Fig. 1. Chest x-ray showing a ‘white-out’ of the right lung field. Note also the significant right breast and arm oedema. There is a kinked left internal jugular dialysis catheter at the level of the right brachiocephalic vein/superior vena cava.

Fig. 2. Post-venoplasty and -stenting of stenosis with clear lung fields and pleural spaces. Significant resolution of the subcutaneous oedema of breast and arm.

in the visceral pleura. In our case, it is likely there was impaired lymphatic absorption as the high venous pressure, resulting from the brachiocephalic stenosis, would impair lymphatic drainage from the right thoracic duct. Additionally, it is possible that there was increased pleural fluid production due to increased venous pressure of the parietal pleural capillaries, which ultimately drain into the SVC.

In conclusion, the finding of a pleural effusion with ipsilateral arm and breast oedema in a dialysis patient with an arteriovenous fistula should prompt investigation for a central venous stenosis.

Conflict of interest statement. None declared.

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1. Davis D, Petersen J, Feldman R et al. Subclavian venous stenosis. A complication of subclavian dialysis. JAMA 1984; 252: 3404–3406
2. McNally PG, Brown CB, Moorhead PJ et al. Unmasking of subclavian vein obstruction following creation of arteriovenous fistulae for haemodialysis. A problem following subclavian line dialysis? Nephrol Dial Transplant 1987; 1: 258–260
3. Agarwal AK, Patel BM, Haddad NJ. Central venous stenosis thrombosis: a nephrologist’s perspective. Semin Dial 2007; 20: 53–62
4. Topf G, Jenkins P, Gutmann FD et al. Unilateral breast enlargement, a complication on an arteriovenous fistula and coincidental subclavian vein occlusion. JAMA 1977; 237: 571–572
5. Wright RS, Quinones-Baldrich WJ, Anders AJ et al. Pleural effusion associated with ipsilateral breast and arm edema as a complication of subclavian vein catheterization and arteriovenous fistula formation for haemodialysis. Chest 1994; 106: 950–952

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The difficult distinction between haemolytic uraemic syndrome and thrombotic thrombocytopenic purpura

Sir,

Haemolytic uraemic syndrome (HUS) and thrombotic thrombocytopenic purpura (TTP) are thrombotic microangiopathies (TMA) once considered the different ends of a spectrum. The recent discovery of mutations in the gene-encoding factors involved in the alternate complement pathway (factors H, I, B and CD46) in HUS and von Willebrand factor-cleaving protease (or ADAMTS-13) in TTP has prompted a new nomenclature ‘complement-dysregulation-related TMA’ for HUS, ‘ADAMTS13-deficiency-related TMA’ for TTP and an ‘indeterminate TMA’ group for TMA of unknown aetiology [1–4]. However, this classification is likely to be useful only retrospectively as most laboratories are unable to give definite diagnostic results for either condition in a short time. So, clinically there is a trend to call a predominant renal picture as HUS (though renal involvement in TTP is not uncommon) and neurological as TTP.
Why platelet microthrombi, which occur in both these conditions, cause different organ predominance has not yet been identified. It is interesting to note that endothelial heterogeneity is an important factor in determining the clotting nature of different diseases [5]. There is a differential distribution of procoagulants and anticoagulants in the endothelium from different sites of the vascular tree to balance local haemostasis which may be perturbed by different mechanisms like the complement pathway or ADAMTS-13.

Another factor which has been increasingly recognized as determining the clinical characteristics of haemolytic microangiopathy is nitric oxide (NO) [6]. The fragmentation of erythrocytes in haemolysis releases free haemoglobin into the plasma, which overwhelms the protective haemoglobin-scavenging mechanisms like haptoglobin [7]. The free haemoglobin has a high affinity for NO and depletes it, causing clinical effects from vasoconstriction and platelet aggregation. This mechanism has been used to explain symptoms of several haemolytic diseases including paroxysmal nocturnal haemoglobinuria, sickle-cell disease and TTP [7–9].

It is important to note that many of the symptoms related to TTP, like gastrointestinal symptoms, and transient neurological deficits, cannot be explained by ADAMTS deficiency but by the depletion of NO [9]. Since plasma exchange has been shown to be effective for patients with TTP who do not have a severe deficiency of ADAMTS-13 activity, it has been hypothesized that this procedure cleans haemolytic products from the plasma and restores the NO (thus inhibiting platelet aggregation) and improves the symptoms [9]. Plasma exchange is also a treatment strategy for severe HUS and NO has been demonstrated to play a protective role in the early pathogenesis of HUS by maintaining the antithrombogenic properties of the renal endothelium [10]. It is possible that the haemolysis associated with HUS depletes NO and thus contributes to the renal impairment which can be halted by plasma exchange, which provides more NO. It is also possible that the endogenous NO production is increased in less severe forms of HUS which explains studies demonstrating this observation [11,12].

Thus, the distinction between HUS and TTP based on pathophysiology may be helpful in research laboratories and for retrospective studies, but more work on the aspect of haemolysis and NO in both these conditions is required to make the distinction clearer and identify novel treatments.

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1. Dragon-Durey MA, Frémeaux-Bacchi V. Atypical haemolytic uraemic syndrome and mutations in complement regulator genes. Springer Semin Immunopathol 2005; 27: 359–374
2. Furlan M, Robles R, Galbusera M et al. Von Willebrand factor cleaving protease in thrombotic thrombocytopenic purpura and haemolytic uremic syndrome. N Engl J Med 1998; 339: 1578–1584
3. Tsai HM, Lian EC-Y. Antibodies of Von Willebrand factor-cleaving protease in acute thrombotic thrombocytopenic purpura. N Engl J Med 1998; 339: 1585–1594
4. Fakhouri F, Frémeaux-Bacchi V. Does hemolytic uremic syndrome differ from thrombotic thrombocytopenic purpura? Nat Clin Pract Nephrol 2007; 3: 679–687
5. Aird WC. Vascular bed-specific thrombosis. J Thromb Haemost 2007; 5(Suppl): 283–291
6. Cappellini MD. Coagulation in the pathophysiology of haemolytic anaemias. Hematology Am Soc Hematol Educ Program 2007; 2007: 74–78
7. Rother RP, Bell L, Hillmen P et al. The clinical sequelae of intravascular hemolysis and extracellular plasma haemoglobin. A novel mechanism of human disease. JAMA 2005; 293: 1653–1662
8. Ataga KI, Cappellini MD, Rachmilewitz EA. Beta-thalassaemia and sickle cell anaemia as paradigms of hypercoagulability. Br J Haematol 2007; 139: 3–13
9. Thachil J. Thrombotic thrombocytopenic purpura: is there more than ADAMTS-13? J Thromb Haemost 2007; 5: 634–635
10. Dran GI, Fernández GC, Rubel CJ et al. Protective role of nitric oxide in mice with Shiga toxin-induced haemolytic uremic syndrome. Kidney Int 2002; 62: 1338–1348
11. Noris M, Ruggenenti P, Todeschi M et al. Increased nitric oxide formation in recurrent thrombotic microangiopathies: a possible mediator of microvascular injury. Am J Kidney Dis 1996; 27: 790–796
12. Herlitz H, Petersson A, Sigstrom L et al. The arginine-nitric oxide pathway in thrombotic microangiopathy. Scand J Urol Nephrol 1997; 31: 477–479
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