Marrow Harvesting From Normal Donors


The experience at a single institution in harvesting marrow for allogeneic transplantation on 1,270 occasions from 1,160 normal donors is presented in detail, together with an analysis of all the donor complications. Four donors were less than 2 years old, and the youngest was 6½ months. No special difficulties were encountered with these young donors. Hospitalization time was three days or less for 99% of the procedures. Six donors had life-threatening complications; three of a cardiopulmonary and two of an infectious nature, and one cerebrovascular embolic episode. Significant operative site morbidity, usually transient neuropathies, occurred in ten procedures. Ten percent of the donations were associated with transient postoperative fever of unknown origin. Increasing donor age was associated with a reduction of the cellularity of the marrow harvest. The use of stored autologous blood permitted the avoidance of blood bank transfusion in 81% of males, 69% of females, and 50% of children. It was concluded that the procedure was associated with a very low risk of complication, but that the involvement of normal donors in such an operation justifies stringent monitoring.

Marrow Transplantation is an increasingly common therapeutic undertaking. Donors have usually been HLA-identical siblings, but improving results have encouraged expansion of the donor pool to include less than perfectly matched family members and fully matched unrelated donors. There will be a further increase in marrow transplants in the next several years, and this will result in a further intensification of the search for acceptable donors.

The decision to perform a marrow transplant involves weighing the risks and benefits to the patient against the risks to the donor. Numerous reports have presented these factors as they affect the marrow recipient, but there is almost no literature discussing the risks to the donor. In conjunction with the International Bone Marrow Transplant Registry, we have reported only the life-threatening complications of marrow aspiration for transplantation. The purpose of this article is to describe in detail all the complications that have occurred in marrow transplant donors in Seattle and to present the large experience at a single institution in collecting marrow from normal donors.

Materials and Methods

The hospital records of all allogeneic and syngeneic donors who gave marrow in Seattle between March 10, 1969, and Feb 1, 1983, were reviewed, and the complications of all separate donor donations analyzed. When a donor gave marrow on two or more occasions, each instance was considered separately for risk of complications. Only records of donors aspirated at the transplant center were analyzed, including all marrow collections at the US Public Health Service Hospital (1969 to 1973), Providence Medical Center (1973 to April 1975), and the Swedish Hospital Medical Center where all donors for patients at the Fred Hutchinson Cancer Research Center underwent aspiration (April 1975 to Feb 1, 1983). Procedures performed at other hospitals and patients aspirated for autologous transplantation were not included in this analysis.

The selection of the method of anesthesia for adult donors was decided by the donor after discussion of the choices with the anesthesiologist. General anesthesia was generally recommended for and administered to children. The marrow aspiration technique has been described. A recent modification has been a change in the type of aspiration needle. Currently, marrow is aspirated with Rosenthal marrow aspiration needles fitted with 3-in balls on the stylet (Techna-Search Labs, Bellevue, Wash). These needles have increased the efficiency and comfort of the operator. The number of nucleated marrow cells in the aspirate was calculated by subtracting the number of peripheral blood leukocytes from the total number of nucleated cells.

When experience in marrow transplantation was limited, marrow was usually aspirated from the anterior and posterior iliac crests and the sternum. With experience, the clinical impression was acquired that an adequate marrow dose could be obtained from the posterior iliac crest alone, which significantly shortened the procedure time by removing the need to turn the donor. The practice has therefore emerged of performing aspirations only from the posterior iliac crest, except in cases where a large marrow dose is considered particularly desirable. The anterior crests and sternum are aspirated when the recipient has aplastic anemia or when there is a major size disparity between donor and recipient. Intraoperative cell counts to determine the number of cells before proceeding to the anterior and sternal aspiration sites were not undertaken.

