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An Effective Therapy by Natural-Interferon-Alfa in a Chemotherapy-resistant Macroglobulinemic Patient

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An effective therapy by natural-interferon-alfa (n-IFN-α) was observed in a previously chemotherapy-resistant 70-year-old female patient with primary macroglobulinemia with IgM-M-protein. Daily injections of 3 megaunits of n-IFM-α responded markedly on clinical and hematological abnormalities. This remarkable improvement was also observed on the including decreased IgM levels from 4,120 mg/dl to 76 mg/dl, disappearance of M-protein, increased background serum IgG and IgA levels, and improvements of anemia and leukopenia.

Key Words

Interferon (IFN),
Natural-Interferon-Alfa (n-IFN-α),
Macroglobulinemia,
Immunoglobulin M monoclonal protein (IgM-Mp),
Hematological improvements.

INTRODUCTION

Among various strategies for hematological malignancies, myeloma and primary macroglobulinemia have been considered to be disorders with regimens of rather conservative "non-total-cell-kill type". Alkylating agents have been major drugs with various combination of other chemotherapeutic drugs and modified schedules.

Interferon (IFN) is currently widely available for routine clinical use (1-8), and IFN's unique reactions sometimes are of great help to induction or maintenance for myeloma patients. Because of lack of literature of IFN in the treatment of macroglobulinemia, we herewith report an effective case with primary macroglobulinemia with a daily intramuscular injection of natural-IFN-α 3 mega units.

CASE REPORT

S. Iwa., 70 y.o. female, started to notice an uncomfortable dysesthesia around her fingers and toes at the age of 64. Three years later at the age of 67, she was found to have a splenomegaly on an occasion of episodic flu symptoms. However, further examinations were not performed due to her refusal. Her past medical history disclosed only an operation of acute appendicitis. Her family history was non-contributory. At the age of 69, five years after the onset, her fingers and toes were unable to move adequately because of advanced dysesthesia in association with lassitude. Furthermore, a combination of nasal bleedings, head

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heaviness, visual disturbance and hardhearings suffered her to hasten her hospitalization. On admission, she was found to be anemic, ophthalmological retinopathy with patchy hemorrhage, and hyperviscosity syndrome. Hyperviscosity of the blood and serum could account for clinical signs of nasal bleedings, retimopathy and visual disturbances. A giant splenomegaly was noted, expanding about 6 cm to the left and about 6 cm downwards from the umblicus. Laboratory examinations disclosed a red cell count of 255 x 10^4 per microliter with reauloux formations, hemoglobin level of 7.0 gm per dl, a hematocrit 23.2%, a white cell count of 5,200 per microliter with a differential 35% of neutrophils, 5% of monocytes, 50% of lymphocytes and 8% of abnormal lymphocytes and a platelet count of 17.7 x 10^4 per microliter. A bone marrow aspiration was performed with an uncleaned cell count of 8.6 x 10^4 per microliter, a ratio of myeloid to erythroid of 2.3, erythroid 15.2%, myeloid 34.6%, monocytes 0.6%, eosinophils 1.0%, lymphocytes 48.4% and plasma cells 0.2%. Surface marker of surface immunoglobulin on the abnormal lymphocytes was examined with a result of IgM and IgD as positive on the surfaces of cells. Significant findings of immunological abnormality were the evidence of IgM(kappa) − monoclonal protein in the serum. A serum total protein was 8.6 gm per dl, including 4.3 gm of albumin, and 3.6 gm of spiky gammaglobulin on an electrophoretic pattern as shown Figure 1 (upper). A serum IgM level was 4,120 mg per dl, IgG 981 and IgA not measurable. Other laboratory data on admission included an elevated LDH of 948 U and BUN of 22 but the rest data showed within normal limits. Therefore, a clinical diagnosis of primary macroglobulinemia was established. An institution of chemotherapy was started consisting of daily oral administration of 50 mg cyclophosphamide and daily 20 mg prednisolone. There were somewhat improvements of size of splenomegaly, signs related to hyperviscosity, LDH titers and percentage of lymphocytes in the peripheral blood. However, no effect was observed on IgM levels in the serum, and acute severe stomatitis resulted in a discontinuation of cyclophosphamide. As to nursing the patient with macroglobulinemia, some responsibilities of nurse were required in the control of infections and bleedings. Thus, careful nursing was accomplished during hospitalization in the present case. An induction of plasmapheresis by double filtration for hyperviscosity once a week with totally 9 times procedures could not help to improve IgM levels. As shown in Figure 2, different regimens were also administered on this patient during her clinical course, first high-dose cyclophosphamide 500 mg intermittently 4 times, secondly vindesine 2 mg per day with 15 mg of prednisolone, and thirdly procarbazine 100 mg per day for 25 days with an increased dose 40 mg per day of prednisolone. These different regimens could not work to decrease serum IgM levels with somewhat remained hyperviscosity in the serum. After these trials for 8 months after the admission, natural interferon alfa (n-IFN-α) was started to use, with a standard dose of 3 x 10^6 unit (3 mega unit) per day

