Simultaneous occurrence of *Clostridium difficile* and *Cytomegalovirus colitis* in a recipient of autologous stem cell transplantation

We report the case of a 59-year old male who underwent autologous transplantation for lymphoma and developed CMV enteritis which was masked by *Clostridium difficile* colitis. Although the incidence of CMV enteritis in the autologous setting is low, simultaneous occurrence of these two diseases can cause significant diagnostic problems.

Sir,

Diarrhea is a major cause of morbidity among recipients of autologous bone marrow transplantation (BMT). The cause is often multifactorial. The use of antineoplastic agents, antibiotics, radiotherapy, alterations in diet and various pathogens have all been implicated. Here we describe a case in a recipient of autologous transplantation who developed life-threatening diarrhea from two different pathogens. A 59-year old male with anaplastic large cell lymphoma underwent an autologous stem cell transplant with BEAM conditioning in first partial remission. After experiencing a stormy post-transplant period with ICU admission due to sepsis and pneumonia he returned to the ward on day +20. (neutrophil engraftment occurred on day +13). Subsequently he developed profuse diarrhea. Abdominal X-ray and CT scan revealed gross bowel dilatation with thickening of the wall of the descending colon wall and thickening of several loops of the small bowel. Sigmoidoscopy revealed abnormal mucosa covered by pseudomembranes: no samples were taken for histologic examination. *Clostridium difficile* toxin was isolated and the patient was treated with oral metronidazole and vancomycin for 13 days. As there was no improvement he underwent a second sigmoidoscopy and a rectal biopsy. This demonstrated the typical viral inclusions consistent with CMV colitis (Figure 1). At the same time whole blood CMV PCR testing was found to be positive. He commenced a two-week course of ganciclovir that resulted in resolution of his diarrhea and conversion to CMV PCR negativity. *Clostridium difficile* is a major cause of nosocomial diarrhea. It accounts for almost all cases of pseudomembranous colitis and up to 20% of antibiotic-associated diarrhea. The severity and the prevalence of the infection in immunocompromised patients and especially in those who undergo BMT has not been fully evaluated. In a retrospective study by Bilgrami *et al*.[1] in 200 autologous transplant recipients the incidence

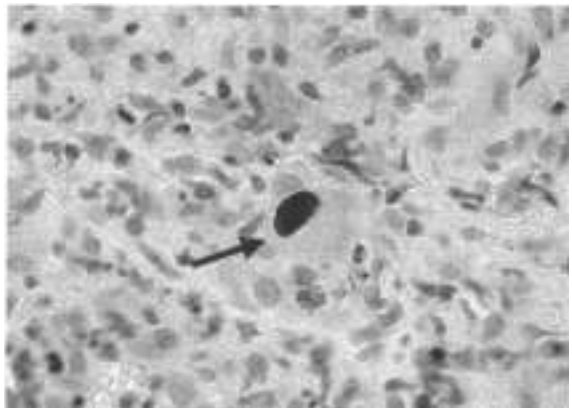

Figure 1. Immunostaining of sections from a gut biopsy: Cytomegalovirus intranuclear inclusion body stained with CCH2 monoclonal antibody (DAKO Limited, UK). Giemsa counterstain x600 (see arrow).

was 7%, with 14 patients experiencing 15 episodes at a median of 33 days after stem cell infusion. All patients responded to standard treatment and no fatalities were reported due to *Clostridium difficile*. CMV infection and disease remains a major problem following allogeneic BMT. Despite a similar incidence of infection, the incidence of CMV disease is extremely low in recipients of autologous transplantation. In a study by Wingard *et al.*[2] the investigators reviewed the occurrence of CMV infection in 143 recipients of autologous transplants. Evidence of CMV infection was detected in 45% of patients but only 2% developed disease (pneumonitis) and died. CMV enteritis is a well recognized complication in immunocompromised patients.[3-7] To our knowledge no documented cases have been previously reported in recipients of autologous transplantation. Another unusual feature of our case is the simultaneous occurrence of two pathogens with similar clinical manifestations creating diagnostic problems. In conclusion diarrhea is a common event in patients having received an autologous transplant. Despite the fact that many other causes are far more common, CMV colitis should be considered in the differential diagnosis. Concomitant infection with other pathogens such as *Clostridium difficile* may mask the diagnosis and we recommend that patients not responding to initial treatment should undergo sigmoidoscopy and biopsy.

