addition of thiamine pyrophosphate, confirmed thiamine deficiency. Parental thiamine 100 mg/d was given. The next day, power of the upper limbs dramatically improved and speech became audible. Over the next 5 days, upper limbs regained full power. As$_2$O$_3$ at 5 mg/d for 28 days as maintenance was given 5 weeks later, with oral thiamine. There was no deterioration in neurology. Lower limb power continuously improved. RBC transketolase during arsenic maintenance was normal, and MRI scan demonstrated complete resolution of all previous abnormalities.

Rapidly progressive neuropathy with a dose level of 10 mg/d and cumulative dose of 280 mg As$_2$O$_3$ is unusual. Moreover, recovery of APL subjects from severe neuropathy had been slow in previous arsenic trials.\textsuperscript{1,2} The rapid improvement in our subject after thiamine administration would not signify a pure arsenic toxicity but would support a contributory role of thiamine deficiency in development of an early severe neurotoxicity during arsenic administration. We have no idea yet whether thiamine or its deficiency has any role in the more frequent but milder form of sensory neuropathy. Yet, we recommend an adequate intake of thiamine during arsenic therapy, and we suggest thiamine deficiency be considered when severe neurotoxicity during arsenic is encountered.

We would like to thank Dr Y. L. Kwong and Dr E. S. K. Ma of Queen Mary Hospital, University of Hong Kong, and Dr S. H. Ng of Tuen Mun Hospital for assistance in patient care and for advice.

To the editor:

Successful double bone marrow and renal transplantation in a patient with Fanconi anemia

In Fanconi anemia (FA), bone marrow failure (BMF) is the major cause of morbidity and mortality, whereas renal failure is less frequent with a possibly underestimated occurrence of between 25% and 30%.\textsuperscript{1,2} and has a lower impact on survival. Bone marrow transplantation (BMT) provides a survival rate of greater than 80% from sibling donors\textsuperscript{2} and of about 30% from unrelated donors.\textsuperscript{3,4}

We present a peculiar case of a patient with FA who, due to clinically prevalent BMF, underwent BMT that was followed by renal transplantation (RT) for end-stage renal disease.

This male patient presented at birth with renal failure caused by congenital single hypoplastic kidney. At the age of 3.5 years, because of thrombocytopenia (74 × 10⁹/L) and a positive dyeoxibutane test, he was diagnosed with FA. At the age of 4.5 years serum creatinine was 278 μM, white blood cells (WBCs) were 3.7 × 10⁹/L, neutrophils 1 × 10⁹/L, Hb 9 g/dL, and platelets 36 × 10⁹/L. At this stage the patient, without previous transfusions, underwent BMT (Table 1).

Two years after the graft, a further impairment of renal function required peritoneal dialysis, and 3.5 years after BMT, the patient underwent RT from a 9-year-old, B-positive, cytomegalovirus (CMV)-positive/Epstein Barr virus (EBV)-negative cadaveric donor. Donor and recipient shared one HLA allele at locus A and one at locus DRB1. Serum creatinine normalized (53 μM) 5 days after the transplant. cyclosporin A (CyA) and steroids were given as posttransplant immunosuppression. No acute rejection occurred during the follow-up.

Currently, 6 years from BMT and 2.2 years from RT, still on steroids and CyA, the patient is well, with no evidence of tumors. WBCs are 7.4 × 10⁹/L; PMN, 4.7 × 10⁹/L; Hb, 10.1 g/dL; and platelets, 188 × 10⁹/L. The hemopoiesis (short tandem repeat polymorphism analysis on peripheral blood) is entirely of donor origin. Serum creatinine is 78 μM.

To the best of our knowledge, this is the first FA patient who underwent a double sequential BMT and RT.

Although double BMT and RT have already been performed,\textsuperscript{5,8} in the context of FA, this experience is peculiar. In fact, in FA patients who have a cancer “proneess” per se, BMT constitutes an additional risk factor for tumors because of the irradiation and alkylating agents used in the conditioning regimen, chronic graft-versus-host disease (cGVHD) occurrence, and posttransplant immunosuppression.\textsuperscript{2,9,10} RT represents another risk factor because of the immunosuppression. Our patient has a high risk of late cancers. In fact, apart from GVHD, he has all the other risk factors, mainly those related to the high immunosuppression load that was required by the 2 sequential transplants from 2 different donors. The choice of an EBV-negative renal donor aimed to diminish the cancer risks by reducing the chances of primary EBV infection which, in turn, is the major risk factor for posttransplant lymphoproliferative disorders.\textsuperscript{11}

No tumors have occurred thus far in our patient during his 6-year follow-up. However, since in FA patients malignancies appear at a mean of 8.2 years after BMT,\textsuperscript{10} a careful lifetime cancer monitoring looks mandatory.

