U/L, ALT 163 U/L, serum amylase 1,402 U/L, uric acid 15 mg/dL, LDH 9,030 U/L, blood urea and creatinine concentrations within the normal limits. An abdominal ultrasound revealed free peritoneal fluid and an enlarged spleen. An emergency laparotomy and splenectomy were performed and the patient was given supportive therapy with blood, platelets, fresh frozen plasma and fibrinogen. Operative findings were two and a half liters of intraperitoneal blood, with marked splenomegaly (size 17×16×8 cm, weight 841 g). Four lacerations were found with an active bleeding. Microscopic examination of the spleen revealed diffuse infiltration with leukemic cells and multiple small hemorrhagic foci in the parenchyma with a subcapsular hematoma.

On the basis of the morphologic characteristics of the peripheral blood and a bone marrow aspirate, cytochemical staining and immunophenotyping of the blast cells, the diagnosis of T-cell ALL was established. The immunophenotype revealed that the blasts were positive for CD1, CD7, CD2, CD5, CD8, CD34, CD38 and TdT, and negative for CD3, CD4, CD19, CD20, CD10, DR, CD14, CD13 and CD33. Immediately after the splenectomy a cytoreductor treatment was initiated with prednisone, vincristine and daunorubicin with intensive prophylaxis of lysis tumour syndrome.

The patient continued to be hemodynamically unstable, in renal failure and have hemorrhagic episodes with disseminated intravascular coagulation and hyperfibrinolysis refractory to supportive therapy. He died 48 hours after arriving at hospital. Permission to carry out a *post-mortem* examination was denied.

The diagnosis of splenic rupture must be considered in all patients with hematologic malignancies and a new abdominal pain, acute or subacute, hypotension and sudden anemia, even more so if there is not previous history of trauma. Diagnosis is based on clinical signs (abdominal pain, splenomegaly, hypotension, tachycardia, etc.) and confirmatory diagnostic tests. Although some authors have reported paracentesis to be the most effective diagnostic procedure,[4,9] we have found that abdominal ultrasound can be a good, non-invasive technique without risk to patients who are hemodynamically unstable . In our case, the abdominal ultrasound was diagnostic and the splenectomy was performed immediately.

The prognosis in splenic rupture is poor; in the non-operative cases reviewed the mortality was 100%. The survival of patients following splenectomy is probably well correlated with the course of the underlying disease. Aggressive management with early surgical intervention and appropriate hemoderivative support is important.

Key words

Spleen, pathological rupture, ALL, initial manifestation

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Interferon-α2b is not effective in the treatment of refractory immune thrombocytopenic purpura

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About 25-30% of patients with immune thrombocytopenic purpura (ITP) are refractory to corticosteroids, splenectomy and other treatments. It has been suggested that interferon-α2b (IFN-α2b) may be useful in the treatment of chronic refractory ITP patients. We treated 9 chronic refractory ITP patients with IFN-α2b: the results were poor.

Immune thrombocytopenic purpura (ITP) is an autoimmune disease mediated by antiplatelet antibodies. Corticosteroids and splenectomy are effective treatment in the majority of patients. However, 25-30% of patients are refractory to these treatments, thus, morbidity increases, and the mortality rate rises to about 16%.[1] It has been suggested that inter-

Table 1. Patients' clinical and laboratory characteristics and response to IFN-α2b therapy.