When feasible, a unit of blood was removed from the donor and stored 1 week prior to marrow donation, and this unit was reinfused during the procedure. Many marrow donors were also subsequently donors of granulocytes for prophylaxis against infection. These donors were usually excluded from donating a unit of blood prior to the aspiration procedure and received blood bank blood when necessary.
NORMAL MARROW DONORS

RESULTS

Donor Characteristics

A total of 1,270 procedures was performed on 1,160 donors. Ninety-nine donors underwent a second marrow aspiration, usually within two months of the first, and 11 donated marrow on three separate occasions. The male–female ratio was 614:546. Table 1 shows the age distribution for donors giving one, two, or three donations. Four donors were less than 2 years old, and the youngest was 6 1/2 months old. No special difficulties or complications were encountered with the very young donors.

Aspirations

Nine hundred twelve procedures (72%) were performed under general anesthesia, 328 (26%) under spinal anesthesia, and 30 (2%) under a caudal block. Table 2 shows the age distribution for donors receiving the different types of anesthesia.

One procedure was interrupted before the aspirations had started [donor for unique patient number (UPN) 561]. The posterior iliac crest only was used in 274 (22%) procedures. In 878 (69%) instances, the anterior crests were also aspirated, and in 117 (9%) instances, the sternum was aspirated as well as the anterior and posterior iliac crests. These proportions were not different in any age group, except that none of the 128 patients less than 10 years of age was aspirated from the sternum.

The median duration of the aspiration procedure was 80 minutes, with a range of 15 to 225 minutes.

Morbidity

Donors were hospitalized from one to 14 days. There was one hospitalization for 13 days and one for 14 days. For 99% of the procedures, hospitalization was three days or less, and 81% involved two days of hospitalization.

Three donors (UPNs 50, 561, 1,085) developed cardiopulmonary problems during the first donation. One donor (UPN 1,493) had a cerebrovascular accident soon after the second donation. Two donors developed bacterial infections (UPNs 1,641 and 1,900) after the first aspiration. These complications, which were sufficiently grave to be considered life-threatening, have been reported elsewhere and are described in detail below. During one second donation (UPN 893), 4 cm of the tip of an aspiration needle broke off, became embedded in the posterior iliac crest, and had to be removed surgically. Examination of the needle revealed a defect that was responsible for the break.

All patients had the expected amount of pain after the aspiration procedure. Greater than expected morbidity due to operative site trauma occurred after ten (0.8%) procedures. In six instances, this appeared to be due to hematomas at the aspiration sites creating pressure neuropathies, which were transient and resolved within three weeks. In one case, sciatic pain was reported to persist for at least 18 months. In one case, there was hip pain of uncertain cause that resolved within three weeks, and in two instances, the donors had pain associated with displaced cortical fractures of the anterior iliac crests.

Eight recipients of spinal anesthesia reported “post-spinal headaches,” and one donor was treated for this with an epidural blood patch. Nine donors were catheterized because of urinary retention. Seven (0.8%) of these had received general anesthesia, and two (0.6%) had received spinal anesthesia.

Postoperative fever greater than 38.2 °C without apparent cause was observed after 121 (10%) procedures. In 99 (10%) instances, fever occurred in donors who were aspirated under general anesthesia, compared with 20 (6%) such instances in patients receiving spinal anesthesia. In 39 (39%) of these 99 episodes, the temperature rose to 38.5 °C or greater. All of these episodes resolved without complication but antibiotics were empirically administered in three instances.

