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LETTER

Allogeneic mesenchymal stem cell transplantation in seven patients with refractory inflammatory bowel disease

We refer to two articles by Duijvestein *et al* and Ciccocioppo *et al*[1 2] in which the authors suggest that administration of autologous bone marrow-derived mesenchymal stem cells (MSCs) is safe and feasible in the treatment of refractory Crohn's disease (CD). However, to date there are few data about allogeneic MSC transplantation (MSCT) for patients with inflammatory bowel disease (IBD).

We wish to report our experience of allogeneic MSCT in seven patients with IBD.

Infused allogeneic MSCs were obtained from the bone marrow or umbilical cord. Bone marrow was aspirated from healthy relatives of three patients. Umbilical cords were obtained from local maternity hospitals after normal deliveries. The isolated MSCs were given by intravenous infusions as 1×10^6 cells per kilogram of body weight.

Four of the included seven patients had CD and three had ulcerative colitis (UC). Table 1 lists the patient demographics and drug regimens received at the time of MSCT. Mean age was 29 years (range 24–41). Mean disease duration was 60.4 months (range 6–120). After MSCT, all patients had a minimum follow-up of 6 months, with a mean follow-up of 19 months (range 6–32). After MSCT, all patients continued their treatment with steroids and/or immunosuppressants as with the therapies before the transplantation. Three patients received a tapering dose of steroids and dosages at the last follow-up ranged from 10 to 12.5 mg. Two patients also tapered the dose of steroids after MSCT, but needed to go back to intravenous steroids because of a relapse. One patient weaned himself off steroids more than 2 years before transplantation, recognising the dangers of continued steroid medication, and never got back to steroids again after MSCT.

Diarrhoea frequency and abdominal pain/cramps gradually improved in all the seven patients, accompanied by a significant reduction in Crohn's Disease Activity Index scores in CD patients and Clinical Activity Index scores in UC patients. At the 3-month visit, five patients achieved remission and maintenance of remission lasted for more than 24 months in two patients. Two patients had a relapse at 6 and 7 months after MSCT. A significant reduction in fistula size and drainage was found in one patient. Endoscopic improvement was observed by a decrease in Endoscopic Index of Severity score from 19.1 to 4.2 points at 4 months and from 14.5 to 3 points at 3 months in two CD patients, as well as a decrease in Endoscopic Activity Index from 7 to 5 at 5 months in a UC patient (figure 1). Rough mucosa, polypoid lesions and ulcers significantly decreased after MSC infusion. The histological features of biopsy specimens changed apparently in these three patients. After MSCT, the extent of the inflamed area and the dense lymphocytic infiltration in the mucosa propria was reduced.

One patient felt hot in the face for no more than 6 hours after MSC infusion. Another patient described insomnia on the first night after infusion. A third patient experienced 2 days of low fever, where the frequency of diarrhoea increased from 6–10 to 12–13 times per day. These symptoms restored quickly without any medical intervention. No other adverse events were observed during or immediately after infusions of MSCs in any of the seven patients with IBD.

In summary, our data show that allogeneic MSCT is safe and may contribute to clinical improvement in patients with refractory CD and UC, although the mechanisms of action underlying the clinical effects of MSCs still need to be clarified. More clinical trials and follow-up periods are warranted to validate our finding.

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Competing interests None.

Table 1 Characteristics of the seven enrolled patients before and after MSCT

	Patient number						
	1	2	3	4	5	6	7
Age	33	27	26	27	41	24	25
Sex	M	M	F	M	F	M	F
Diagnosis	CD	CD	CD	CD	UC	UC	UC
Disease duration (m)	40	6	120	34	62	113	48
Extent of disease	Ileum and colon	Terminal ileum	Ileum and colon	colon	Pancolitis	Pancolitis	Pancolitis
Previous treatment	CS 5-ASA CYC Antibiotics	CS MTX SASP Etanercept	CS SASP CYC	CS SASP Infliximab Antibiotics	CS SASP MMF CYC 5-ASA	CS SASP 5-ASA	CS SASP 5-ASA
Therapies used within 3 months before MSCT	CS CYC Antibiotics	CS SASP	CS SASP	CS CYC	CS MMF CYC	5-ASA	CS SASP
Baseline CDAI/CAI score	223	335	295	378	8	10	9
Baseline EIS/EAI score	18.7	19.1	14.5	20.3	7	9	8
Concomitant medication	CS CYC	CS SASP	CS SASP	CS CYC	CS 5-ASA	5-ASA	CS SASP
CDAI/CAI score at 3 months after MSCT	187	140	126	284	2	5	5
EIS/EAI score after MSCT	NA	4.2 (4 months)	3 (3 months)	NA	5 (5 months)	9	NA
Adverse events	NA	NA	Face hot	NA	Insomnia	Low fever	NA

5-ASA, 5-aminosalicylic acid; CAI, Clinical Activity Index; CD, Crohn's disease; CDAI, Crohn's Disease Activity Index; CS, corticosteroids; CYC, cyclosporine; EAI, Endoscopic Activity Index; EIS, Endoscopic Index of Severity; m, month; MMF, mycophenolate mofetil; MSCT, mesenchymal stem cell transplantation; MTX, methotrexate; NA, not available; SASP, sulfasalazine; UC, ulcerative colitis.