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Key words

Clostridium difficile, CMV colitis, autologous marrow transplantation.

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Expression of CD34 by megakaryocytes in myelodysplastic syndromes

We report that increased numbers of megakaryocytes in bone marrow biopsies from patients with myelodysplastic syndromes express the CD34 antigen. A significant correlation was observed between CD34 positivity on megakaryocytes and a low platelet count, as well as the occurrence of cytogenetic abnormalities.

Sir,

The CD34 antigen is expressed by hematopoietic progenitors, endothelial cells and bone marrow (BM) stromal precursors.[1] In myelodysplastic syndromes (MDS) the number of CD34$^+$ blasts varies widely, exceeding in most cases the normal threshold of 1%,[2] and their number has been associated with an unfavorable clinical outcome.[2] Studying BM biopsies we noticed that in MDS, CD34 positive cells included megakaryocytes (Mks); this phenomenon was

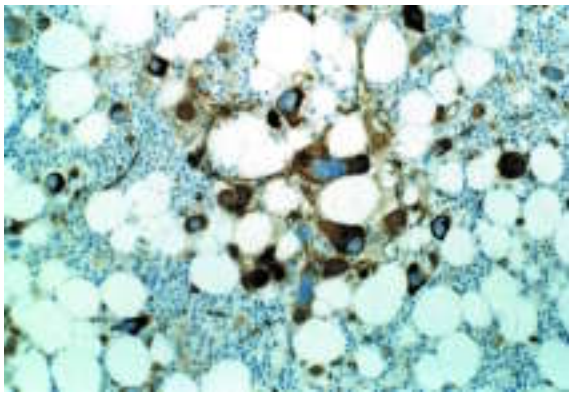

Figure 1. Bone marrow biopsy in a case of MDS, stained for CD34: the numerous dysplastic megakaryocytes, including several micro-megakaryocytes, are strongly CD34 positive. Note that only a few scattered CD34$^+$ small blasts are present in the biopsy.

analyzed in detail in 57 BM biopsies obtained from 22 patients with MDS (diagnosed and classified according to FAB criteria)[3] (Table 1) and compared with biopsies from age-matched patients without hematologic disorders (19 cases) and from patients with idiopathic thrombocytopenic purpura (ITP)(9 cases). In normal marrows and in the ITP patients rare mature Mks were found to express CD34, but only in 1

Table 1. Clinical and cytogenetic features, and bone marrow findings in patients with myelodysplastic syndrome.

Pts	Gender/ age (yrs)	Diagnosis at onset (FAB)*	Plts (10^9/L)°	Cytogenetic characteristics	BM biopsy: CD34$^+$ small immature cells (%)	BM biopsy: CD34$^+$ Mks on the total no. of Mks (%)
1#	F/65	RA	56	+8	15	10
2#	M/62	RA	285	Normal	70	3
3#	M/60	RAEB-T	91	Normal	4	60
4#	F/55	RAEB-T	55	t(14;14)	30	5
5#	M/65	RAEB	88	nd	1	0
6#	F/49	RAEB-T	24	-5	0	0
7	M/48	RAEB-T	38	Normal	15	95
8#	F/71	RA	96	nd	1	0
9	M/72	RAEB-T	215	nd	15	8
10#	M/53	RA	179	nd	0	0
11	M/76	RAEB-T	28	4p+/der(12)/mar	10	25
12	F/89	RAEB-T	23	Complex rearrangements	4	30
13	F/73	RA	120	+8	25	60
14	F/70	RA	76	Normal	0	0
15	F/80	RA	140	5q-	25	15
16	F/85	RARS	242	Normal	0	2
17#	M/31	RAEB-T	13	t(5;9)	10	10
18	M/76	RAEB-T	71	nd	15	10
19	M/75	RARS	6	der(5)/-7/12p-/ -19/miscellaneous defects	1	10
20	F/75	RA	301	Normal	0	0
21	F/69	RA	na	nd	0	2
22#	M/42	RAEB	16	Normal	0	0

*#patients with multiple biopsies; *RA: refractory anemia, RARS: refractory anemia with ringed sideroblasts, RAEB: refractory anemia with excess of blasts, RAEB-T: RAEB in trasformation; °values at the time of first bone marrow biopsy; Pts: patients; Plts: platelets; nd: not determined.*