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## Colostrum and severe gut GVHD

Treatment of severe gut graft-versus-host disease (GVHD) after allogeneic hematopoietic stem cell transplantation (HSCT) remains problematic even though there have been many advances in immunosuppressive therapy. Recently we have treated nine patients who suffered from severe gut GVHD: large volumes of watery and bloody stool, paralytic ileus and severe abdominal pain. We gave them colostrum for the treatment of severe gut GVHD and six out of nine showed clinical improvement. A dose of colostrum was set at 20 ml daily and given for 5 consecutive days. Colostrum was obtained from random donors. Clinical data of these nine patients are summarized in Table 1. Two of them (UPN 151 and 157) were not evaluated because of poor compliance. Rectal biopsies were performed in six cases (UPN 147, 151, 159, 164, 166 and 173) and histological findings were compatible with enteric GVHD in all cases. Thrombotic microangiopathy combined with GVHD was proven in UPN 151 and also CMV infection was confirmed by *in situ* hybridization in UPN 159. One typical case (UPN 147) is presented.

This patient was diagnosed with B-precursor ALL (CD10 negative) when she was 3 months old and transplanted from an unrelated HLA-matched donor in second complete remission when she was 1 year old. Conditioning consisted of TBI (12 Gy), etoposide (60 mg/kg) and cyclophosphamide (120 mg/kg). FK506 and methylprednisolone (mPSL) were used for GVHD prophylaxis. Ganciclovir was administered from days −8 to −1 because she was CMV-seropositive. Engraftment was prompt. Neutrophils rose to $0.5 \times 10^9$/l on day 14. Platelets rose to $20 \times 10^9$/l on day 17. Reticulocytes reached 1% on day 57. Complete chimerism was confirmed by VNTR on day 47.

She developed grade III acute GVHD. A rash appeared on day 15 followed by bloody diarrhea complicated by paralytic ileus. The peak value of TB was 4.4 mg/dl on day 34. A rectal biopsy was performed and histological findings were compatible with acute GVHD. CMV infection was not detected by *in situ* hybridization. Symptoms of gut GVHD persisted in spite of high-dose mPSL (pulse therapy), methotrexate and anti-thymocyte globulin (ATG). We therefore decided to use colostrum and low-dose etoposide (VP16) as a systemic immunosuppressive agent. Colostrum obtained from random donors was administered orally at 20 ml/day for 5 consecutive days. Her gut GVHD disappeared soon after the colostrum therapy as shown in Figure 1. In addition, the liver and skin GVHD improved.

It is well known that breast feeding plays an important role for babies in preventing infection and in developing the digestive system. Human milk, especially colostrum, contains many materials such as cytokines (TGF$\beta$, EGF, etc) and sIgA.[1] The present trial is still preliminary and the efficacy of colostrum therapy for gut GVHD should be confirmed in more cases. In the same setting oral immunoglobulin may be an alternative choice.[2] However, in our

**Table 1** Summary of nine cases who underwent colostrum therapy for severe gut GVHD

| *UPN* | *Age (years)* | *Disease* | *Preconditioning regimen* | *SCT* | *GVHD prophylaxis* | *aGVHD grade* | *Prior therapy of GVHD* | *Immunosuppressive agent administered with colostrum* | *Stage of gut GVHD* | | *Effectiveness of colostrum* |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | *pre-colostrum* | *post-colostrum* | |
| 147 | 1 | ALL | TBI+VP16+Cy | UBMT | FK506+mPSL | III | Pulse, MTX, ATG, Pred | VP16 | 4 | 0–1 | + |
| 151[a] | 1 | JCML | TBI+thioTEPA+LPAM | RBMT | CSA+mPSL | III | Pulse, Pred, MTX | VP16 | 4 | 4 | NE |
| 157[a] | 16 | ALL | TBI+CA+LPAM | UBMT | FK506+mPSL | III | Pulse, mPSL | — | 4 | 4 | NE |
| 159[a] | 14 | MDS | TBI+thioTEPA+LPAM | UBMT | FK506+mPSL | III | Pulse, Pred | MTX | 4 | 3 | + |
| 162 | 4 | ALL | TBI+CA+LPAM | CD34PBSCT | FK506 | III | Pulse, Pred | MTX | 4 | 0–1 | + |
| 164 | 13 | AML | TBI+thioTEPA+LPAM | UBMT | FK506+mPSL | III | Pulse, mPSL | MTX | 4 | 4 | – |
| 166 | 13 | AML | TBI+LPAM | UBMT | FK506+mPSL | III | Pulse, Pred | MTX | 3 | 2 | + |
| 167 | 1 | JCML | TBI+thioTEPA+LPAM | UBMT | FK506+mPSL | III | Pulse, Pred, MTX | — | 3 | 1 | + |
| 173 | 6 | ALL | TBI+thioTEPA+LPAM | UBMT | FK506+mPSL | III | Pulse, Pred | — | 3 | 1 | + |

UBMT = HAL-matched BMT from unrelated donor; RBMT = HLA-matched BMT from related donor; CD34PBSCT = PBSCT using CD34-positive cells from HLA haploidentical father; Pulse = high-dose methylprednisolone therapy (0.5 g/m$^2$/day for 3 consecutive days); NE = not evaluable.