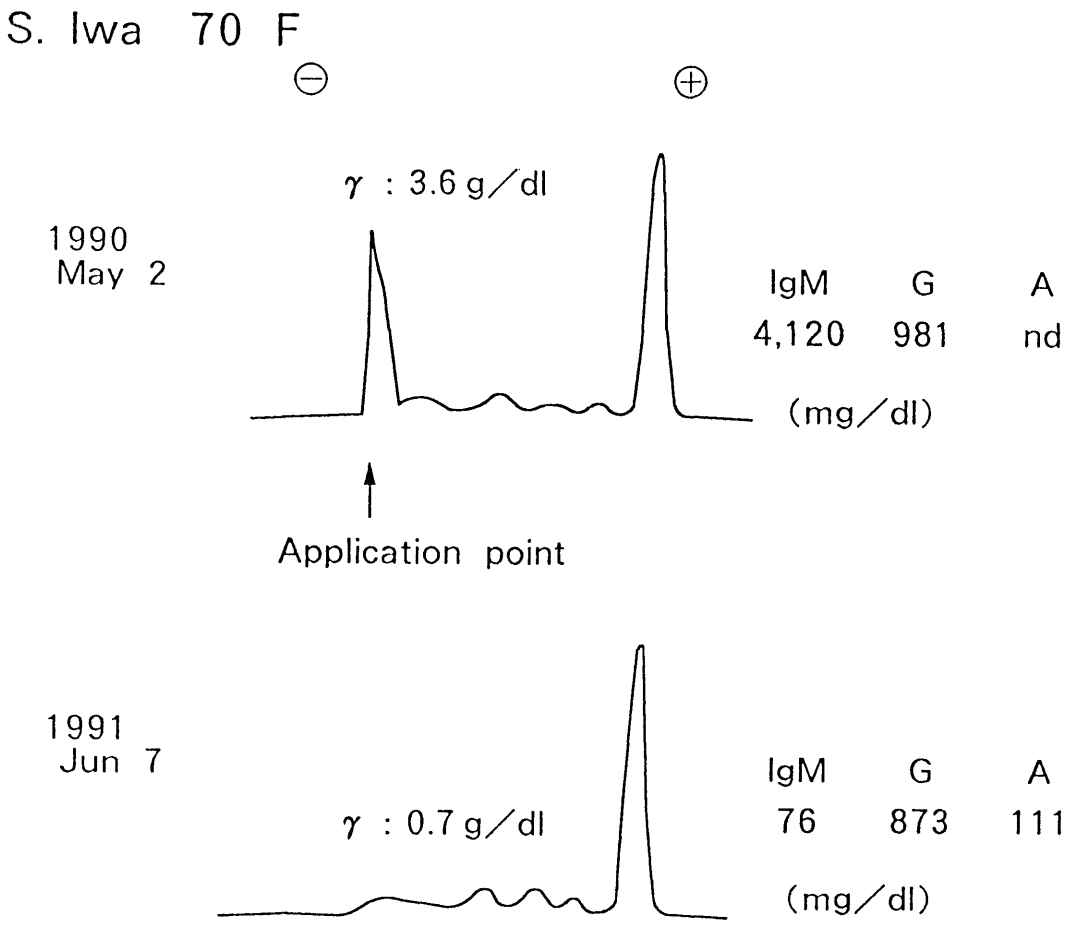

Figure 1. An unusual contour of gamma-globulin peak on an electrophoretic pattern on admission (upper) disappeared after IFN administration (lower).

intramuscularly with a combination of low dose of prednisolone as shown in Figure 2.

