

Ken Murata
 Yasuaki Yamada
 Shimeru Kamihira
 Naoki Sadamori
 Michito Ichimaru
 Masao Tomonaga

A Case of Adult T Cell Leukemia Complicated by Monoclonal Gammopathy in the Course of Chemotherapy

Adult T cell leukemia (ATL) [1] patients display several peculiar clinical features including skin rash, hypercalcemia and rarely monoclonal gammopathy [2]. We recently encountered a patient with ATL who developed monoclonal gammopathy in the course of chemotherapy. We discuss the possible causes of monoclonal gammopathy in this patient.

The patient was a 58-year-old male who was admitted to our clinic with lymphadenopathy in May 1988. Clinical and hematologic findings on admission are shown in table 1. Electrophoretic analysis of serum protein did not reveal an M component. Chest X-ray showed bilateral pulmonary infiltrates, and transbronchial lung biopsy was therefore performed, which identified *Pneumocystis carinii* organisms. The diagnosis of *Pneumocystis carinii* pneumonia was made, and he was treated with pentamidine isethionate and sulfamethoxazole trimethoprim. Combination chemotherapy using vincristine, cyclophosphamide and adriamycin for ATL was also started (fig. 1).

Although chemotherapy was continued, his pneumonia resolved completely. ATL cell count decreased gradually, and a partial remission was obtained. After several days of intramuscular injection of α -interferon (α -IFN) for consolidation chemotherapy, skin eruption and fever developed. Herpes zoster was diagnosed, and he was treated with acyclovir, resulting in improvement. Serum electrophoresis showed an abnormal peak in the gamma globulin area. The peak gradually increased as shown in figure 1, and IgG-kappa monoclonal immunoglobulin was detected by immunoelectrophoresis (IgG 3,362 mg/dl; IgA 180.0 mg/dl; IgM 271.5 mg/dl).

Table 1. Clinical and hematologic findings

WBC, $\times 10^9/l$	153	LDH, mU/ml	3,861
ATL cells, %	77	Ca, mg/dl	10.5
Hb, g/dl	17.7	IgG, mg/dl	765
Platelets, $\times 10^9/l$	315	IgA, mg/dl	168.1
Lymphadenopathy	+	IgM, mg/dl	198.1
Hepatomegaly	+	Surface markers, %	CD3 51.4
Splenomegaly	-		CD4 97.6
Skin lesions	+		CD8 0.4

Since this patient had a complicated presentation with *Pneumocystis carinii* pneumonia on admission, his prognosis was thought to be quite poor. However, pentamidine isethionate and sulfamethoxazole trimethoprim had a remarkable effect on the pneumonia in spite of simultaneous initiation of chemotherapy for ATL, and a partial remission was obtained. He developed herpes zoster infection after α -IFN therapy, and M protein was detected shortly after.

Monoclonal gammopathy is rarely associated with ATL. It has been reported that monoclonal gammopathy occurs in ATL as a result of the functional activity of ATL cells [2]. Since ATL cells constitutively express interleukin-2 (IL-2) receptor and show activated mature helper/inducer T cell phenotype, it seems likely that they secrete various lymphokines, similarly to normal activated T lymphocytes. It has been demonstrated that fresh ATL cells produce lymphokines, such as IL-1, parathyroid hormone-related protein, transforming growth factor- β , and B cell

