



## Autologous Ascitic Fluid Transfusion: A Therapeutic Option in a Child with Nephrotic Syndrome Associated with Recalcitrant Edema in a Low Resource Setting

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**Abstract:** Nephrotic syndrome is a clinical entity that is characterized usually by generalized edema, hypoalbuminaemia (<25g/L) and massive proteinuria (>40mg/m<sup>2</sup>/day). It is seen more commonly in children than adults. The most prominent clinical feature of edema makes the caregiver to seek attention. Most times the edema responds to diuretics by marked reduction in size of a previously bloated child and with the commencement of anti-proteinuric drugs, complete resolution of edema is possible. We present the management of a 7-year-old boy with relapsed nephrotic syndrome complicated with massive generalized edema and marked ascites unresponsive to diuretics and eventually had autologous ascitic fluid transfusion.

**Keywords:** Nephrotic syndrome; recalcitrant edema; ascites; autologous transfusion.

### INTRODUCTION

Nephrotic syndrome is seen more in children than adults (Siddall, E. C., & Radhakrishnan, J. 2012). It is characterized by edema, massive proteinuria (>40mg/m<sup>2</sup>/day) and significant hypoalbuminaemia (<25g/L). The most prominent clinical feature is edema which may vary from mild per orbital and pedal edema to generalized fluid accumulation otherwise known as anasarca. In its management, it is imperative that massive edema should be controlled in patients with nephrotic syndrome before instituting steroid which is the mainstay of the treatment (Bagga, A., & Mantan, M. 2005). This is because gross edema can be complicated by skin breakdown and infection (Lewis, M. A., & Awan, A. 1999), both of which can be enhanced by the therapeutic dose of steroid.

Management of edema in patients with nephrotic syndrome involves the use of diuretic agents. Patients generally respond to the combination of dietary sodium restriction and usually loop diuretic therapy and occasionally thiazide diuretics. However, in some patients, resistances to these agents are recognized leading to the development of refractory edema.

Edema is considered refractory if therapy with bed rest, salt and water restriction, and diuretics (which must include a thiazide) at maximum doses fail to result in diuresis. Administration of intravenous diuretic alongside infusion of salt poor albumin has also been used to manage recalcitrant edema (Arroyo, V. *et al.*, 1996). However, failure of this combined intervention has been recorded and paracentesis with intravenous infusion of albumin has been associated with untoward effects (Bagga, A., & Mantan, M. 2005; Lewis, M. A., & Awan, A. 1999). Some other interventions have been attempted, including a successful use of a combination of mannitol and furosemide in three grossly edematous children with nephrotic syndrome reported by (Lewis, M. A., & Awan, A. 1999). We report our experience in a 7- year-old patient who had relapse of nephrotic syndrome (frequently relapsing steroid sensitive nephrotic syndrome) with Recalcitrant edema who did not respond appreciably to any of the described interventions above and eventually had autologous ascitic fluid transfusion.

## CASE STUDY

C. A was a 7-year-old boy who presented at the Ekiti State University Teaching Hospital, Ado Ekiti, Nigeria that was managed as a case of frequently relapsing steroid sensitive nephrotic syndrome. His serology tests for hepatitis B and C as well as HIV were negative. His hemoglobin genotype was AA and the random blood glucose was within normal limit. He was on oral prednisolone which was tapered to 10mg on alternate days alongside tab levamisole. He defaulted from his regular clinic attendance for about 3months but claimed he had been on his medication. He re-presented and was admitted on account of a relapse with gross ascites and associated breathlessness that was attributed to splinting of the diaphragm by the distended abdomen. There was no fever or reduction in urine output. He weighed 35kg (his pre-morbid weight was 25kg) and he had a normal blood pressure of 90/50mmHg. Picture of the patient is as shown in fig 1.

He had severe hypoalbuminaemia (14.2g/L) and proteinuria of 4+ but there was no hematuria on urinalysis. His electrolyte, urea and creatinine as well as his full blood count results were essentially normal. The blood film for malaria parasite was negative. He was commenced on salt restriction, daily weighing, strict fluid input and output chart, the vital signs as well as abdominal girth were also monitored. He was commenced on diuretics, fresh frozen plasma transfusion, and intravenous albumin and simultaneously placed on prednisolone and steroid sparing anti-proteinuric medications as outlined below.

### Diuretic Medications

At admission, he was commenced on intravenous furosemide (2mg/kg/day) and spironolactone 25mg daily with the weight remaining at 36kg over 2 days, despite a marginal increase in his urine output. Tab hydrochlorothiazide at 25mg daily was thereafter added but the abdominal girth remained the same over 7days with no significant reduction in weight. Adequate fluid intake was ensured and his urine output was averagely 2mls/kg/day. The serum albumin marginally increased to 15g/L, proteinuria was 3+, and the child had gross ascites. Subsequently, the child was placed on intravenous furosemide (2mg/kg), mannitol (1g/kg) and

salt poor 20% albumin. After 24 hours the weight remained unchanged, serum albumin slightly increased to 16g/L. The patient had only two doses of salt poor albumin as parents could no longer afford it. The cost was about 200US dollars per vial of 50mls which contains 10g of human plasma protein. Consequently, the patient was placed on fresh frozen plasma at 10ml/kg daily with intravenous furosemide still, his weight ranged between 34kg and 35 kg. The ascites was worrisome and patient was considered for autologous ascitic fluid transfusion to augment the control of the edema while planning for renal biopsy.

### Autologous Ascitic Fluid Transfusion

In preparation for this procedure, screening for infection was done. The full blood count with differentials was essentially normal and his clotting profile was within normal limits. Under sterile conditions, ascitic aspirate was sent for culture and cytology to exclude infection and presence of malignant cells respectively; both were negative.

