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Recurrent Urinary Tract Infections with Multidrug Resistance Bacteria in a 50-Year-Old Man Living Donor Kidney Transplant Recipient with Adult Polycystic Kidney Disease: The Issues for Native Nephrectomy

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ABSTRACT

A 50-year-old man with polycystic kidney disease had living donor kidney transplant. Simultaneous right sided native nephrectomy was done to give a space for graft kidney. He developed three episodes of urinary tract infections within 2 months after transplant; one episode was associated with septic shock and rise serum creatinine. Two urine culture results taken two weeks apart revealed *Klbsiella pneumoniae.* It was sensitive to amikacin and resistant to nearly all antibiotics including quinolone, imepenum, colistin, cefepime and tigecycline. The remaining left native kidney was removed as the cysts were nidus to hide bacteria; no more recurrence after second nephrectomy.

KEYWORDS: polycystic kidney disease, native nephrectomy, multidrug resistance, recurrent urinary tract infections

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INTRODUCTION

Autosomal dominant polycystic kidney disease (ADPKD), the most common hereditary kidney disease, accounts for approximately 10% of the patients on kidney transplantation waitlists (Copur et al., 2024) (Čellár et al., 2022). Autosomal dominant polycystic kidney disease (ADPKD) was seen in 2.5%-10% of dialysis patients in Europe (Torres et al., 2007). Kidney transplantation in ADPKD has several obstacles: (1) narrow space for allograft kidney; (2) recurrent urinary tract infections (UTIs); (3) massive hematuria requiring repeated transfusions; (4) abdominal pain and discomfort; (5) weight loss; and, (6) resistant hypertension. There were several controversies in doing native nephrectomy in patients with ADPKD. Generally, if they were not infected and not too big, native nephrectomy was not necessary. Native nephrectomy was indicated in the following situations: (1) active bleeding causing repeated leuko-depleted pack red cell transfusions; (2) abdominal pain due to cyst rupture; (3) narrow space for the allograft kidney; and (4) partial obstruction of the large intestine. Repeated transfusions before surgery will increase human leukocyte antigen sensitivity; and, the chances of early and late-phase graft loss increase (Waiser et al., 2024). Nonetheless, they found that the prognosis was good after kidney transplantation in patients with ADPKD.

Three timing for native nephrectomy were prior to transplant (pretransplant nephrectomy), during transplant (simultaneous nephrectomy) and after transplant (post-transplant nephrectomy). Simultaneous unilateral nephrectomy and kidney transplantation had some advantages. The need for routine native nephrectomy and timing of such procedure in ADPKD patients being prepared for transplantation were debating. Pre-transplant nephrectomy had fewer infectious complications due to lack of immunosuppressive medication use; however, the disadvantage was loss of residual kidney function and need for dialysis. On the other hand, simultaneous nephrectomy and transplantation had longer perioperative duration, perioperative complications and the requirement for blood transfusions. Copur et al studied the current evidence regarding the need and timing of nephrectomy in ADPKD patients in relation to kidney transplantation. They found that no significant difference in graft or patient survival across different nephrectomy timings. And, current trend was simultaneous or post-transplant approaches for optimal outcomes (Copur et al., 2024).

Doing unilateral or bilateral nephrectomy in patients with ADPKD was arguable too; unilateral nephrectomy was preferred to preserve renal function and reduce complication (Copur et al., 2024) and preemptive nephrectomy produced a small benefit to reduce the chance for a cyst infection. In addition, recurrent cyst infections were seen after transplantation, indicating that post-transplantation nephrectomy was an overtreatment in these patients. Geertsema et al found that cyst infections were caused by an ascending lower urinary tract infection (Geertsema et al., 2022).

Urinary tract infection (UTI) after transplant was related with graft dysfunction and morbidity. The prevalence of UTI was highest in the first 3 months after transplant (Säemann & Hörl, 2008). They also reported that age, female gender, co-morbidities and type of immunosuppressive found to be the determinants of UTI. UTI may worsen graft function and patient survival.

