In conclusion, neither histopathological evaluation nor DNA analysis predicted subsequent distant metastasis in pathological stage II NSGCT patients. Until predictors of subsequent distant (chest or serological) recurrence are found in pathological stage II patients, the options of immediate adjuvant chemotherapy or observation after RPLND must be presented to the patient. No known biological parameter mandates adjuvant chemotherapy in this group of patients.

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Exceptional Toxicity of 5-Fluorouracil and Interferon-α in a Patient with Hepatocellular Carcinoma

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WE OBSERVED severe mucosal toxicity and thrombocytopenia after a first course of fluorouracil (5-FU) and interferon-α (IFN-α) in a patient suffering from liver cirrhosis and hepatocellular carcinoma.

The patient was a 67-year-old man who, in 1992, had been diagnosed as having liver cirrhosis due to prolonged alcohol consumption. An inoperable hepatocellular carcinoma was diagnosed in April 1994. At the time of diagnosis he had a normal blood count, but the highest pretreatment value of alphafetoprotein (AFP) was 2500 U/l (normal values shown in Table 1).

Treatment with 5-FU, 500 mg/m^2 and IFN-α (Introna) 3 million units/day was given for 5 consecutive days (days 1–5). By the end of treatment, the patient started to have symptoms of stomatitis and was admitted on day 6 with severe mucosal bleeding of the oral cavity, epistaxis, fever and ascites. The thrombocyte count was 9 × 10^9/l. He had surface antibodies IgG, IgM and IgA against thrombocytes. Ultrasound examination showed a small, cirrhotic liver, a small spleen and some ascites. The leucocyte nadir of 1.1 × 10^9/l was observed on day 16. Bone marrow examination was performed when thrombocytes were recovering and showed normal haematopoiesis.

Table 1. Blood chemistry prior to, and 1 and 4 weeks after treatment with 5-fluorouracil and interferon-α

	Before treatment	Day 7	Day 28	Normal values
Hb (g/l)	103	90	106	128–168
WBC (×10^9/l)	7.6	3.0	12.8	3.7–10
Thrombocytes (×10^9/l)	158	9	65	150–400
GT (U/l)	839	364	273	<90
AFOS (U/l)	1147	597	649	110–300
Albumin (g/l)	29	18	16	37–50
Creatinine (μmol/l)	52	52	65	<135
Bilirubin (μmol/l)	29	38	46	<20
AFP (kU/l)	2500	800	812	<10–10

Hb, haemoglobin; WBC, white blood cell count; GT, glutamyltranspeptidase; AFP, alphafetoprotein.

The patient was treated with parenteral feeding, transfusions of thrombocytes (four times) and red cells (once), antibiotics and diuretics. His blood values prior to, on admission and on discharge from the hospital are presented in Table 1. He recovered and was discharged on day 30.

Haematologic and hepatic toxicities of IFN-α are usually dose related and occur more commonly with doses exceeding 10 MU. The incidence of severe bleeding and clotting disorders or grade 3–4 somatitis was less than 1% in a series of 800 treated cancer patients [1]. The tolerance of combined treatment is dose dependent; mucositis, myelosuppression and electrolyte waste are dose limiting [2]. Mucositis occurs usually at days 10–14 after combination treatment [3]. Liver cirrhosis decreases the metabolism of 5-FU, which is potentiated by IFN-α, and causes an exceptionally intense effect on mucosa and bone marrow, and slow recovery of blood values. Although IFN-α can usually be safely used with chemotherapy in the treatment of malignancies, the presence of a cirrhotic liver can cause exceptional severe synergistic toxicity, as seen in our patient. The presence of antibodies against thrombocytes in this patient indicates an immunological thrombocytopenia, but a direct inhibitory effect of IFN-α on promegakaryocytes in the bone marrow [4] cannot be dismissed.

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