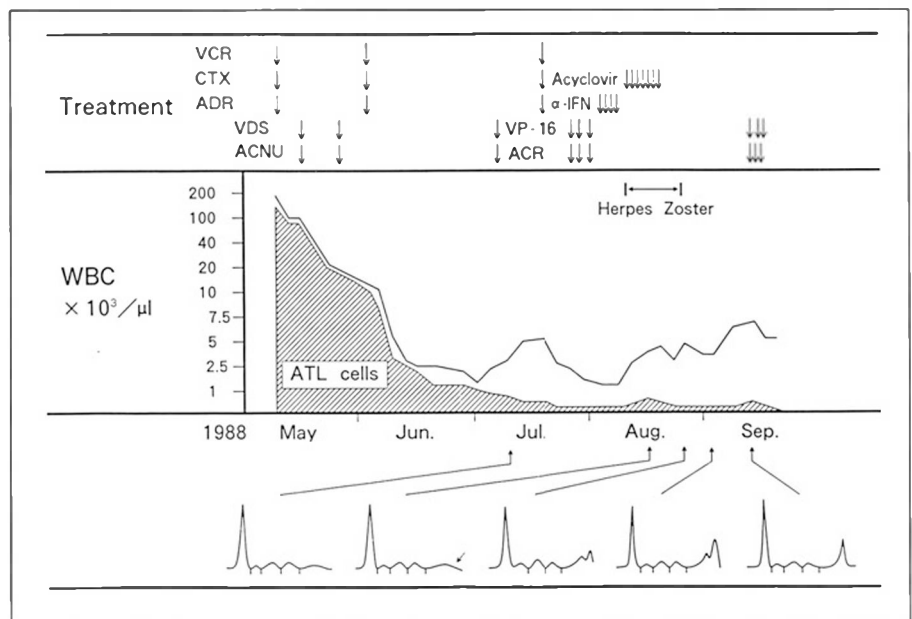


Fig. 1. Clinical course, treatment regimen and cellulose-acetate membrane electrophoresis. An abnormal peak detected for the first time in mid-August, 1988 gradually increased. VCR = Vincristine; CTX = cyclophosphamide; ADR = adriamycin.

differentiation factor (BCDF) in vitro [3–6]. These findings suggest that ATL cells also produce lymphokines in vivo, which may complicate the clinical features of ATL.

Recent studies have revealed that three lymphokines, IL-4, IL-5 and IL-6, are involved in the activation and differentiation of B cells [7–9]. Since it has been shown that ATL cells secrete BCDF, the rare occurrence of mono-

clonal gammopathy in ATL patients may be the result of continuous stimulation of B cells by BCDF secreted from ATL cells [6], although in this case we were not able to examine lymphokine production. To our knowledge, this is the first paper to report the development of monoclonal gammopathy in an ATL patient during the course of chemotherapy.

References

- 1 Uchiyama T, Yodoi J, Sagawa K, Takatsuki K, Uchino H: Adult T-cell leukemia: Clinical and hematologic features of 16 cases. *Blood* 1977; 50:481–492.
- 2 Kamihira S, Taguchi H, Kinoshita K, Ichimaru M: Monoclonal gammopathy in adult T-cell leukemia/lymphoma: A report of three cases. *Jpn J Clin Oncol* 1984;14:699–704.
- 3 Wano Y, Hattori T, Matsuoka M, Takatsuki K, Chua AO, Gubler U, Greene WC: Interleukin 1 gene expression in adult T cell leukemia. *J Clin Invest* 1987;80:911–916.
- 4 Watanabe T, Yamaguchi K, Takatsuki K, Osame M, Yoshida M: Constitutive expression of parathyroid hormone-related protein gene in human T cell leukemia virus type 1 (HTLV-1) carriers and adult T cell leukemia patients that can be trans-activated by HTLV-1 tax gene. *J Exp Med* 1990;172:759–765.
- 5 Niitsu Y, Urushizaki Y, Koshida Y, Terui K, Mahara K, Kohgo Y, Urushizaki I: Expression of TGF-beta gene in adult T cell leukemia. *Blood* 1988;71:263–266.
- 6 Yamada Y, Ichimaru M, Shiku H: Adult T cell leukemia cells are of CD4⁺ CDw29⁺ T cell origin and secrete a B cell differentiation factor. *Br J Haematol* 1989;72:370–377.
- 7 Rabin EM, Ohara J, Paul WE: B-cell stimulatory factor 1 activates resting B cells. *Proc Natl Acad Sci USA* 1985;82:2935–2939.
- 8 Kinashi T, Harada N, Severinson E, Tanabe T, Sideras P, Konishi M, Azuma C, Tominaga A, Bergstedt-Lindqvist S, Takahashi M, Matsuda F, Yaoita Y, Takatsu K, Honjo T: Cloning of complementary DNA encoding T-cell replacing factor and identity with B-cell growth factor II. *Nature* 1986;324:70–73.
- 9 Hirano T, Taga T, Nakano N, Yasukawa K, Kashiwamura S, Shimizu K, Nakajima K, Pyun KH, Kishimoto T: Purification to homogeneity and characterization of human B-cell differentiation factor (BCDF or BSFP-2). *Proc Natl Acad Sci USA* 1985;82:5490–5494.