In patient with ADPKD, the prevalence of UTI before transplant was ten percent; and, the prevalence increased double after renal transplant. The source of organism in UTI was from cysts of native ADPKD.

Waiser et al reported that ADPKD patients were at increased risk of UTI and liver cyst infection after transplantation; nephrectomy seemed to reduce it. Steroid medication and recipient age were the possible risk factors for UTI/urosepsis. However, the survival rate after renal transplant in ADPKD patients was the same as that of non-ADPKD patient (Waiser et al., 2024).

Common uro-pathogens were *E coli*, *Enterococcus* spp (24%), *Staphylococcus* spp (12%), and *Klebsiella* spp (10%) in renal transplant recipients who developed UTI (Chuang et al., 2005).

CASE PRESENTATION

The patient was 50 years old man; He had incidental found polycystic kidney disease and initial creatinine was 2.8 mg/dl when he had gotten left brachial plexus injury due to motorcycle accident for 39 years of age. His creatinine was gradually increase year by year but his urine output was estimated (1500-2000 ml) per day. He had felt two times urinary tract infections before transplantation. He had planned to do renal transplantation.

He has three sibling brothers; he is the eldest and two younger brothers are healthy without polycystic kidney disease. His parents had also no kidney disease. The youngest brother is his donor, the same blood group (o), Rh (+) ve. Last 2 months ago before operation, He had taken hemodialysis with tunneled lumen permanent catheter, one time per five days. His blood pressure was 140-160/90-100 mmHg on Nifedipine 20mg TDS, Carvidilol 12. 5mg BD, Duracard 2mg OD, Lasix 40mg BD and Atorvastatin 10 mg OD, Ferrium XT 1 OD.

In pretransplant work up, NECT KUB showed that Right kidney size was 16.3 x 10.9 x 14.8 cm, multiple cysts and Left kidney size was 18.05 x 9.8 x 14.8 cm, multiple cysts. Liver was multiple small hepatic cysts (1.8 x 2 cm) size.

He received ABO matched living kidney from the youngest brother who was 43 years old. Regarding immunological typing, CDC crossmatch was negative. DSA was positive at A 11 MFI 1237.

As he had standard immunological risks, he was given Anti-thymocyte globulin ATG (Equine) and methylprednisolone. He received triple immunosuppressive therapy (steroid, mycophenolate mofetil and tacrolimus). He has already taken trimethoprim - sulfamethoxazole for prophylaxis of *pneumocystis jirovecii* and vegacytes for cytomegalovirus prophylaxis.

In intraoperative, right nephrectomy and renal transplantation were done. Graft kidney was placed in Right iliac fossa. Anastomosis by renal artery to external iliac artery (end to side), renal vein to external iliac vein (end to side). Ureter to bladder by extravesical Lich-Gregoir method and J stent 6/16 was inserted.

In post-operative periods was uneventful. Unfortunately, Urine C & S results had 99% probability of *Klbsiella pneumoniae spp.*, three antibiotics were merely got sensitive (Amikacin, Tigecycline and Fosfomycin) and urine RE showed pus cells (4-6 HPF), few bacteria one-week after transplantation. C-reactive protein was also high. He is not febrile. After giving IV Tigecycline and amikacin in two weeks, urine culture (recheck), twelve day later was sterile.

He stayed at home in total 11 days and later, he presented with features of uro-septicshock; high fever (Temp – 103'F) with chills and rigor for two days; low blood pressure 90/60 mmHg; pulse rate 100/min; and, respiratory rate 22 breaths/min. There were no abdominal pain, hematuria, dysuria, frequency and urgency. Urea and creatinine (56.9

and 2.03 mg/dl) results were two times increased from previous result. High TWBC count (14.0 x 10^9/L) (Neutrophil leucocytosis), mild anemia and normal platelet are resulted. Urine C&S on this admission showed *Klebsiella pneumoniae spp*. and the same previously sensitive antibiotics. C-reactive protein was also high. According to urine C&S results, IV Tigecycline was given in total 6 days and subsided signs and symptoms of urinary tract infections, urine C & S was sterile and discharged from hospital.

