

# Acute interstitial nephritis associated with cosmetic soft-tissue hyaluronic acid filler injections: Two case reports from Sarawak, Borneo

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## SUMMARY

**We report two cases of acute interstitial nephritis occurring in two women after having received cosmetic breast augmentation with breast filler injections. Both patients deteriorated rapidly developing acute kidney injury which required acute haemodialysis. They remained dialysis dependant but started to have renal recovery by week 7 and eventually were successfully weaned off dialysis. At 6 months post event, they remain dialysis free but continue to have chronic kidney disease with an eGFR 27 and 42 mL/min/1.73m<sup>2</sup> respectively.**

## INTRODUCTION

Cosmetic soft tissue fillers have been used to augment the appearance of facial contours, breasts, buttocks and other areas. Adverse effects associated with these cosmetic fillers have been reported however acute interstitial nephritis (AIN) associated with soft tissue filler injections is uncommon. We report two cases of AIN associated with hyaluronic acid cosmetic breast filler injections done by the same unlicensed practitioner.

## CASE PRESENTATION

### Case 1

We describe a 41-year-old lady, with no known medical illness who underwent a cosmetic bilateral breast filler procedure by an unlicensed practitioner on 17th March 2022. She received 500 mls of hyaluronic acid gel breast filler, injected at multiple sites bilaterally. Thirty minutes after the procedure, she developed dizziness and shortness of breath, with pain over bilateral breasts up to the neck region and she returned to the unlicensed facility to seek treatment.

She was then sent to the Emergency and Trauma Department (ETD) 4 hours post procedure, where she was hypotensive (BP 75/35 mmHg) and tachycardic (HR 107/min). There was no rash, fever or joint pains. Her initial blood investigations revealed a total white cell count of 39 000 and creatinine of 89 µmol/L. She was empirically treated as anaphylactic shock and intramuscular adrenaline and intravenous hydrocortisone was administered. Subsequently her blood pressure normalised and hydrocortisone was stopped after 1 day. Interestingly her urine pregnancy test was noted to be

falsely positive. She was confirmed not pregnant by negative transabdominal and transvaginal ultrasonography and negative serum beta-HCG.

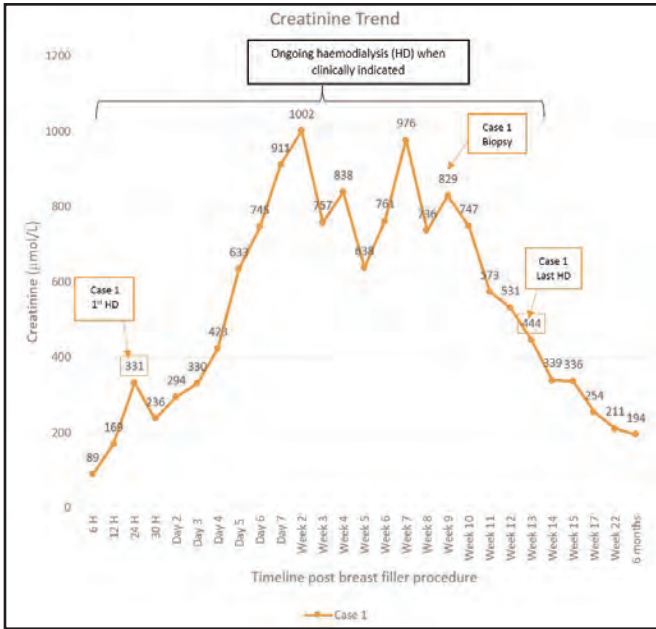
Despite adequate fluid resuscitation and blood pressure optimisation, she became oliguric and her renal function rapidly deteriorated with creatinine increasing to 169 µmol/L and 331 µmol/L at 12 hours and 24 hours respectively post filler. She also developed refractory hyperkalemia (K 7.3 mmol/L) despite medical therapy and a decompensated metabolic acidosis with a blood pH of 7.038, and bicarbonate of 5 mmol/L. She was admitted to the intensive care unit (ICU) and underwent acute haemodialysis.

On day 2 of ICU admission, infective changes over the breast wounds were noted, and an ultrasound was done which showed collections bilaterally. An ultrasound guided aspiration was performed and 20 mls of pus was aspirated. The pus culture grew *Pseudomonas aeruginosa* spp and the patient was treated with appropriate antibiotics. Throughout her hospital stay, multiple aspirations and wound desloughing were carried out however due to persistent and severe infection, bilateral mastectomy needed to be performed at week 4 post filler. Intraoperatively it was noted that the infection had extended to the pectoralis major muscle bilaterally. Histopathological examination showed extensive fat necrosis with neutrophilic microabscesses and areas of haemorrhage, as well as a marked foreign body inflammatory reaction surrounding some amorphous material, postulated to be the breast filler substance used.

