally water-borne gram-negative bacilli as contaminants, and in three studies fungal isolates were recovered [8, 9, 15]. The greater number of fungal isolates in our study likely reflects that fungal cultures were performed on all samples, and contamination probably occurred in the microbiology laboratory at or after plating. For three patients, cultures were repeated and negative, confirming the strong suspicion that the progenitor cell sample was not truly infected.

Our review of the literature revealed that, in some cases, there is another explanation for a positive progenitor cell culture—namely, contamination of the bag at any point from the time of harvesting to the time of infusion of the preparation, representing true infection of the hematopoietic progenitor cell preparation.

In all but two studies [5, 11], infusion of contaminated components was reported. Overall, 277 (88%) of 316 contaminated preparations were infused in previous investigations. No ultimately adverse outcomes were reported. Four patients developed bloodstream infection with the same species as that recovered from the contaminated preparation (two, Staphylococcus epidermidis; two, Pseudomonas species). One case of bacteremia was due to a preexisting infection rather than infusion of contaminated bone marrow [6]. The three remaining patients did well after receiving systemic antibiotics [4, 15]. Overall, three preventable cases of bacteremias occurred among 4,762 patients.

The actual cost (not patient charges) of bacterial and fungal cultures for bone marrow or peripheral stem cell harvests at our institution is $18.41. Thus, the true cost of 1,937 cultures over the 39-month study period was $35,660.

Approximately 4,500 allogeneic and 8,000 autologous transplantsations were done in North America in 1995 [17]. Based upon our own institutional data, the extrapolated cost to the health care system was ~$755,600 for routine culture of harvests in that year. Approximately 12,000 allogeneic and 18,000 autologous transplantsations were performed worldwide in 1995 [17]. We estimate the actual cost of routine cultures of these harvests to have been $1.77 million. Routine hematopoietic progenitor cell cultures might have prevented 7.9 cases of bacteremia in North America at a cost of $95,600 per bacteremia prevented, and worldwide, 18.9 cases of bacteremia at a cost of $93,500 per bacteremia prevented.

In summary, routine culture of all hematopoietic progenitor cell harvests intended for transplantation is expensive and yields low microbial contamination rates. Positive culture results seldom influence the decision to infuse contaminated samples. Infusion of a contaminated preparation rarely results in clinically significant sequelae. Finally, in this era of cost-containment at the individual hospital level and the national level, routine culture of all harvests adds significant cost to an already expensive procedure.

Occasional cultures should still be done for quality control purposes, but we agree with Attarian et al. [13] and believe that cultures of each and every hematopoietic progenitor cell preparation need not be performed routinely. We suggest that the AABB revise its recommendation.

### References