And then, He stayed at home in total 11 days and third time readmitted to hospital because of presenting fever with chills and rigor off and on, and features of urosepsis. On this occasion, white blood cells are normal, creatinine was 1.6 to 1.9 range and urea were 38 to 51 range. He was on IV Tigecycline 50mg 12 hourly, IV Amikacin 500mg OD to 250 mg OD depends on creatinine results.

Because of having recurrent UTI in this immunocompromised patient and the most likely source from remaining left APCKD, we decided to do nephrectomy to left APCKD to reduce frequent urinary tract infections and preserve graft function. As shown in photo (5), the cut section revealed pus containing cyst in one of them. Post nephrectomy period was uneventful. Serum creatinine level gradually decreased. There was no more UTI till now- 4 months.

DISCUSSION

Patients with autosomal dominant polycystic kidney disease attributed nearly 10% of dialysis patients and waiting list for kidney transplant. The outcome of kidney transplantation in patients with polycystic kidneys particularly pre-emptive transplant was better than that of non- polycystic kidneys namely diabetic kidney disease, SLE kidney disease etc. The nutritional status of those with PKD was better; they did not have associated other organ damage like stroke, ischemic heart disease, peripheral neuropathy and anemia.

However, kidney transplantation in PKD has several obstacles. Firstly, a large PKD left less space for the new allograft kidney. Therefore, unilateral native nephrectomy was performed either prior to transplant or simultaneously at the time of transplant. Approximately one-fifth of patients with polycystic kidneys required unilateral or bilateral nephrectomy (Harris & Torres, 2009). Secondly, those with massive hematuria requiring repeated blood transfusions native nephrectomy was indicated. Repeated transfusions before surgery would result in increased sensitivity of human leukocyte antigen though it was prevented by leuko-depleted pack red cell transfusions. And, the chances of early and late-phase graft loss would be higher. Nonetheless, it was reported that kidney transplantation in patients with polycystic kidneys had a good prognosis (Waiser et al., 2024).

However, many controversies exist concerning the need, indication, and timing for native nephrectomy in patients with polycystic kidneys scheduled for kidney transplantation (Akoh, 2015).The indications for pretransplant nephrectomy include ongoing hematuria, pain or discomfort, gastrointestinal symptoms such as early satiety, and risk of malignancy (Kirkman, Van Dellen, et al., 2011). However, pretransplant nephrectomy is associated with increased morbidity and mortality in patients with ESRD, may deprive patients of residual diuresis, and may cause overall worsening of symptoms or renal failure(Patel et al., 2011). Hence, routine pretransplant nephrectomy was no longer recommended (Fuller et al., 2005).

This patient had recurrent UTI , four episodes within 8 weeks after transplant; one episode caused septic shock and deterioration in renal function. He had simultaneous unilateral nephrectomy (right) during transplant. The remaining native left kidney had source of infection as evidenced by pus filled cyst in cut section of nephrectomy specimen. And, culture from cyst was sterile.

Brazda et al suggested to remove polycystic kidneys before transplantation if cyst-related complications occurred repeatedly (Brazda et al., 1996). Waiser et al reported that patients with polycystic kidneys were at increased risk of UTI and liver cyst infection after transplantation; nephrectomy seemed to reduce such complication. Steroid medication and the age of recipient were the possible risk factors for UTI/urosepsis (Waiser et al., 2024). They found that preemptive nephrectomy had a relatively small benefit; it reduced the chance of a cyst infection. If we removed both native both polycystic kidneys during transplant in this patient, he would not have recurrent UTI. Moreover, the graft function would be better.