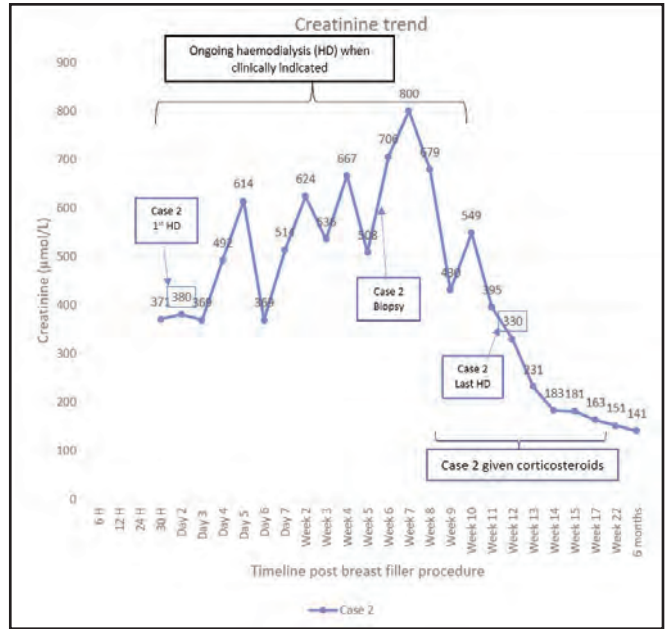
Another complication was noted about 2 weeks post filler procedure. The patient unexpectedly developed bilateral hearing loss. She was referred to the otorhinolaryngology (ENT) team and after assessment was deemed to have bilateral sensorineural hearing loss, postulated to be associated with the hyaluronic acid filler procedure. She was regularly assessed by the ENT team but despite all efforts this hearing loss persisted.

Throughout the admission, she needed multiple sessions of intermittent haemodialysis. Serum creatinine peaked at 1002 µmol/L at week 4 post filler (Graph 1) with her urine output at that time being 500 mls per day. Urinalysis showed leukocyturia and proteinuria, with urine protein:creatinine

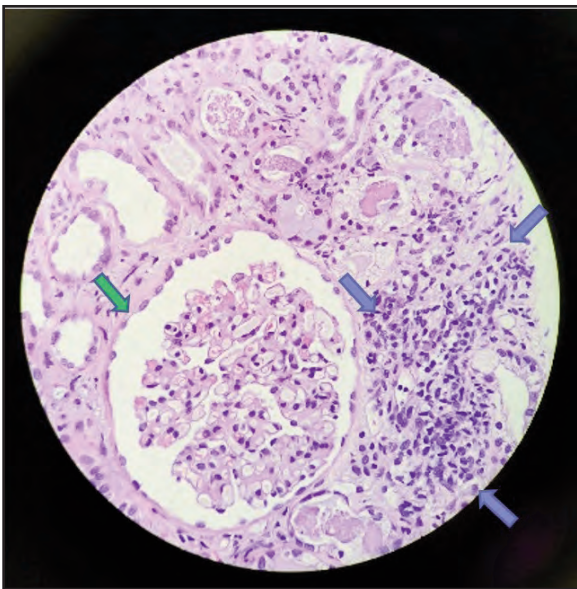
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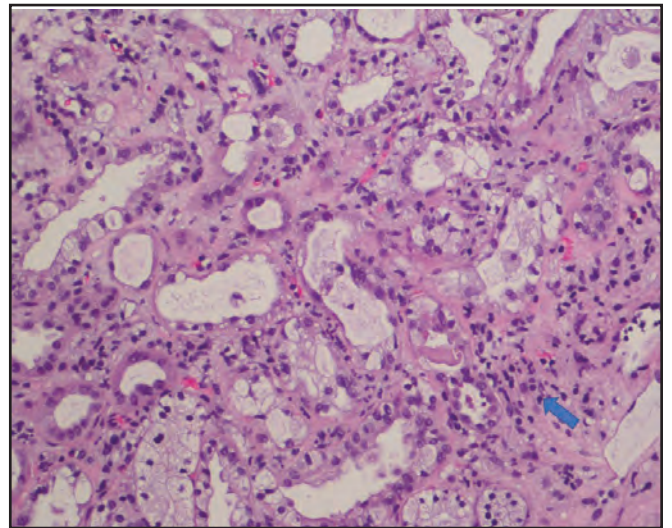
Graph 1: Creatinine trend of Case 1