An abrupt and successful decrease of serum IgM levels was clearly observed along with an improvement of already diminished background serum IgG, improved hemoglobin levels as well as white cell counts and complete disappearance of hyperviscosity syndrome. Figure 1 also demonstrated the disappearance of IgM monoclonal spike on the routine serum protein electrophoretic pattern, after the IFN therapy. Continuous administration of IFN in the present case, however, tended to decrease of cytopenia of hemoglobin, white blood cells and platelets, about 40 days after the induction of IFN.

DISCUSSION

IFN comprises a class of protein

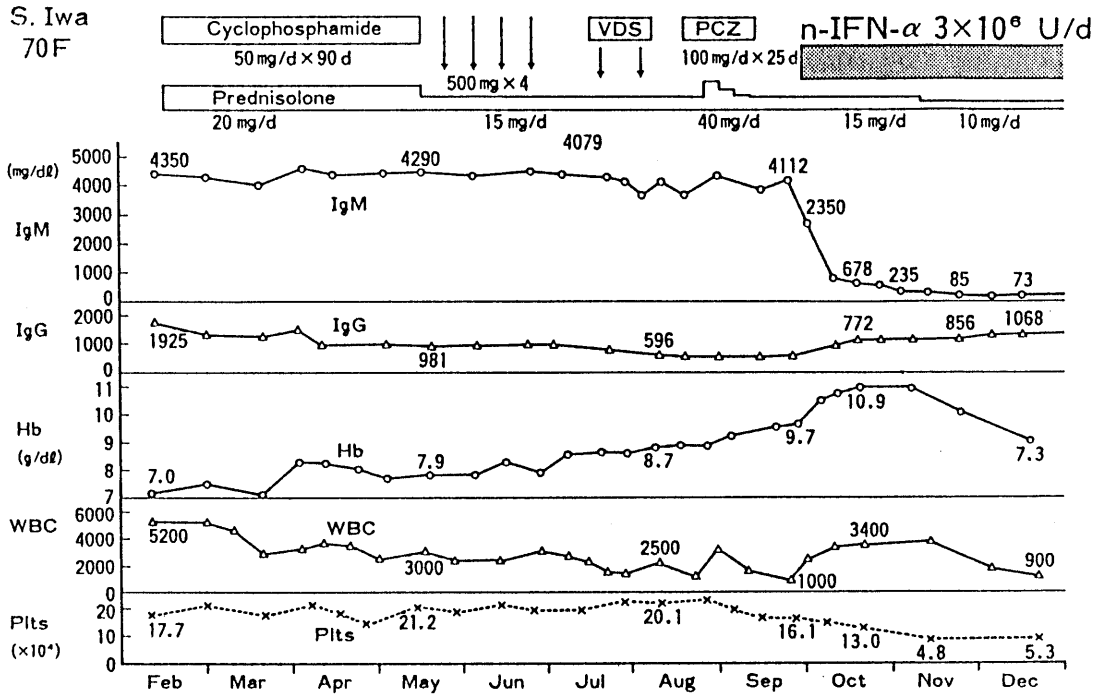

Figure 2. An obvious effect of a daily injection of n-IFN-alfa 3 mega units in the course of the patient, with a decrease of serum IgM levels and an improvement of serum IgG levels.

factors, originally associated with antiviral properties, which also have antiproliferative, immunomodulatory and differentiation-induction effects (1, 2). A large number of preclinical studies have shown that the therapeutic effect of IFN increases various types of immunity (3), natural-killer cell activity, antigen-elicited cell-mediated cytotoxicity and antibody-dependent cellular cytofoxicity (4).

Interferon-α is currently widely available for routine clinical use (2). Furthermore, strategies for combining with chemotherapy have been considered such as in the treatment of multiple myeloma (2, 5). The evaluation of IFN on myeloma cases were now world widely established (5-8). Within a same group of plasma cell dyscrasia, macroglobulinemia other than myeloma is reasonably considered to be treated by IFN, although the published data on macroglobulinemia are still scarcely seen in the literature (9). As seen in Figure 2 in the clinical course of this patient, an intermittent schedule of IFN might well be tolerated without any obvious side effects such as gradual cytopenia. This line of experience on macroglobulinemic cases are worthy of trial in the future.

As to nursing the patient with cancer as in the present case, some responsibilities of the nurse were required in

the control of infections and bleeding in two different aspects, first the care of the patient, and secondly the prevention of infectious or bleeding during chemotherapy. In detail, the nurse have to keep in mind to pay attention on preventing spread, increasing the resistance of the host and minimizing the infection (10), since infections and bleeding are two major factors among cancer hosts.

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