Copur et al studied the current evidence regarding the need and timing of nephrectomy in patients with polycystic kidneys in relation to kidney transplantation. They found that no significant difference in graft or patient survival across different nephrectomy timings: before transplant; simultaneously during transplant; and, after transplant. And, current trend was simultaneous or post-transplant approaches for optimal outcomes (Copur et al., 2024). It recommended Argyrou et al (2017); the performance of the simultaneous procedure could be of benefit (ARGYROU et al., 2017). However, there were some controversial issues in timing of native nephrectomy in patients with polycystic kidneys and renal transplant.

Casteleijn et al studied 257 patients with polycystic kidneys for kidney transplantation. A restrictive nephrectomy policy in patients with polycystic kidneys for kidney transplantation was suggested based on the following findings. Simultaneous nephrectomy together with transplantation was not performed in their center. They found that there was no significant difference between two group, pre-transplant nephrectomy and post-transplant nephrectomy, in terms of surgery related complications, 10-year patient survival and in 10-year death-censored graft survival (Casteleijn et al., 2023). Nephrectomy was performed only in patients with lack of space for the

allograft, recurrent cyst infections, persistent cyst bleedings, or chronic refractory pain.

Suggestions by Alkaissy et al was against 'restrictive nephrectomy policy; they encouraged bilateral nephrectomy prior to kidney transplantation as it was safe. It had minimal complication and mortality rates; moreover, it facilitated a subsequent transplant procedure without mechanical or hemodynamic limitations for the graft (Alkaissy et al., 2020). There were no statistically significant differences in postoperative morbidity after nephrectomy nor overall kidney transplant outcome. The findings in 2011 was contrary. Post-transplant unilateral nephrectomy was the safest approach with fewest complications (Kirkman, van Dellen, et al., 2011); they found that native nephrectomy in patients with polycystic kidneys was associated with significant morbidity especially in the pre-transplant group.

The suggestion by Rozanski et al was 'individualized approach' if there was cyst-related infection. They were against pretransplant unilateral nephrectomy because there was no advantage over transplantation (Rozanski et al., 2005). Similar finding was found by Maxeiner et al. Higher rates of more severe complications were observed in those group of patients who underwent pre-transplant nephrectomy prior to receiving a kidney transplant even though this was not statistically significant (Maxeiner et al., 2019). Generally, both short-term and long-term transplantation outcomes in two groups (pre-transplant nephrectomy and post-transplant nephrectomy) were not different (Maxeiner et al., 2019).

No consensus exists on the appropriate timing for native nephrectomy in patients with polycystic kidney. Several issues to be addressed in the decision-making process are the importance of residual diuresis, the longer operative time along with the associated prolonged ischemia time and higher complication rate of the combined procedure. In symptomatic cases, pre-transplant unilateral or bilateral native nephrectomy seems appropriate, in order to alleviate symptoms. 'Individualized approach' seems to be the best. Abrol et al reported that 'laparoscopic simultaneous bilateral nephrectomy and kidney transplant' for symptomatic patients was safe and feasible at the time of living donor kidney transplant. It had longer cold ischemia time; it required more intensive care; it required increased blood transfusions; and, it had longer hospital stays (Abrol et al., 2021).

The prevalence of urinary tract infections (UTIs) during the first year after renal transplantation varied; the lowest was 30% and the highest was 60% (Gołębiewska et al., 2014) (Ma et al., 2020) (Muñoz, 2001) (Mahon et al., 1973). And, recurrent UTI was seen in more than 75% of kidney transplant recipients (Giessing, 2012). Giessing highlighted that UTI in kidney transplant recipients was under-represented (Giessing, 2012). This patient had recurrent UTI with multidrug resistant organism. This is one reason for case reporting.

