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Acute interstitial nephritis induced by glucosamine

Sir,

Acute tubulointerstitial nephritis (TIN) is an important cause of acute renal dysfunction resulting from immune-mediated tubulointerstitial injury. The commonest causes of TIN include drugs and infection. Acute interstitial nephritis accounts for up to 15% of patients hospitalized for acute renal dysfunction. Glucosamine is a relatively new alternative therapy for the treatment of osteoarthritis (OA). We present a case of possible glucosamine-induced TIN.

A 75-year-old man was admitted with a history of difficulty in passing urine, urgency, nocturia and hesitancy. There was no history of fever, rash or arthralgia. Past history was uneventful; he denied known drug allergy and the only medication he had been exposed to had been glucosamine (2–3 months) used for treatment of his osteoarthritis. General and systemic examination was unremarkable except for dehydration. Investigation revealed haemoglobin 10.3 g/dl; white cell count 15.1×10^9 (neutrophils 13.98, eosinophils 0.02), platelets 179×10^9 /l, sodium 140 mmol/l, potassium 4.3 mmol/l, urea 45.8 mmol/l, creatinine 97 μ mol/l, bicarbonate 19 mmol/l, bilirubin 2 μ mol/l, alanine transferase 36 IU/l, alkaline phosphatase 183 IU/l, albumin 26 g/l and CRP 221 mg/l. He was initially fluid-resuscitated aggressively and catheterized, draining approximately 2000 ml of urine. Despite the above, his renal functions deteriorated. During the same period, he also had a series of blood tests which included normal complement and negative serum electrophoresis, auto-immune screen, ANCA and anti-GBM. Ultrasound demonstrated normal sized kidneys with good cortical thickness and a simple cyst in the left kidney. Prostatic volume was mildly increased at 48 cm³ and prostatic specific antigen was within normal limits. Renal biopsy demonstrated a heavy mixed inflammatory cell infiltrate within the interstitium, suggestive of acute TIN. A minor degree of age-related atherosclerosis, involving the small and slightly larger blood vessels, was also noted. Glucosamine was discontinued and the patient received haemodialysis along with a short course of steroids. His symptoms improved significantly and he was dialysis-independent on discharge.

Drug-induced acute TIN is an inflammatory process involving the tubules and the space between the tubules and the glomeruli. It is mediated by T cell hypersensitivity reaction and cytotoxic T cell injury. Renal biopsy is the gold standard for diagnosis. Stopping the suspected medication forms the main component of treatment, with most patients recovering rapidly on withdrawal of the offending drug. Corticosteroid and immunosuppressants, in cases where there is no significant improvement in the renal function, may be of value. Recovery is more rapid in those individuals who have been exposed to the drug for less than 2 weeks, in comparison with those who have taken the suspected medication for more than 3 weeks.

Glucosamine is a commonly used alternative therapy in OA. Glucosamine is an aminosaccharide derived from chitin

that takes part in the synthesis of glycosaminoglycans and proteoglycans by chondrocytes. It serves as a substrate for the biosynthesis of chondroitin sulfate, hyaluronic acid and other macromolecules located in the cartilage matrix. Experience with the use of glucosamine in OA is limited. There is no available literature reporting a direct link between glucosamine and nephrotoxicity, but there have been reports stating that additives like aristolochic acid, used in the preparation of glucosamine, can be nephrotoxic. Among the commonly known documented side effects of glucosamine, non-specific gastrointestinal tract symptoms lead the list, followed by worsening insulin resistance in diabetics. There have been no reports of glucosamine-induced TIN. In this case, there was no obvious precipitating factor other than glucosamine for the histological changes and impaired renal function. We therefore believe that glucosamine contributed to the pathogenesis of TIN in this case.

The results presented in this article, have not been published previously in whole or in part.

Conflict of interest statement. There is no conflict of interest to be reported by the authors.

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Transhepatic venous access as an alternative for Tesio catheter in the case of a patient on haemodialysis with antiphospholipid syndrome

Sir,

We report on a case of a patient with antiphospholipid syndrome with exhaustion of vascular accesses for haemodialysis. The transhepatic route through the suprahepatic vein

was used to place a tunnelled catheter for permanent haemodialysis without complications and with an excellent permeability rate.

A 54-year-old woman with end stage renal failure of unknown origin, on haemodialysis since April 1991 and who had had numerous permanent vascular accesses which were lost due to thrombosis, required the placement of double-lumen, transitory catheters on several occasions. The patient began peritoneal dialysis, but it was interrupted two years later, due to multiple peritonitis episodes which caused the loss of the peritoneal membrane. She, therefore, had to restart haemodialysis. Clinical and laboratory tests performed on the patient led to the diagnosis of antiphospholipid syndrome [1]. The angiographic test showed thrombosis in both subclavian veins and compromised both femoral and iliac veins (Figure 1).