Graph 2: Creatinine trend of Case 2



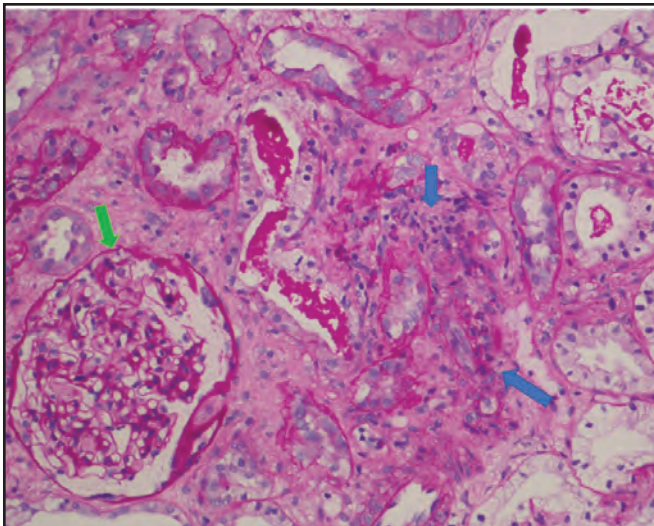
**Renal histopathology for Case 1**  
**Fig. 1:** Renal tubular granular cast with interstitial lymphocytic infiltrates depicting AIN (blue arrows). The glomerulus is normal (green arrow) (H&E stain, magnification 400 x)



**Renal histopathology for Case 2**  
**Fig. 2:** Dilated tubules with desquamated epithelium and casts within the lumen. Interstitial oedema with mixed mononuclear and neutrophilic infiltrate (blue arrows), occasional eosinophils are seen depicting AIN changes (H&E stain, magnification 200 x)

ratio of 166 mg/mmol. She had no evidence of a urinary tract infection. As she continued to require dialysis support, a renal biopsy was carried out 8 weeks after the initial breast filler procedure. It revealed acute tubular necrosis (ATN) and AIN with interstitial lymphocytic infiltrates (Figure 1). No steroids were given for her AIN due to the recent severe infection.

Her haemodialysis was gradually weaned down to once weekly and she was discharged after 2 months of hospital admission. She was successfully weaned off dialysis 3 months after filler injection and at last follow up at 6 months, her creatinine was 194 µmol/L, with an eGFR 27 mL/min/1.73m<sup>2</sup>. Urinalysis is negative for proteinuria and hematuria. Her hearing however still remains impaired.



**Renal histopathology for Case 2**

**Fig. 3:** Tubules are separated by oedema and inflammatory infiltrate (blue arrows) depicting AIN changes  
No change to glomerulus (green arrow) is noted  
(PAS stain, magnification 200 x)

**Case 2**

A previously healthy 33-years-old lady also underwent the same cosmetic bilateral breast filler procedure the next day, at 4 pm on 18th March by the same unlicensed practitioner. She also received 500 mls of hyaluronic acid gel injected at multiple sites bilaterally. Post procedure, she experienced swelling and pain over bilateral breast until her neck region which worsened and 30 hours later, she presented to the ETD with shortness of breath.

At ETD, her blood pressure was 122/79 mmHg with normal oxygen saturation but she was tachycardic (122 beats/min) and tachypneic (33 breaths/min). No rash, fever or joint pains were noted. Her electrocardiogram showed sinus tachycardia but no other features of pulmonary embolism was demonstrated. Initial blood investigations, revealed severe decompensated metabolic acidosis with a pH of 6.948 and bicarbonate of 3.1 but no hypoxemia. Other parameters taken showed acute kidney injury (AKI) with a serum potassium of 7.5 mmol/L, urea 14.4 mmol/L, and creatinine of 371 µmol/L. Her calcium was 1.6 mmol/L, phosphate 4.48 mmol/L and sodium was 116 mmol/L. Her total white count was high at 39 200 but other blood investigations including liver function tests were normal. Of note, the patient also had persistent false positive urine pregnancy test, but confirmed not pregnant after repeated assessments by the obstetric and gynaecology team.

She was intubated and resuscitated with intravenous (IV) crystalloids and sodium bicarbonate therapy. However in view of persistent metabolic acidosis and anuria, acute haemodialysis was initiated and the patient was admitted to ICU. Lung fields on her initial chest radiograph were clear, however 3 days later, she developed bilateral pleural effusion which required chest tube drainage due to persistent hypoxia. Pleural fluid analysis was transudative in nature. She was successfully extubated on day 5 of admission.

The patient underwent breast ultrasonography which revealed features suggestive of right breast mastitis which was treated conservatively and improved with antibiotics.

Similar to the first patient, she also developed bilateral sensorineural hearing loss about 2 weeks after the filler procedure and was seen multiple times by the ENT team.

In view of persistent anuria and dependence on dialysis, a renal biopsy was done 5 weeks post filler procedure which revealed AIN with eosinophilic, mononuclear and neutrophilic mixed interstitial infiltrates (Figure 2). She was started on IV methylprednisolone 500 mg for 3 days at week 8 post filler, followed by oral prednisolone 1 mg/kg/day for her AIN, which was tapered over 14 weeks.