This patient had cyst infection as evidenced by gross appearance of pus in cut section of nephrectomy specimen. According to Ronsin et al, the incidence of cyst infection in polycystic kidneys after kidney transplantation was low; history of cyst infection prior to transplant was the main risk factor (Ronsin et al., 2022). This patient had history of urinary catheterization twice when he had road traffic accident; he had past history of UTI twice prior to transplant (2023 and 2024 january).

Predisposing factors such as old age, female sex, history of UTIs, deceased donor, long-term use of an indwelling catheter, diabetes mellitus, use of ureteric stent, native kidney disease with urological malformations like polycystic kidneys, vesicoureteral reflux and neurogenic bladder, hypertension, diabetes mellitus, , calculi, pyelonephritis as their original renal disease, concomitant cytomegalovirus (CMV) disease, re-transplantation, acute rejection process and delayed graft function were more prone to UTIs (Alangaden et al., 2006)(Dupont et al., 2007) (Ma et al., 2020) (Mahon et al., 1973)(Hosseinpour et al., 2023).

Therefore, the reasons for having recurrent UTI in this patient, living donor kidney transplant recipient, history of urinary catheterization, history of recurrent UTIs before KT, native left polycystic kidneys, induction of ATG (Equine) and triple immunosuppressant therapy and use of ureteral stent. We did not identify other risk factors including vesico-ureteral reflux, and stricture at the uretero-vesical junction. The ureter length seemed to be associated with the incidence of UTI after living donor kidney transplant in one urosurgical study (Influence of Graft Ureter Length, a Donor-Related Factor, on Urinary Tract Infections After Living-Donor Kidney Transplantation: A Single-Center Analysis of 211 Cases, n.d.) . The long ureter was trimmed, and the widest part was used for anastomosis; therefore, it might increase the possibility of reflux from the bladder to the ureter in living donor kidney transplant. The ureter length in this patient was neither long nor short according to urosurgeon.

Escherichia coli, Klebsiella species and *Enterococcus faecalis* were reported to be common organisms causing UTI in post-renal transplant (Jackson et al., 2021) (Silva et al., 2013). The urine culture results in this patient revealed growth of Klebsiella species in 3 different specimens taken at 2 weeks interval. It was resistant to all antibiotics including tigecycline except amikacin. Giving aminoglycoside might damage graft kidney. In the era of anti-microbial resistant, therapeutic usage of antibiotics was very limited. Hopefully, this patient would not have another recurrence after nephrectomy.

CONCLUSION

In potential renal transplant recipient with PKD, screening for UTI prior to transplant is paramount important. Screening includes urine for microscopy, urine culture, urodynamic studies, prostate assessment in male, post-void residual urine

by ultrasonogram should be done. Recurrent UTI in renal transplant recipient with PKD in post-transplant period in is one of the indications for native nephrectomy. Treatment of UTI with drug resistant microorganism in an immunocompromised patient is not easy; it may cause recurrent attack and graft failure in kidney transplant recipient. In kidney transplant recipient with PKD, the cysts may favor the growth of organism. Higher dose of antibiotics for longer duration are required to get access to cysts. Antibiotics like aminoglycosides may impair graft function.