Patient	Plts ($x10^9$/L) PRE	Plts ($x10^9$/L) POST	Hb (g/dL) PRE	Hb (g/dL) POST	WBC ($x10^6$/L) PRE	WBC ($x10^6$/L) POST	Hemorrhage PRE	Hemorrhage POST	Anti-platelet autoantibodies PRE	Anti-platelet autoantibodies POST	Previous treatments
1	33	39	14.9	14	7.9	4.8	–	–	-----	PaIgG + SBIgG	C
2	14	14	14	14	8.1	7.6	–	–	–	PaIgG	S, C, A
3*	36	18	10.3		4.5		–	+	PaIgG	PaIgG + SBIgG	C, A
4*	7	1	13.6	13.9	6.2	4.4	–	+	PaIgG + SBIgG	N.E.°	C,A, S, Ig
5*	30	2	12.9		13.3		–	+	-	N.E.°	C, S, A
6	30	28	13.2	13.7	3.9	4.3	–	-	PaIgG + SBIgG	PaIgG + SBIgG	C, A, Ig
7*	14	2	11.6	11.9	4.2	5.8	–	+	PaIgG + SBIgG	PaIgG + SBIgG	C, S, A
8	45	46	14.6	13.7	4.5	3.8	–	–	PaIgG	PaIgG	C, A
9	21	106	14.9	14.2	9.1	4.9	–	–	PaIgG	PaIgG	C, A

**Therapy was withdrawn due to hemorrhage and/or worsening of thrombocytopenia; °N.E.= Not evaluated. C = Corticosteroids; A = Azathioprine; S = splenectomy; Ig = Immunoglobulins.*

Table 2. Phenotype of peripheral blood lymphocytes in ITP patients treated with IFN-α2b. Values are expressed as percentages.

	CD3 PRE	CD3 POST	CD4 PRE	CD4 POST	CD8 PRE	CD8 POST	CD57 PRE	CD57 POST	CD20 PRE	CD20 POST
1	52	64	34	31	25	32	12	18	7	11
2	71	68	42	45	28	28	7	9	10	12
3	57	61	23	33	30	30	16	20	9	11
4	62	/	40	/	28	/	11	/	5	/
5	43	/	39	/	11	/	7	/	4	/
6	59	65	22	31	40	39	17	22	9	13
7	44	56	29	31	20	22	6	9	5	8
8	79	81	55	59	26	29	9	12	6	6
9	67	66	50	45	14	24	5	12	5	9

PRE= before α-IFN treatment. POST= after α-IFN treatment.

feron-α (IFN-α) may be beneficial because of its immunomodulant activity,[2,3] but the data in the literature are not concordant.[4,5]

We used IFN-α2b to treat 9 refractory ITP patients (3 males, 6 females; median age 55 yrs, range 37-70 yrs) with a diagnosis of chronic ITP made according to the criteria of McMillan,[6] and who were negative for hepatitis B and C and HIV. The patients had a median duration of disease of 37 months (range 21-357), a platelet count <50×10^9/L, and had been off-therapy for at least one month. IFN-α2b was administered alone at a dosage of 3 MU s.c. × 3/week for five weeks. Antiplatelet autoantibodies (PaIgG and SBIgG) were detected by the standard immunofluorescence method and flow cytometer analysis (Table 1), as already described.[7] A study of main lymphocyte subsets was also performed (Table 2). Clinical examination and platelet count were evaluated weekly.

Therapy was well tolerated, but 4/9 patients withdrew from treatment owing to worsening of the thrombocytopenia and/or appearance of a hemorrhage syndrome. Two patients needed hospitalization and platelet transfusions. Autoimmunity increased in 3 patients. Only one patient (#9) developed a significant increase in the platelet count (21 →106×10^9/L) after administration of IFN-α2b (Table 1), but she lost the response 2 months later.

As regards the lymphocyte subset study, no true differences were seen between before and after treatment with IFN-α2b. The CD3 and CD20 levels remained unchanged throughout the treatment, while CD4/8 ratio was highly variable (Table 2).

Our short series of chronic refractory ITP patients showed a remarkably poor response to IFN-α2b therapy. It is possible that our series largely comprised a subset of patients in whom more aggressive disease and/or prolonged immunosuppressive therapy were associated with a different pathogenetic pathway that obviated the action of IFN-α2b.