A Tesio haemodialysis catheter (27cm in length) was inserted at the suprahepatic vein level, leaving its distal end in the right axillary region (Figure 2). The procedure was well tolerated by the patient and complications were not observed. Anticoagulation was started after 24 h with enoxiparine dose of 30 mg/day, labelled according to the anti-Xa specific

activity. From the beginning, this approach achieved an effective blood flow of 300 ml/min. There are as yet no complications with this access.

Eleven years after the beginning the renal replacement therapy, it was necessary to look for a new alternative venous access such as the suprahepatic vein. The selection of this route over the translumbar was based on our previous experience with the approach of the suprahepatic vein.

The transhepatic venous access as a catheter placement site has been known for many years, not only for dialysis but also for chronic parenteral nutrition [2,3].

It is a safe and simple route for venous access with complications and infections, comparable with other places of venous access. Although others suggest that the direct translumbar access is a better alternative [4], to date our patient maintains an excellent primary permeability, with an effective functioning for haemodialysis 980 days after the placement of the catheter. The excellent permeability rate can probably be explained by the combination of a suitable anticoagulation, our experience with this unconventional route and the type of catheter used [5].

The transhepatic venous access under ultrasound and radiosopic guidance is a simple and safe method. It is an

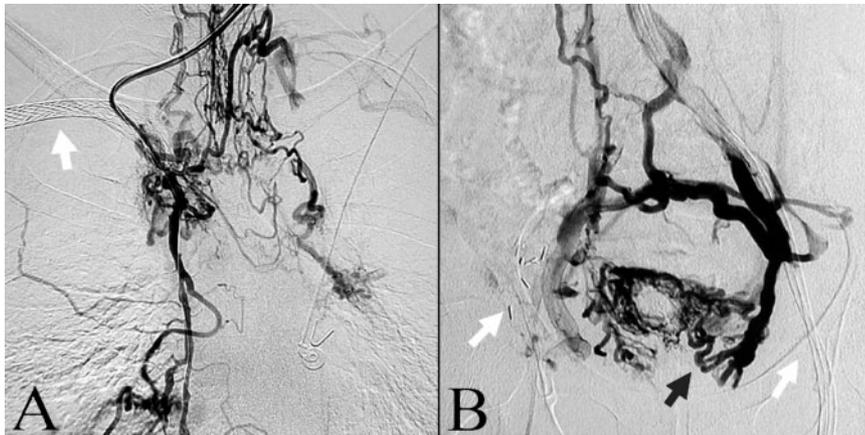


Fig. 1. Main accesses thrombosis: (A) Jugular and subclavian veins thrombosis with collateral circulation. Thrombosed Stent in right subclavian vein (white arrow). (B) Femoral and iliac veins thrombosis (white arrows) with collateral sacral circulation (black arrow).

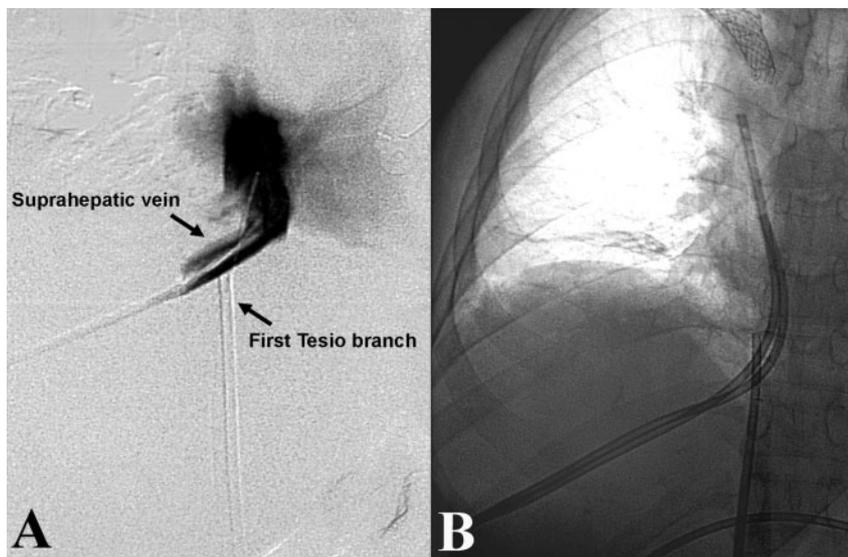


Fig. 2. Tesio catheter placed in right suprahepatic vein. Angiographic control of the first Tesio branch (A) and second branch (B).

acceptable alternative for permanent haemodialysis catheters when other venous accesses are exhausted, and when it is performed by a well-trained team.