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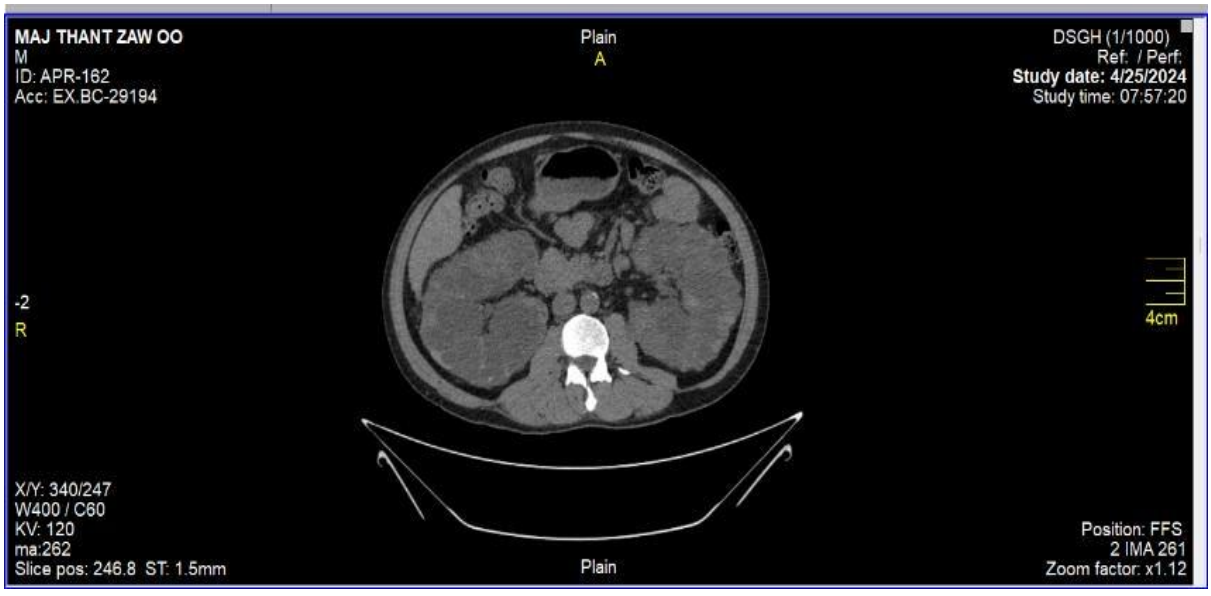

Photo (1) Non-contrast CT abdomen showing multiple large cysts in both kidneys

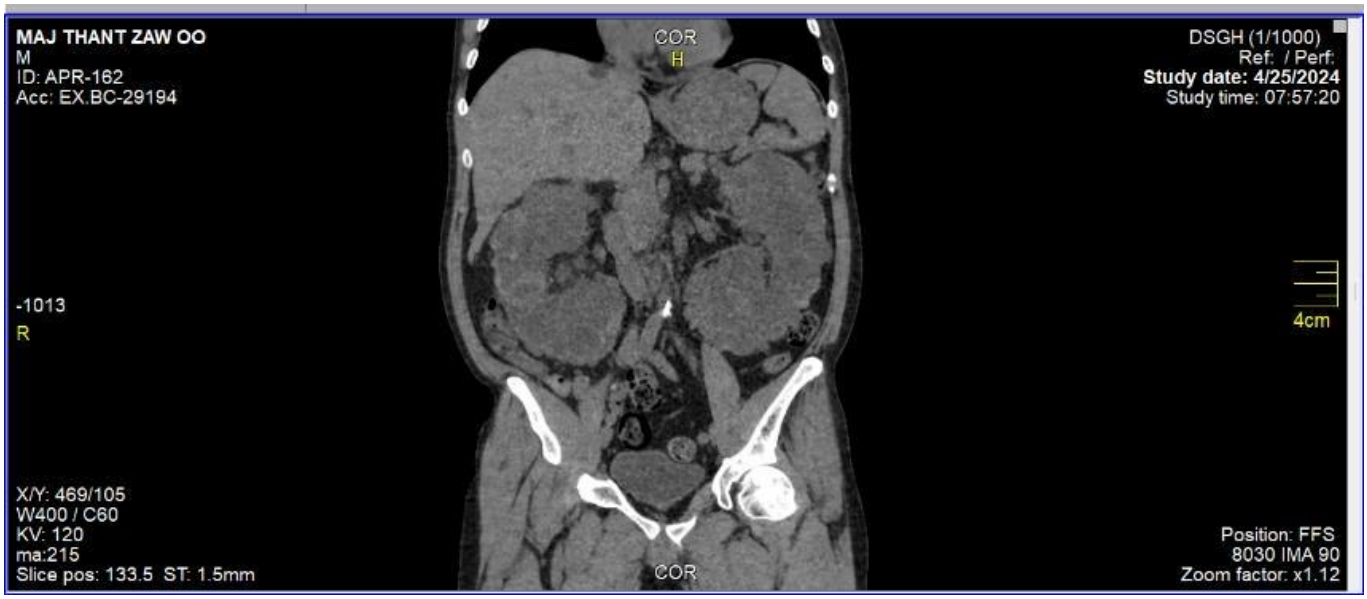

Photo (2) Non-contrast CT abdomen showing multiple large cysts in both kidneys occupying whole abdomen and multiple liver cysts