Table 1. Marrow Donors: Donation Number and Age Distribution

<table>
<thead>
<tr>
<th>Age in Years</th>
<th>One Donation</th>
<th>Two Donations</th>
<th>Three Donations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 10</td>
<td>123</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>10 to 19</td>
<td>343</td>
<td>31</td>
<td>5</td>
</tr>
<tr>
<td>20 to 59</td>
<td>681</td>
<td>62</td>
<td>6</td>
</tr>
<tr>
<td>60 and over</td>
<td>13</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>1,160</td>
<td>99</td>
<td>11</td>
</tr>
</tbody>
</table>

Characteristics of the Marrow Harvest

The volume of marrow aspirated varied from 1.9 mL/kg donor body weight to 26.9 mL/kg; the nucleated cell content ranged from 0.3 x 10^7/kg to 14.4 x 10^7/kg. The concentration of nucleated marrow cells in the marrow harvests ranged from 0.6 x 10^7/mL to 10.5 x 10^7/mL. Table 3 presents an analysis of the median values for these assays in terms of donor age and donation number. The median cell concentra-
tion for first donation marrows collected was $2.5 \times 10^7$/mL from both male and female donors, with a mean of 2.7 for males and 2.8 for females.

**Red Blood Cell Transfusion Requirements**

The transfusion requirements associated with 1,008 procedures involving 923 marrow donors, who were not also donors of granulocyte transfusions, are summarized in Table 4.

**Case Histories**

Four donors had major cardiopulmonary complications during the aspiration procedure, and two had grave infections as a consequence of the operation. These six complications were sufficiently serious to be described as life-threatening. The case histories relating to these episodes are presented here.

**UPN 50.** A 19-year-old man was aspirated under general anesthesia. While being extubated, he developed bronchospasm. The next morning he had dyspnea, and a chest x-ray revealed infiltration in the right lung, which was compatible with aspiration pneumonitis. He was treated with steroids and antibiotics and was discharged after a five-day hospitalization with a normal chest x-ray.

**UPN 561.** This 26-year-old, 65-kg woman received 10 mg morphine and 0.4 mg scopolamine intramuscularly before spinal anesthesia. This was followed in one hour by 5 mg diazepam intravenously and five minutes later by instillation of 12 mg tetra-caine hydrochloride intrathecally, followed by 5 mg diazepam intravenously. Thirty minutes later, soon after starting the marrow aspiration procedure, the donor had a cardiopulmonary arrest. The surgery was abandoned, epinephrine and dexamethasone were administered, and the donor was resuscitated with external cardiac massage. The donor recovered without sequelae, and the marrow aspiration was performed under general anesthesia without complication 24 hours later.

**UPN 1,085.** A 4-year-old girl underwent marrow aspiration from the posterior iliac crest under halothane anesthesia. Ten minutes into the procedure, after the collection of 35 mL of marrow, she developed a sinus bradycardia that evolved into ventricular tachycardia. The surgical procedure was halted and a precordial blow administered. The donor reverted to normal sinus rhythm with occasional ventricular ectopy, which disappeared following an infusion of lidocaine. Subsequent monitoring and investigations did not reveal any underlying abnormality that might have contributed to this episode. There were no sequelae.

**UPN 1,493.** A 43-year-old man with a positive family history for cerebrovascular disease was evaluated as a potential marrow donor in August 1981. He was noted to be hypertensive, with a blood pressure of 160/110 for which he was treated with metoprolol tartrate and diuretics. In September 1981, he donated marrow under general anesthesia without complication. In February 1982, he underwent a second marrow donation procedure, again under general anesthesia, without complications. His blood pressure before and during the procedure was within normal limits. Thirty-six hours later, he suddenly developed a left-sided hemiparesis. A CAT scan was consistent with a cerebral infarction in the distribution of the right middle cerebral artery. Electroencephalograms showed temporal slowing, and an echogram showed stenosis of the right carotid bifurcation. In March 1982 he underwent a carotid endarterectomy. By July 1983, he had made a complete recovery.

**UPN 1,641.** A 44-year-old man donated marrow for his brother in an uneventful procedure and was discharged from the hospital on the following day. Three days later, he developed pain, swelling, and purulent drainage from the right anterior aspiration site. He was treated empirically with dicloxacillin and, when cultures produced *Enterobacter cloacae*, with
trimethoprim-sulfamethoxazole. This therapy failed to control the infection, and he was readmitted to the hospital for incision and drainage of the infected area and for parenteral antibiotic therapy. The infection resolved and, after 11 days of hospitalization, he was discharged.