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Impact of upper extremity abduction on arteriovenous fistula (AVF) blood flow

Sir,

It is important to avoid early arteriovenous fistula (AVF) failures in order to achieve maturation of native AVFs. In one case, we experienced a weakened shunt murmur immediately after AVF surgery when the patient's upper extremity AVF side was placed on the trunk in the supine position while the patient was on the operating table. Re-abducting the patient's upper extremity at 90° restored a desirable shunt murmur. Therefore, AVF blood flow (Q_a) is thought to be altered not only by bending or extending the hand or elbow joints, but also by shoulder joint abduction. We sought to investigate whether the difference in a patient's upper extremity abduction affects Q_a and brachial artery blood flow (Q_b).

We recruited 16 patients (five females, age 61 ± 10 years, the age of the AVFs 52 ± 34 months) undergoing maintenance haemodialysis (HD). All AVFs were primary native radiocephalic AVFs at the wrist.

Q_a was measured immediately after starting HD. Patients were placed in the supine position with the upper extremity AVF supinated and the elbow and hand joints extended. A patient's upper extremity AVF was abducted at an angle of 0, 45, or 90°, and Q_a was measured three times for each position, using the opotodilutional method with the Crit-Line TQA III device.

When significant changes were recorded in the AVF Q_a measurement due to altering the position of the upper extremity, Q_b was measured using a colour Doppler ultrasound.

There were no significant changes in blood pressure during the Q_a and Q_b measurements. Of the 16 patients, AVF Q_a changes due to upper extremity abduction were recorded in nine patients (56%). Moreover, of these nine patients, Q_b changes were observed in six patients (67%) due to abduction of the upper extremity AVF. Based on analysis of the relationships between maximal Q_a and Q_b and the upper extremity AVF abduction angle, the primary contributed vessel was thought to be a vein in five patients (56%), an artery in two patients (22%), and both a vein and an artery in two patients (22%) (Table 1). It is unclear whether the values of Q_a or Q_b measured using the Crit Line TQA III or the Doppler ultrasound are correct as the absolute values but those are correct as the relative values. Although the pathophysiology of early AVF failures is not fully understood, many possible risk factors associated with vessel quality and several haemodynamic parameters at AVF creation have been considered [1,2].

Using venous angiography, Schumacher *et al.* [3] examined 78 patients whose AVF Q_a values were insufficient, and found that an occlusion or significant stenosis of far proximal venous vessels (axillary and/or subclavian vein) could be detected in 14% of these patients. Therefore, in patients whose cephalic vein in upper arm is thin or stenosed, venous blood in upper arm tends to flow into the basilic or brachial veins, such that it tends to be affected by axillary compression. Furthermore, in patients whose deep median cubital vein, a *rami communicantes* to deep veins, is stenosed, venous blood flows into either the cephalic or basilic veins, such that it is strongly affected by the valve at the brachial junction. Thoracic outlet syndrome (TOS) is caused by compression of the brachial and subclavian arteries or veins at the thoracic outlet region where is the space between the rib cage and the clavicle by excessive arm abduction and external rotation of the upper extremity, and results in diminished blood flow of radial and brachial arteries [4]. Therefore, in a manner similar to TOS, not only Q_b but also Q_a changes due to positional changes of the upper extremity are likely caused by the compression of both the brachial and subclavian arteries and veins at the thoracic outlet region.

Because of an increasing number of patients with type 2 diabetes mellitus and elderly patients with decreased vascularity, the incidence of early access failure of native radiocephalic AVFs is increasing. Furthermore, in addition to diseased vessels, patients of old age or with diabetes more frequently have degenerated bones, muscles and connective tissues in the shoulders and armpits, as in the TOS patients; therefore, a positional change of the upper extremity may more easily compress arteries and veins. In this study, the patients exhibiting AVF Q_a changes due to upper extremity AVF abduction were significantly older than those without AVF Q_a changes [5].

Based on the present study, we propose the following guidelines for proper AVF management: (1) prior to AVF creation, the upper extremity position most effective at maintaining the maximal Q_b is to be determined and (2) immediately after the operation, the patient is to maintain the upper extremity position that ensures the maximal AVF Q_a as measured by auscultation or colour Doppler ultrasound. Although the number of patients in our study was small, our findings will hopefully provide the basis for future prospective studies in more patients, and the incidence of early AVF failures will decrease.