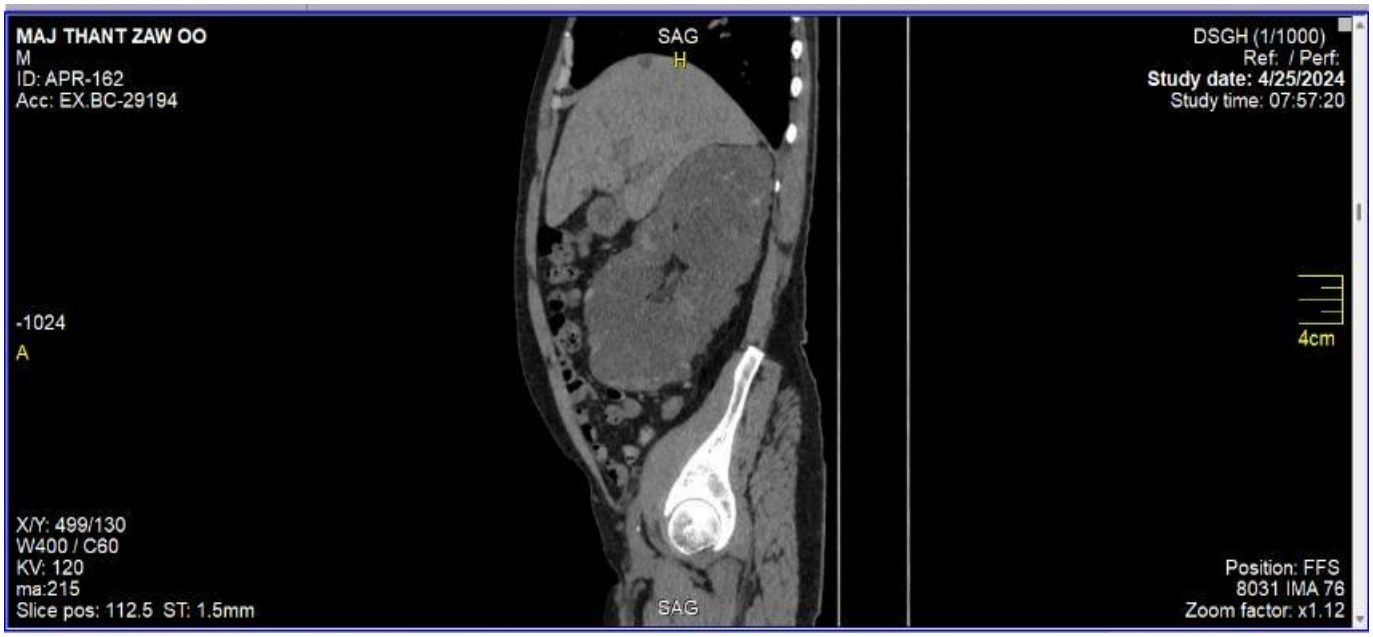

Photo (3) Non-contrast CT abdomen showing multiple large cysts in kidney and liver cysts

Photo (4) External surface of resected kidney revealing multiple cysts filled with blood

Photo (5) Cut section of resected kidney revealing multiple cysts filled with blood and the central cysts containing pus