**UPN 1,900.** A 60-year-old man donated marrow under spinal anesthesia. On return to the ward, he was febrile, and *Klebsiella pneumoniae* was grown in one of four blood cultures. He was treated with antibiotics for two weeks and discharged without complication. No source for the bacteremia was identified.

**DISCUSSION**

The life-threatening complications associated with 3,290 marrow donations have been reported. In that study, which contains part of the experience reported here, the incidence of such events was 0.27%, and the authors also reported that a fatality had occurred in connection with a marrow donation. This relatively low incidence of dangerous complications does not fully describe the impact of marrow donation upon the health and comfort of the donor. There is no large body of reported experience dealing with the relationship between donor characteristics and the quality of the marrow collected.

In our study, increasing donor age appeared to be associated with reduction in the number of nucleated cells collected, but when this was examined in linear regression by the method of least squares, this reduction was not statistically significant.

Most marrow donors who also provide granulocytes for prophylactic transfusion require red cell transfusions in addition to stored autologous blood. The analysis of blood transfusion experience was therefore restricted to donors who did not give prophylactic granulocyte transfusions. The use of stored autologous blood enabled us to avoid the transfusion of blood bank blood in 81% of males, 69% of females, and 50% of children under the age of 10 years. The decision not to store autologous blood for subsequent transfusion was made on the basis of a variety of indications, including the hematocrit of the donor after the phlebotomies associated with intensive study, the state of the donor's veins, and the age and size of the donor. As a consequence, such blood was stored for 82% of male donors, 75% of female donors, and 51% of donors less than 10 years of age. A small proportion of donors required red cell transfusions from the blood bank in addition to autologous blood. The main reason for the use of extra red cell transfusions was a decrease in hematocrit out of proportion to the volume of marrow aspirated. This probably occurred because some patients had a significant amount of hemorrhage into the soft tissues around the posterior iliac crest. The proportion of donors who required blood bank-derived red cell transfusions in addition to their stored autologous blood was 1% for males, 8% for females, and 2% for children aged <10 years. For donors without stored autologous blood, there was no difference among males or females or children in the proportion of patients who required blood bank red cell transfusions. The finding that 155 donors received only a single unit of blood bank blood is cause for concern. Forty-five of these donors were less than 10 years old, but in many of the other 110 donors, these transfusions may have been avoidable. No cases of hepatitis attributable to blood transfusions were suspected, but long-term follow-up studies were not performed, although the experience of these donors after transfusion was readily accessible for 100 days. Obviously, an attempt should be made to eliminate the use of blood bank transfusions in normal individuals, and whenever practical, autologous blood should be stored from marrow donors for use during the aspiration procedure. Moreover, the removal of red cells from donors in the course of collecting samples for investigation should be stringently controlled.

It has always been anticipated that marrow donation would be associated with a risk of complications resulting from the use of general or spinal anesthesia. Three of the six life-threatening complications reported here were related to anesthesia. These occurred in relatively young healthy donors, two following general and one following spinal anesthesia. We were not able to distinguish any difference in complication rate following these two modes of anesthesia.

Multiple marrow aspirations result in major trauma to the iliac bones. Despite this fact, morbidity from damage to bone and adjacent structures was minimal, with a very low complication rate. The complications were mainly prolonged pain and symptoms of neuropathy. Infection of aspiration sites occurred in only one of 1,270 procedures.

The increase in the number of marrow transplants occurring in an increasing number of widely distributed centers presents the need for consolidating the dispersed experience with normal donors. Small centers should be encouraged to report their donor experience to the established registries to monitor the complications that occur. The information that such a process could generate, together with the more uniform records from the large centers, would permit early recognition of the risks involved and provide a body of data that is needed for the informed counselling of potential marrow donors.
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