This case outlines the relevance of renal malformations on the outcome of the FA patients. In addition, it shows that sequential BMT

Table 1. BMT characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donor</td>
<td>HLA identical brother</td>
</tr>
<tr>
<td>ABO match</td>
<td>Donor B pos, Rec O pos</td>
</tr>
<tr>
<td>Conditioning regimen</td>
<td>Cy 20 mg/kg recipient body weight + TAI 500 cGy</td>
</tr>
<tr>
<td>Cell infused</td>
<td>19.8 × 10⁹/kg</td>
</tr>
<tr>
<td>GVHD prophylaxis</td>
<td>CyA 3 mg/kg. Then reduced to maintain serum through levels between 50-100 ng/mL for 15 months</td>
</tr>
<tr>
<td>Engraftment</td>
<td>PMN (&gt;0.5 × 10⁹/L) day + 5, Plt (&gt;50 × 10⁹/L for 3 consecutive days) day + 35</td>
</tr>
<tr>
<td>Toxicity</td>
<td>Grade 1 mucositis</td>
</tr>
<tr>
<td>GVHD</td>
<td>No</td>
</tr>
</tbody>
</table>

References
References


To the editor:

Cytomegalovirus infections in cancer patients receiving granulocyte transfusions

Because of the high risk of transfusion-transmitted cytomegalovirus (CMV) infection associated with the use of granulocyte concentrates, it is common blood bank practice to provide only CMV-seronegative granulocytes to patients who are CMV seronegative.1 Recently, Narvics et al challenged this practice.2 In their case series of 100 cancer patients who received CMV unscreened granulocyte transfusions, they report that only 4% developed CMV infection and that all 4 patients were CMV seropositive prior to the granulocyte transfusions. Thus, they suggested that screening granulocyte donors for the presence of CMV infection is not needed.

Several problems with this conclusion are evident. The primary CMV-related concern with unscreened granulocyte transfusions is for transfusion-transmitted CMV infection (TT-CMV) in the CMV seronegative recipient, yet no details regarding the CMV serostatus of the granulocyte recipients were presented. The prevalence of CMV seropositivity in their cancer patients is likely to be even higher than that of their donor pool (70%-80%), as cancer patients are commonly multiply transfused. Thus, CMV-seronegative granulocyte recipients likely represent a minority (< 20%) of patients in the cohort. Second, it is unclear whether CMV infection or CMV disease (such as pneumonitis) is being reported. There is also no information provided whether prospective monitoring for primary CMV infection was performed in this cohort of mostly chemotherapy recipients. Thus, the true incidence of CMV infection cannot be obtained from these figures. What is at issue in this context is the true rate of CMV infection associated with granulocyte transfusions. Thus an analysis that focused upon CMV-negative recipients and included prospective monitoring for CMV infection would have been more informative. Fortunately, such studies have been performed in the setting of stem cell transplantation (SCT),3,4 and they demonstrated a very high rate of primary CMV infection when granulocytes from CMV-seropositive donors are administered to CMV-seronegative recipients. These studies are the basis for present blood center recommendations.5

The authors also failed to distinguish important differences in patient populations with regard to risks associated with CMV infection; the risk for progression from CMV infection to CMV disease is in parallel with the degree of immunosuppression. Certainly, SC transplant recipients are at the highest risk for CMV disease, but recently published data from the authors’ own institution suggest that CMV disease is “an emerging problem” in adults with leukemia receiving conventional chemotherapy as well.6(p391) In that report, immunosuppressive regimens containing fludarabine, steroids, cyclophosphamide, or, interestingly, granulocyte transfusions from CMV-unscreened donors were implicated.7 Current guidelines for the use of “CMV-safe” blood products include the use of either CMV-seronegative or leukocyte-reduced cellular blood products for CMV-seronegative patients at high risk for CMV-related morbidity and mortality. As such, the use of granulocyte transfusions from CMV-positive donors (products that are obviously leukocyte-rich and, thus, more likely to transmit virus) for CMV-negative SC transplant recipients is untenable. Given the poor outcome associated with CMV seropositivity in patients who undergo SCT8 those who are candidates for SCT should also receive CMV-negative products. “CMV-safe” components should be strongly considered for CMV-seronegative patients with significant chemotherapy-induced T-cell immunodeficiency (such as those receiving fludarabine or other T-cell suppressing therapies) given the data presented above.

The argument that the requirement for CMV-seronegative donors diminishes the potential donor pool has also been raised.9 In our experience of 76 recipients of granulocytes from related or unrelated donors,10 the CMV-seronegative rate was approximately 40%. We did not encounter problems in recruiting CMV-seronegative donors for these patients. While it is true that communities with a high CMV-seroprevalence rate have a smaller seronegative donor pool, it should also be pointed out that the demand for such products may be less.

Finally, the authors indicate that granulocyte colony-stimulating factor (G-CSF)–stimulated granulocyte transfusions are “clearly . . . effective.”11(p199) But this point remains controversial. In that uncontrolled case series, 47% of patients demonstrated a favorable response to granulocyte transfusions, though response was dependent on underlying infection type.10 The interpretation of uncontrolled series is difficult,
Successful double bone marrow and renal transplantation in a patient with Fanconi anemia

Maurizio Miano, Fabrizio Ginevri, Arcangelo Nocera, Sandro Dallorso, Iris Fontana, Francesco Perfumo, Giorgio Dini and Carlo Dufour