IFN-α2b is known to have an antiproliferative action,[8] and can induce the appearance of autoimmune thrombocytopenia[9] or autoimmune disorders.[10] Data from the literature suggests that IFN-α2b is capable of modifying immunologic response by enhancing NK response and by leading some T cells to differentiate into the Th1 subset that secretes IL2 and IFNγ. It has recently been reported that ITP patients who respond to IFN show an increase of IL2 and IFNγ production, accompanied by a decrease in IL4 production.[5] A likely explanation for the therapeutic effect of IFN-α is that by inducing T cells to differentiate into the Th1 subset it indirectly exerts a cytotoxic action on autoreactive cell clones. Non-responder patients might be not capable of producing IL2 and IFNγ in response to IFN-α2b.

In view of this, we think that due to its unforeseeable effects on autoantibody production IFN-α2b should not be considered a safe or satisfactory treatment for refractory ITP patients.

Key words

Chronic refractory ITP, IFN-α2b, immune system

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Long-term disappearance of previous chromosomal abnormalities in myelodysplastic syndromes treated with low dose cytosine arabinoside and granulocyte/macrophage-colony stimulating factor

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Most therapies for elderly patients with myelodysplastic syndromes offer few short responses and little improvement in survival. We describe two patients who, after several cycles of low dose cytosine arabinoside and GM-CSF, achieved and maintained complete remission and became tranfusion independent. Previous chromosomal abnormalities also disappeared and karyotype remains normal.

No uniformly accepted treatment is available for elderly patients with myelodysplastic syndromes (MDS).[1] We present two MDS patients treated with combined low-dose araC and GM-CSF who achieved a complete (CR) clinical, hematological and cytogenetic response.

Case #1. A 71-year-old-woman diagnosed in 1992 as having refractory anemia was referred in 1995 because of severe cytopenias and elevated transfusional requirements. Bone marrow (BM) aspirate was hypercellular with trilineal dysplasia and 12% myeloblasts. Cytogenetics: 46,XX (45% metaphases)/46, XX, t(5;13)(q13; q14) (35%)/47,XX,+8 (20%). She started low-dose ara-C (10 mg/m^2/d) and GM-CSF (150 mg/d), days 1 to 14, every month. After the fourth cycle she did not need further transfusions. Data in August 1996: normal karyotype; less than 1% of blasts in BM; WBC count, 3.3×10^9/L; hemoglobin (Hb), 143 g/L; 124×10^9 platelets/L. Side-effects were mild (except for flu-like syndrome related to GM-CSF), thus allowing us to administer up to 20 cycles of this protocol. The patient remains stable without complications 24 months after the onset of treatment (Figure 1).

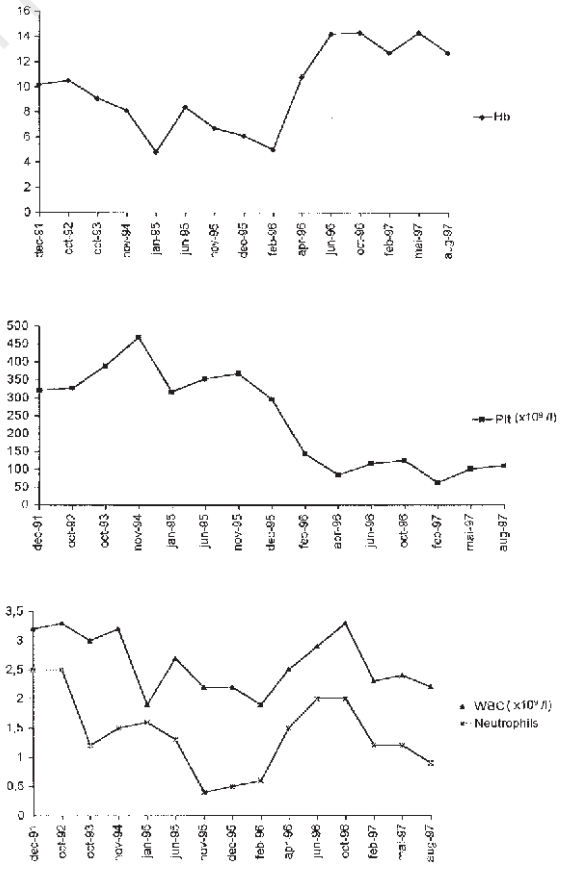

Figure 1. Case #1.