Her serum creatinine peaked at 800 µmol/L (Graph 2) at week 7 post filler and she required regular intermittent haemodialysis. After this however, her urine output started to improve and her hemodialysis was gradually weaned down to once a week and she was discharged after 2 months of stay in hospital.

Her urine output and renal function continued to improve and the dialysis was successfully stopped 3 months after the filler procedure. Six months post filler procedure, her creatinine tapered to 141 µmol/L with an eGFR of 42 mL/min/1.73m<sup>2</sup> and repeated urinalysis is negative for proteinuria and hematuria. Her hearing however did not recover and she continues to have bilateral sensorineural hearing loss. The relevant authorities were notified regarding both cases and the unlicensed practitioner.

**DISCUSSION**

Cosmetic enhancement with fillers are not without complications. These include infection, dislocation of the injected gel, early degradation of gel, firm breasts and nodules, and visible nodules.<sup>1</sup>

An article published in the CDC Mortality and Morbidity Weekly Report reported three cases of acute renal failure associated with cosmetic buttock soft-tissue filler injections in North Carolina in 2007.<sup>2</sup> Records indicated that the injections contained liquid silicone. Of the three reported cases, creatinine on presentation was 4.2 mg/dL (371 µmol/L), 4.0 mg/dL (353 µmol/L) and 11 mg/dL (972 µmol/L) respectively. The second and third patients had a renal biopsy done. The second case showed ATN with casts, and the third demonstrated AIN. These two patients who underwent a biopsy required haemodialysis that was successfully weaned off and eventually their renal function returned to normal. The article highlighted the dangers of receiving cosmetic injections from unlicensed practitioners.

AIN is a condition which is characterised by inflammatory infiltrate in the interstitium of the kidneys. AIN has been found most often as a result of drugs, but infection, systemic diseases and idiopathic forms have also been identified.<sup>3-5</sup> AIN is a common cause of acute kidney dysfunction but interestingly, articles have described only a minority of patients (<10-15%) presenting with the classical triad of fever, rash and eosinophilia,<sup>3,6,7</sup> however a proportion of the cases needed renal replacement therapy.<sup>7</sup>

The use of corticosteroids in AIN is still controversial as data is limited. A few studies have shown benefits with corticosteroid usage.<sup>6,8</sup> In the study by González et al, patients who were not given steroid therapy had significantly higher final serum creatinine level and significantly higher proportion of patients required chronic dialysis.<sup>6</sup> This study also found benefit with earlier steroid initiation. Predecki et al found that steroid-treated patients had better eGFR at all time points post biopsy up to 2 years and fewer steroid-treated patients were dialysis dependant by 6 and 24 months.<sup>8</sup> Muriithi et al demonstrated that longer duration of drug exposure and longer delay in starting steroid therapy was associated with poorer renal recovery.<sup>9</sup> Overall, studies have shown that earlier offending drug withdrawal and earlier steroid usage was associated with better renal outcomes.<sup>4,6</sup>

We describe two cases of AIN associated with bilateral hyaluronic acid breast filler procedure which most likely had systemic absorption and was excreted through the kidneys.

Both patients developed the same clinical course of pain and swelling at bilateral breasts up to the neck region. Both patients' serum creatinine levels rose to 330-370 mmol/L one day post filler injection and both needed emergent dialysis. Thereafter both patients remained dialysis dependent for about 3 months but were successfully weaned off dialysis eventually with partial renal recovery

Case 1 presented earlier with anaphylactic shock, but had more severe infection of the breast injection sites requiring surgical intervention and hence did not receive steroids for her AIN. This could explain the more marked ATN seen on her renal biopsy. The AIN changes were not as pronounced possibly because her renal biopsy was performed 3 weeks later than case 2. After stopping dialysis, Case 1's creatinine remained higher compared to Case 2 up until 6 months.

Case 2 had a more delayed presentation resulting in severe anuric AKI but her infection was not as severe and she received a course of steroids for her AIN. These measures may have potentially aided in more rapid renal recovery as compared to case 1. The AIN was postulated to be due to an immune related response secondary to the hyaluronic acid filler injection which likely had systemic absorption. It is uncertain if earlier use of steroids would have made any difference in the final outcome as both cases were very ill in the early stage and steroid use was not considered then.

## CONCLUSION

To the best of our knowledge, these are the first two reported cases in Malaysia of AIN due to hyaluronic acid cosmetic breast filler injections resulting in severe dialysis requiring acute kidney injury, with eventual partial renal recovery. The public should be aware of potential adverse reactions with various cosmetic procedures and should be educated to seek treatment by licensed personnel.

Written informed consent was obtained from the patients for the publication of this case report and any accompanying images.

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