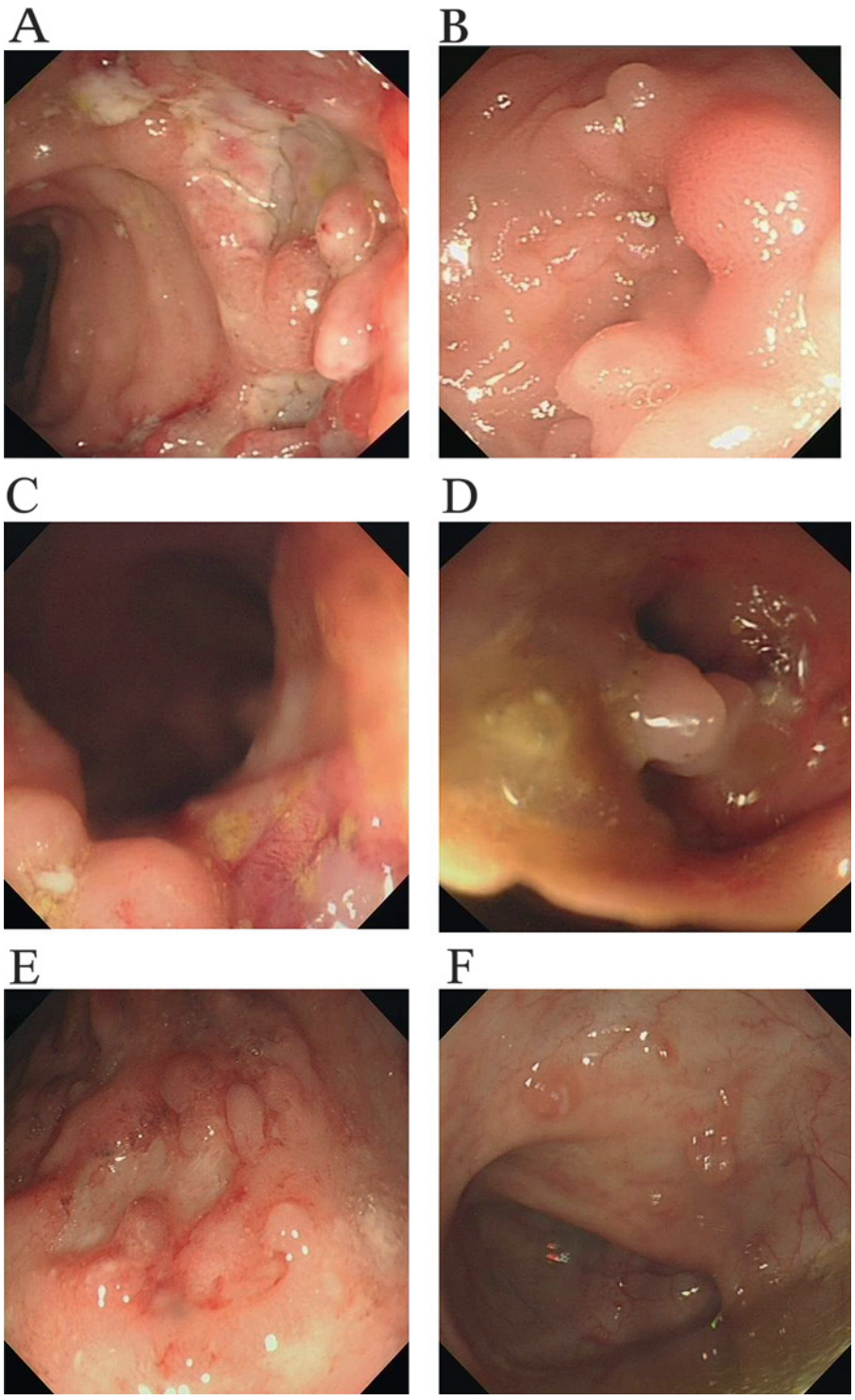

Figure 1 Endoscopic healing was found in three patients after mesenchymal stem cell transplantation (MSCT). (A, B) From patient 2 at 0 and 4 months after infusion, respectively. (C, D) From patient 3 at 0 and 3 months after infusion, respectively. (E, F) From patient 5 at 0 and 5 months after infusion, respectively (0: at the time of MSCT).

Patient consent Obtained.

Ethics approval This study was conducted with the approval of the Affiliated Drum Tower Hospital of Nanjing University Medical School.

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