anemia was observed in 10/18 patients (7 grade 1-2 and 3 grade 3-4), neutropenia in 13/18 patients (5 grade 2 and 8 grade 3-4) and thrombocytopenia in 8/18 patients (4 grade 1-2 and 4 grade 3-4). Supportive treatment with G-CSF was given to 12 patients. Blood transfusions were given to patients with grade 3-4 anemia, while platelet transfusion was used in only one case with bone marrow involvement.

The prognosis of patients with NHL who have relapsed or were resistant to front line treatment remains poor. Several conventional salvage protocols are available for such patients. Overall response rates (CR+PR) of up to 60% have been reported, depending on the characteristics of the patients including i.e. age, primary resistance, early or late relapse. The prognosis is particularly dismal for elderly patients or those with primary refractory disease.

Idarubicin is an interesting agent whose use in the treatment of NHL is worth investigation. Idarubicin was initially tested as monotherapy in patients with relapsed or refractory disease to confirm its activity. Next it was combined with other agents with known activity either in relapsed or refractory patients or as a first line treatment, often used in place of doxorubicin. In relapsed or refractory disease the response rates to idarubicin-containing regimens are up to 60%.

This study included 18 patients with unfavorable prognostic according to the international index and the majority of them (14/18) exhibited resistance to front line treatment. The response rate was 33% which is lower than that obtained in other studies. The lower remission rate in the present study can be attributed to the unfavorable clinical characteristics of the patients.

Hematotoxicity, mainly neutropenia, was common with this regimen, but no toxic death occurred. Supportive treatment with G-CSF was used in the majority of patients.

In summary the IVPP regimen was effective in some relapsed or refractory patients with intermediate or high grade NHL and unfavorable clinical characteristics. It may be an alternative treatment for elderly or other patients not eligible for intensive regimens.

References


Genetic polymorphism of methylenetetrahydrofolate reductase (MTHFR) and venous thromboembolism: a case-control study

Sir,

Moderately high total plasma homocysteine (Hcy) levels have been demonstrated to be an independent risk factor for arterial and venous diseases. This situation can result from genetic defects and folate, B6, B12 vitamin deficiencies. Recently, a point mutation (C677T) in the gene encoding methylenetetrahydrofolate reductase (MTHFR), a key enzyme involved in Hcy remethylation, has been reported by Frosst et al. This polymorphism in the homozygous variant (TT) has been associated with increased enzymatic thermolability and consequently, was involved in some cases of hyperhomocysteinemia, especially in fasting conditions, when folate intake is low. In some reports about coronary heart disease, the risk was elevated in the homozygous variant, but in others did not. In venous thromboembolism, moderate hyperhomocysteinemia has also been found to be a significant risk factor, but the MTHFR genetic condition is

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We assessed the MTHFR polymorphism in a non-matched case-control study: 107 consecutive thromboembolic patients (deep venous thrombosis and pulmonary embolism), aged 54 years (range 18 to 80) and 200 healthy donors (42 years, range 25 to 54). Venous blood samples in EDTA were obtained for DNA analysis by PCR. The amplified fragments were cut with TaqI which recognized the C→T substitution. Additionally, we measured plasma homocysteine levels in fasting conditions by EIA in all the patients.

The overall frequencies of the three MTHFR genotypes were similar among patients and control subjects. The thermolabile variant (Val/Val equivalent to T/T homozygosity in 677 position) was found in 13/107 (12.1%) patients and in 20/200 (10%) controls (NSD) with an odds ratio of 1.24 (CI95%=0.6-2.9), and the normal homozygous variant (C/C or Ala/Ala) occurred in 44% of the patients and 46% (92/200) of the controls. After adjustment for FV R506Q and FII G20210A mutations, the estimated risk of venous thrombosis among T/T carriers increased up to 1.33 (CI95%=0.6-2.9), but did not reach statistical significance (p=0.50).

Those with abnormal genotype (T/T), have higher total homocysteine levels (11.3±4.6 μmol/L) than the others (10.1±6.6 μmol/L in C/T and 9.2±5.3 μmol/L in C/C) however, without statistical significance (p=0.19).

In conclusion, our data show that homozygosity for the C677T mutation in the MTHFR is not associated with increased risk of venous thromboembolism or, at least, suggest that a multicenter study would be necessary to obtain a definitive answer.

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References

Recombinant human tissue plasminogen activator without heparin is effective in the treatment of hepatic veno-occlusive disease

Sir,
We report on 6 patients with veno-occlusive disease (VOD) who have been treated with recombinant human tissue plasminogen activator (rh-tPA) alone, without heparin, at a dose of 50 mg daily for 4 days. Four of them responded. Major bleeding was not observed in any of the patients.

The most effective therapy for VOD after bone marrow transplantation (BMT) has not yet been established. Rh-tPA has been employed both alone and in combination with heparin, but its efficacy remains unclear, and hemorrhagic complications are often described.14 We describe our successful experience in the treatment of VOD with rh-tPA alone.

Our series consisted of 6 patients, (4 males, 2 females), who developed VOD after autologous BMT (5 cases) or syngeneic BMT (1 case). Five patients had multiple myeloma, and one had T-lymphoblastic lymphoma. Median age at BMT was 42 years (range 20-54). Conditioning regimens for transplantation were: Bus 16 mg/kg and Cy 200 mg/kg for 3 patients, Bus 16 mg/kg and melphalan 100 mg/m² for 2 patients and melphalan 140 mg/m² plus single dose TBI (1000 cGy) for 1 patient. VOD was defined according to the Seattle criteria. The clinical diagnosis of VOD was made at a median of 21 days after BMT (range 15-30). Rh-tPA was administered by 3-4 hours intravenous infusion at a dose of 50 mg daily for 4 days. No patient received heparin in addition to rh-tPA. No patient had renal or pulmonary failure or encephalopathy. The median total serum bilirubin at diagnosis of VOD was 3.14 mg/dL (range 0.87-5.51), while the median serum levels of ALT and AST were 671 U/L and 588 U/L, respectively.

Four patients (66%) responded to rh-tPA, with a complete resolution of painful hepatomegaly or ascites and normalization of hepatic function. Improvement of clinical symptoms was fast, starting...