The procedure was explained to the patient and his primary caregivers; assent and informed consent were given. Using sterile technique, abdominal paracentesis was done with an 18G needle and the fluid was collected by gravity into a pediatric Citrate- Phosphate- Dextrose-Adenine (CPDA) blood bag. About 200mls of ascitic fluid was removed gradually into the bag over 30minutes (taking precaution not to remove more than 10% of the patient's blood volume without replacement) and same was infused via intravenous route into the child while simultaneously removing the second 200mls of ascitic fluid. The rate of ascitic fluid transfusion was 20ml/kg over 3hrs. Intravenous furosemide at 2mg/kg was administered intra-transfusion and he was also given intravenous ceftriaxone at 50mg /kg. His vital signs (blood pressure, pulse rate, temperature), urine output, weight and abdominal girth were closely monitored. This procedure was repeated after 48 hours while standard care was maintained. There was significant reduction in the edema, as shown in figure 2 below. He had six sessions of autologous ascitic fluid transfusion over a period of two weeks. The weight of the child reduced to 24kg by the second week.



**Figure 1:** pre treatment



**Figure 2:** post treatment

#### **Antiproteinuric Medications**

He was on long term alternate day steroid (tab prednisolone at 10mg alternate day) and tab levamisole 2mg/kg alternate day prior to relapse which was managed with tab Prednisolone at 60mg/m<sup>2</sup> daily alongside with diuretics, however remission was not attained. The steroid was tapered gradually to 10mg alternate days and tab enalapril was added at 5mg daily while working him up for renal biopsy. Patient eventually had renal biopsy done with the result showing focal segmental glomerulosclerosis (FSGS). Mycophenolate mofetil (MMF) was added to his medication, he was able to attain partial remission.

#### **Follow Up**

On follow up, he achieved partial remission on oral Mycophenolate mofetil, enalapril and alternate day prednisolone at 10mg.

### **DISCUSSION**

The patient in our case report had massive edema, associated with ascites that was unresponsive to diuretics, including hydrochlorothiazide at 2mg/kg which made it fit the description of refractory edema (Arroyo, V. *et al.*, 1996; European Association For The Study Of The Liver. 2010). The index patient had severe hypoalbuminaemia with serum albumin of 14.2mg/dl, impairing the delivery of loop diuretics that require protein to convey them to their site of action; this may have accounted for the sub-optimal effectiveness of furosemide in this case report. (Lewis, M. A., & Awan, A. 1999) recorded successful management of recalcitrant edema in three children with combination of furosemide and mannitol, however,

this was not the case in the index patient. The reason for this might be traceable to variability in clinical features and neuro-hormonal responses in edematous patients with nephrotic syndrome which has been earlier reported (Jethwani, P., & Krishnan, N. 2021; Walle, J. V. *et al.*, 1995).

The use of combination diuretic therapy was to achieve multi-site nephron blockade and overcome diuretic resistance, however, the risk of iatrogenic hypovolaemia leading to hypoperfusion of the kidneys, acute kidney injury, activation of the renin–angiotensin–aldosterone system, and secondary renal sodium retention as well as edema cannot be overlooked. The vital signs, hydration status of the patient, urine output, electrolyte, urea and creatinine were all closely monitored to prevent this. Increased risk of thrombotic events that may be associated with combined diuretic use was not observed in this case report.

The histologic diagnosis of focal segmental glomerulosclerosis made in the index patient is similar to the histologic pattern reported by (Lewis, M. A., & Awan, A. 1999) in children with recalcitrant edema. Non-minimal change nephrotic syndrome appears to be related to the development of recalcitrant edema. It stands to reason therefore that recalcitrant edema in a child with nephrotic syndrome should warrant renal biopsy to identify the histologic pattern. Autologous ascitic fluid transfusion can be done after proper screening to have optimal access to the kidney during biopsy.

The use of salt poor albumin has also been promoted (Dharmaraj, R. *et al.*, 2009; Chalasani, N. *et al.*, 2001), however, in a low resource center, salt poor albumin is not readily accessible because of the cost. Our patient was given two doses but there was financial constraint, and it could not be sustained.

Autologous ascitic fluid transfusion in combination with diuresis was opted for having reached a brickwall in the management of the patient. In adults with nephrotic syndrome associated with recalcitrant edema, the use of modified peritoneo-venous shunt for ascitic fluid transfusion has been reported with successful outcome in terms of reduction in edema according to the study by (Hassan, M. O. *et al.*, 2019). They reported that modified peritoneo-venous shunt using a peripheral vein was an effective and safe technique for treating refractory edema in nephrotic syndrome (Hassan, M. O. *et al.*, 2019). (LeVeen, H. H. *et al.*, 1979) following their study done in the late 70's recommended that patients with refractory ascites should be considered for peritoneo-venous shunting as this offers a method of continuous reinfusion of ascitic fluid which corrects avid sodium retention, oliguria and azotemia. Disseminated intravascular coagulopathy and sepsis have been previously reported in few of the patients who had peritoneo-venous transfusion (LeVeen, H. H. *et al.*, 1979) but in our patient, there was no untoward complication except for the oozing of the ascitic fluid from the access site and this resolved with sterile pressure dressing with gamgee. The use of infection screened autologous ascitic fluid may explain why these complications were not recorded in our patient.

## CONCLUSION

Autologous ascitic fluid transfusion following standard sterile procedure and after screening for infection might be a therapeutic option to consider for children in resource poor setting with recalcitrant edema when salt poor albumin is not accessible/affordable.

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