[a]UPN151 and UPN157, Compliance of colostrum was poor because of nausea and vomiting. UPN151, histological finding of rectum was aGVHD accompanied with thrombotic microangiopathy. UPN159, histological finding of rectum was compatible with aGVHD, and CMV infection was confirmed by *in situ* hybridization.

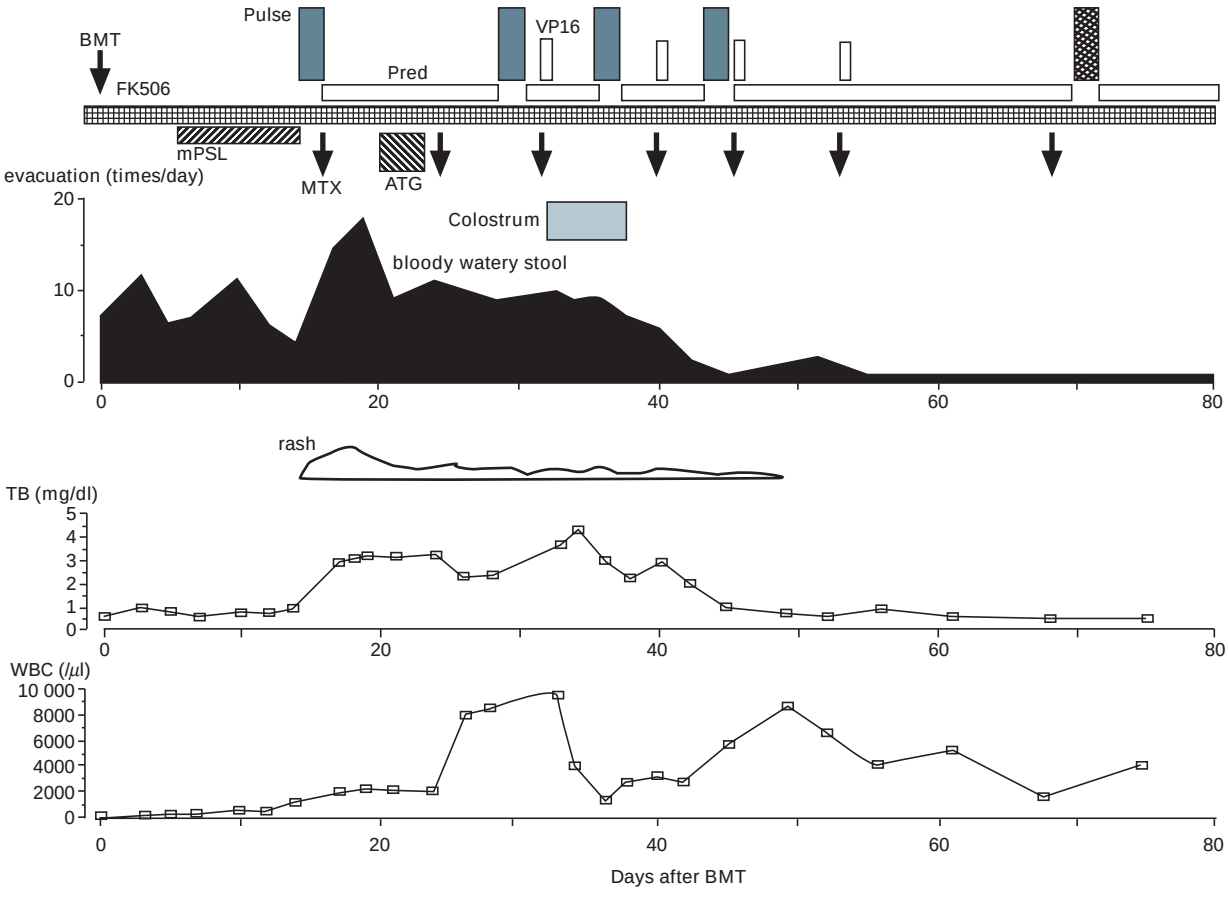


**Figure 1** Clinical course of UPN 147.

limited experience colostrum seems to be superior. On the basis of these findings we suggest a potential benefit of colostrum for severe gut GVHD.

M Inoue
T Okamura
A Sawada
K Kawa

*Department of Pediatrics, Osaka Medical Center and Research Institute for Maternal and Child Health, 840 Murodo-cho, Izumu, Osaka 594–1101, Japan*

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## Myasthenia gravis post allogeneic bone marrow transplantation revisited

We feel that it is appropriate to extend our previous report, 'Myasthenia gravis in association with allogeneic bone marrow transplant',[1] in which we describe a 15-year-old female with AML who underwent BMT in 1985. As we noted, her clinical course was complicated by the development of chronic graft-versus-host disease as well as generalized myasthenia gravis treated successfully with corticosteroids, pyridostigmine and thymectomy.

In March 1997, 37 months after the initial diagnosis of myasthenia gravis, the patient presented to a peripheral hospital with progressive dysphagia, dysphonia, ptosis and shoulder and pelvic girdle weakness. These symptoms occurred while tapering prednisone to 5 mg/day. The patient did not improve with prednisone 40 mg/day and reinstitution of pyridostigmine. Despite hospitalization and