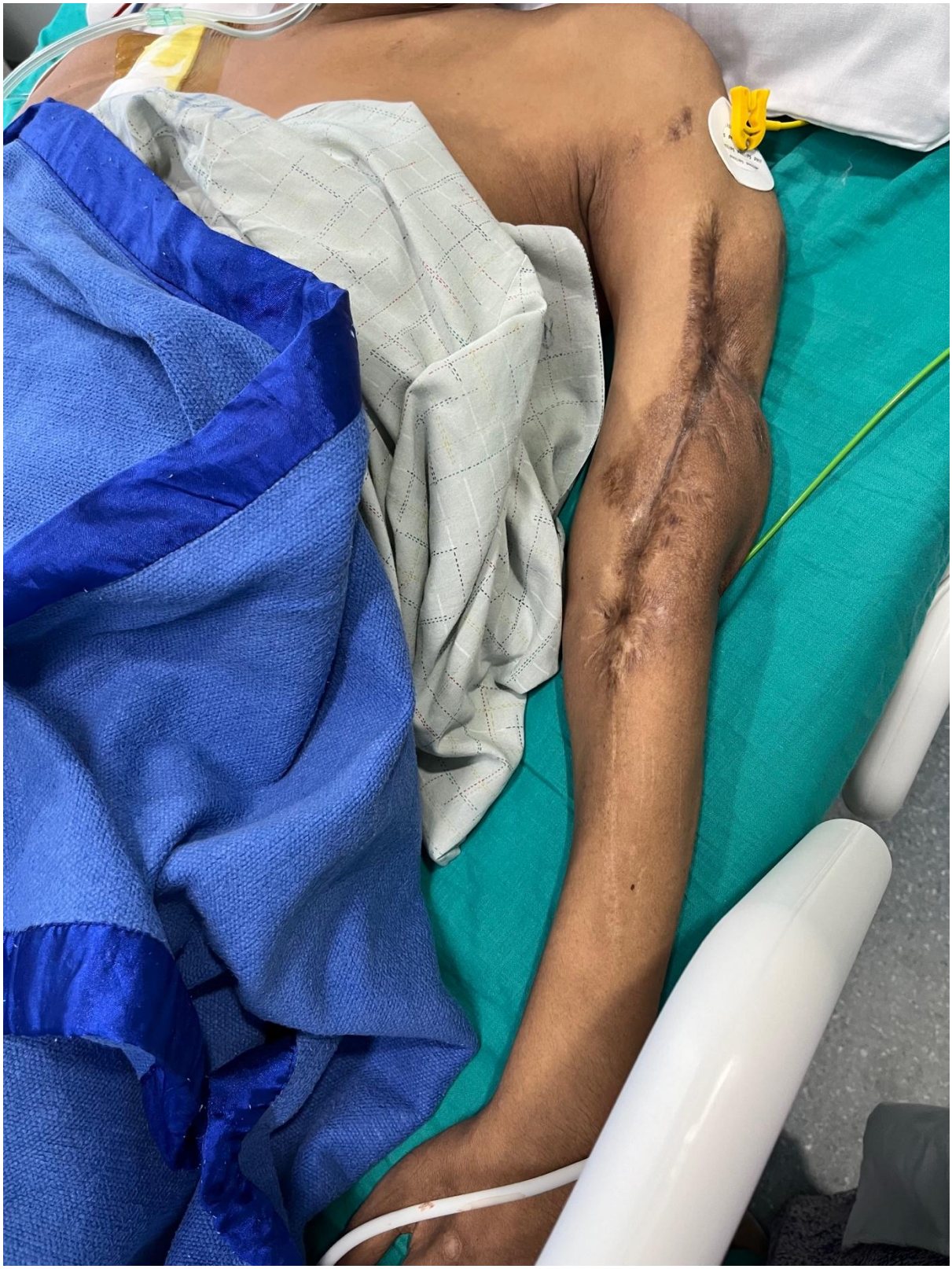

Photo (6) A large scar in arm healed from open fracture, wasting and contracture resulting from open fracture humerus due to Road Traffic Accident