ties of aggregation with various agonists. No inhibitors of coagulation factors were detectable. Levels of von Willebrand factor (vWF) antigen and fibrinogen were high, but the functional property of vWF assessed by ristocetin cofactor activity (vWF:RCo) assay reached 30% of that of normal reference plasma only.

The possibility of inhibitor-induced AvWD was confirmed by a subsequent inhibition test. We mixed the patient’s plasma and pooled normal plasma in a 1:1 ratio, incubated it at 37°C for 2 h, and repeated the ristocetin cofactor activity assay. The mixture showed similarly decreased activity.

The patient then received therapy with epirubicin and interferon-alpha, with satisfactory response. Clinically, his bleeding diathesis abated. Laboratory work-up showed an improved hemostatic profile. His platelet count dropped dramatically without a concurrent fall of white cell count, which ruled out the possibility of marrow suppression effects of chemo-immunotherapy.

Our patient here exhibited two unique features: AvWD due to presence of vWF inhibitors and RT mediated by increased TPO production.

Non-hematological malignancies with coexisting AvWD are most commonly seen in patients with Wilms tumor. Other cancers sporadically reported include adenocortical carcinoma, lung cancer, gastric carcinoma and primitive neuroectodermal tumor [1]. There have not been similar reports in patients with HCC. Generally, excessive tumoral adsorption of vWF was the pathogenesis of AvWD in cancer patients [1]. Nevertheless, we demonstrated vWF inhibitors as the underlying causes in our case.

Autoantibody-induced AvWD was typically associated with autoimmune or hematoproliferative disorders. In most patients, the antibody–vWF immune complexes were cleared from the circulation, which resulted in low levels of factor VIII and vWF antigen and reduced vWF:RCo activity [2]. Sometimes, these antibodies had restricted specificity, interfering with the binding of vWF to platelet glycoprotein Ib receptors without causing clearance of vWF antigen [3]. This could lead to normal antigen level with disproportionately reduced functional activity of vWF, as in our patient.

Various neoplasms have been associated with RT. The most widely accepted mechanism is that the endogenously increased IL-6 in cancer patients leads to excessive TPO production and resultant thrombocytosis [4]. Newer evidence has also revealed that tumor cells could over-express TPO. In a large series, thrombocytosis occurred in 2.7% of HCC patients and was the result of overproduction of TPO by HCC [5]. The contrast levels of IL-6 and TPO in our patient suggest a similar mechanism.

Both thrombocytosis and AvWD are rare paraneoplastic syndromes of HCC patients. Although RT rarely causes bleeding, hemorrhagic complications associated with AvWD could be problematic. When bleeding occurs, careful evaluation of hemostatic parameters is mandatory. If AvWD is documented, treatment must be planned accordingly.

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Limitations of Wright formula estimates of renal function

It was with interest that we read the publication by Marx et al. [1] who examined a number of formulae to estimate renal function in cancer patients over 70 years of age. They concluded that the Wright formula would provide an adequate estimation of glomerular filtration rate (GFR) in patients with a GFR within the normal range (50–120 ml/min). However, the key practical question relating to this work was not addressed, that is, the performance of the formulae in accurately predicting renal function for all patients across the full range of renal function, and particularly those with poor renal function (GFR <50 ml/min). This is an especially relevant issue for elderly patients, who were the patient group in this study. It would appear from the data that there were 40 patients with a GFR <50 ml/min; however, no details of the bias and precision of the Wright formula was presented for this group. Visual inspection of the data presented (Marx et al. [1], figure 1A) would indicate that the Wright formula significantly overestimates GFR in patients with poor renal function. The authors make no comment on the utility of the formula for this group of patients. It is worth noting also, that the original Wright paper did not provide an analysis for low levels of renal function [2].

In their paper, Marx et al. comment that our group have also shown the Wright formula to be superior over the
Cockroft–Gault and Jelliffe formulae [3]. In our study this was correct when comparing the various formulae over all ranges of GFR; however, we actually showed that the Wright formula did have a significant positive bias for low GFR (i.e. overestimates) and a significant negative bias for high GFR (i.e. underestimates). This led us to conclude in our paper that the Wright formula provides a biased and imprecise estimate of GFR. This interpretation is further supported in that we have recently analysed data on 525 patients (as yet unpublished) who have had GFR determined by Tc99m DTPA clearance at our centre. In this group there were 41 patients >70 years of age with a GFR <50 ml/min. The mean percentage error of the Wright formula was 26.5% (95% confidence interval 13.1% to 39.8%). Consequently, we cannot recommend the use of the Wright formula. From a clinical perspective, a tool is needed that provides a reliable estimate across the full range of renal function. Our data, and possibly that of Marx et al. [1], indicate that the Wright formula has substantially limited applicability.

Further research is required to develop reliable methods of bedside estimates of GFR, as there is no precise formula available. Recently, the Modification of Diet in Renal Disease formula has been advocated, but this too requires validation in different situations. This expensive and often unavailable test may be avoided. Ongoing research to provide more accurate and precise estimates as accuracy and precision in this range is limited. Provided that the degree of variation is acceptable for the particular clinical situation, this estimate would be a reasonable estimate of renal function. The clinical appropriateness would be based on treatment goals, disease state and chemotherapy agent. If the degree of variation is not acceptable for the particular situation then the clinician would need, at this stage, to continue to use EDTA or DTPA GFR measures. We specifically did not include the lower range of GFR in our conclusions as accuracy and precision in this range is limited. Our results were similar to those described by Poole et al. [4], with an overestimation seen with the Wright formula in the lower GFR range. We agree that this group of patients is of particular interest for the development of reliable formulae that estimate renal function. At this stage, however, the data suggest that all available formulae have limitations in renal function estimation in the lower range of renal function, and these patients should continue to rely on Tc99m DTPA and CS1 EDTA measurements. In the higher range of GFR, provided that the degree of bias is acceptable for the clinical situation, these expensive and often unavailable tests may be avoided. Ongoing research to provide more accurate estimates across the whole range of GFR is still required.

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It is with interest that we read the letter by Dooley and Poole [1]. As expected with any surrogate measure of renal function evaluation, there are limitations. This is particularly so when evaluating renal function using creatinine as a variable. As renal function declines there is an increase in the active tubular secretion of creatinine. This results in reduced accuracy and precision in the lower renal function range. Our study demonstrates that in the range of glomerular filtration rate (GFR) from 50–120 ml/min the Wright formula [2] is the most accurate and precise estimate of renal function [3]. We have reported the degree of bias that can be expected within a particular range of GFR. This provides clinicians with an expected degree of variation within various ranges of GFR. Provided that the degree of variation is acceptable for the particular clinical situation, this estimate would be a reasonable estimate of renal function. The clinical appropriateness would be based on treatment goals, disease state and chemotherapy agent. If the degree of variation is not acceptable for the particular situation then the clinician would need, at this stage, to continue to use EDTA or DTPA GFR measures. We specifically did not include the lower range of GFR in our conclusions as accuracy and precision in this range is limited. Our results were similar to those described by Poole et al. [4], with an overestimation seen with the Wright formula in the lower GFR range. We agree that this group of patients is of particular interest for the development of reliable formulae that estimate renal function. At this stage, however, the data suggest that all available formulae have limitations in renal function estimation in the lower range of renal function, and these patients should continue to rely on Tc99m DTPA and CS1 EDTA measurements. In the higher range of GFR, provided that the degree of bias is acceptable for the clinical situation, these expensive and often unavailable tests may be avoided. Ongoing research to provide more accurate estimates across the whole range of GFR is still required.

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