CASE REPORT

Acute kidney injury after breast augmentation using hyaluronic acid injection – A case series and review of literature

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SUMMARY

Breast augmentation (BA) is a common aesthetic surgery to attain the desired breast fullness or to rectify potential asymmetries. The use of injectable hyaluronic acid (HA) has become conveniently popular as an alternative to breast implant. We reported a series of four individuals who underwent BA with HA and subsequently experienced severe kidney injury requiring kidney replacement therapy (KRT). These individuals had their procedures done by unlicensed personnel. HA however is not a licensed product in Malaysia as breast implants. We aim to raise the awareness of the implications of such malpractice, including potential toxic effects and severe complications associated with HA injections.

INTRODUCTION

Breast augmentation (BA), is a popular surgical technique to enhance breast size and shape. This procedure involves the insertion of breast filler, enabling individuals to achieve their desired breast size with the use of injectable materials. Unlike traditional surgical interventions, BA with injectable fillers offers several advantages, including reduced hospitalization requirements and shorter recovery periods.[1]

One of the newest products utilized in BA procedures is Hyaluronic acid (HA).[2] However, the safety and efficacy of using HA specifically for BA remain unknown due to the scarcity of published scientific data.

By presenting this case series, we aimed to shed light on the potential risks and common complications associated with the use of HA for BA. Understanding such adverse outcomes is crucial for both medical professionals and patients, as it can aid in making well-informed decisions regarding the most appropriate and safe choices for breast enhancement procedures.

CASE PRESENTATION

Case 1

A 35-year-old woman with a history of bronchial asthma presented to the hospital with symptoms of dizziness, nausea, vomiting, and seizures, approximately four hours after her second BA procedure: involving the injection of 200ml of HA into her breasts under local anesthesia (LA). Her first BA, done a month prior, had no complications.

Upon arrival at the emergency department, the patient exhibited a Glasgow Coma Scale (GCS) score of E4V2M1 and required double inotropic support. She experienced two generalized tonic-clonic seizures and displayed physical signs of breast engorgement and erythema at the injection sites.

Blood tests revealed leucocytosis, high anion gap metabolic acidosis with serum lactate level of 9.1 and acute kidney injury (AKI). The patient was intubated for airway protection and admitted to the intensive care unit (ICU). In the ICU, she received continuous veno-venous hemodiafiltration (CVVHDF) and intravenous (IV) antibiotics.

After 19 days in the hospital, she was discharged home with improved kidney function. In her three-month follow-up, the patient exhibited full kidney recovery.

Case 2

A 42-year-old female patient, with no prior medical history, underwent her second BA procedure, receiving an injection of 2ml of LA followed by 200ml of HA as a breast filler. Immediately after the injection, she experienced dizziness, nausea, and multiple seizure episodes. Her condition upon arrival was critical, with a low GCS score and hemodynamic instability, necessitating inotropes and intubation.

The patient exhibited hypertonicity, hyperreflexia, and clonus during neurological examination, alongside erythema and swelling of the right breast at the injection sites. Blood investigations revealed leucocytosis, severe metabolic acidosis, AKI, and urine analysis showed proteinuria and microscopic hematuria.

She was admitted to the ICU and underwent CVVHDF while receiving IV antibiotics. Blood culture results were negative. Throughout her admission, she was closely monitored, underwent extubation, and received intermittent hemodialysis (IHD) as needed. A kidney biopsy was advised but declined by the patient. Ultimately, the patient chose to discharge herself against medical advice and was lost to follow-up.

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Table I: Clinical characteristics and outcome of the patients

Clinical Data	Patient No.			
	1	2	3	4
Age, yr	35	42	41	31
Sex	F	F	F	F
Race	M	M	M	M
Comorbidities	None	Bronchial Asthma	None	None
CKD status	No history of CKD	No history of CKD	No history of CKD	No history of CKD
Treatment Centre	Temporary Rental Apartment	Temporary Rental Apartment	Aesthetic Centre	Aesthetic Centre
Admission Urea, mmol/L	3.8	4.2	31.9	23.4
Admission Scr, mcmol/L	105	108	1097	616
Peak Urea, mmol/L	14.6	36.4	42.3	20.7
Peak Scr, mcmol/L	388	1014	1261	1142
Urinalysis Protein	3+	3+	NA	2+
Urinalysis Blood	4+	4+	NA	1+
Blood Culture	NG	NG	Serratia marcescens	NG
Breast Tissue Culture	NG	NG	Burkholderia cenocepacia	Candida and Aspergillus species
Kidney size, cm, right/left	NA	10.5/10.5	12.9/13.1	13.0/12.5
Vasopressor use at time of AKI	Yes	Yes	Yes	Yes
Risk factors for AKI	Hypotension, Infection	Hypotension, Infection	Hypotension, Infection	Hypotension, Infection
Kidney biopsy diagnosis	NA	NA	NA	Acute Interstitial nephritis and acute tubular injury
Dialysis	Yes	Yes	Yes	Yes
ICU admission	Yes	Yes	Yes	Yes
Mechanical Ventilation	Yes	Yes	Yes	Yes
Length of Hospital Stay, days	19	87	24	39
Clinical outcome of the AKI	Patient needed dialysis; AKI subsequently improved and patient came off dialysis	Dialysis dependent, however patient discharge against medical advice and defaulted follow up.	Dialysis dependent, patient died	Patient needed dialysis and became dialysis independent; develop CKD (eGFR 24 mls/min/1.73m^2)
Death	No	No	Yes	No

F, female; M, Malay; CKD, chronic kidney disease; Scr, serum creatinine; AKI, acute kidney injury; ICU, intensive care unit; NA, not available/applicable; NG, no growth.

Table II: Presenting signs and symptoms in Case 1 – 4,

Clinical signs and symptoms	Case No.			
	1	2	3	4
Seizure	•	•	×	×
Hypotension	•	•	•	•
Nausea/Vomitting	•	×	•	•
Body weakness	×	×	•	•
Urinary Retention	×	×	•	•
Breast infection	•	•	•	•
Blindness	×	×	•	×
Hearing loss	×	•	•	×

•, Indicates the presence of the clinical signs or symptoms; ×, Indicates the absence of the clinical signs or symptoms

Case 3

A healthy 41-year-old female sought BA at an aesthetic center who receiving 500ml HA injection. She later presented at a district hospital with a 3-day history of anuria after few days. Blood tests indicated AKI, transaminitis, and hypercalcemia, prompting her transfer to a tertiary hospital. During her hospitalization, the patient experienced sudden bilateral sensorineural hearing loss, and bilateral papilledema. She also developed bilateral breast abscesses due to breast filler injections. Her kidney function continued to decline, necessitating intubation and CVVHDF. Wound debridement was performed. Blood cultures revealed Serratia marcescens while breast tissue and pus cultures showed Burkholderia cenocepacia. Unfortunately, her condition continued to deteriorate and she succumbed to severe infection with multi-organ failure.

Case 4

A previously healthy 31-year-old woman was admitted to the hospital with epigastric pain, vomiting, and reduced urination two days after underwent a bilateral BA procedure involving HA filler injections at multiple sites. Physical examination revealed signs of sepsis, lethargy, and gangrenous tissues at the breast injection sites. She developed

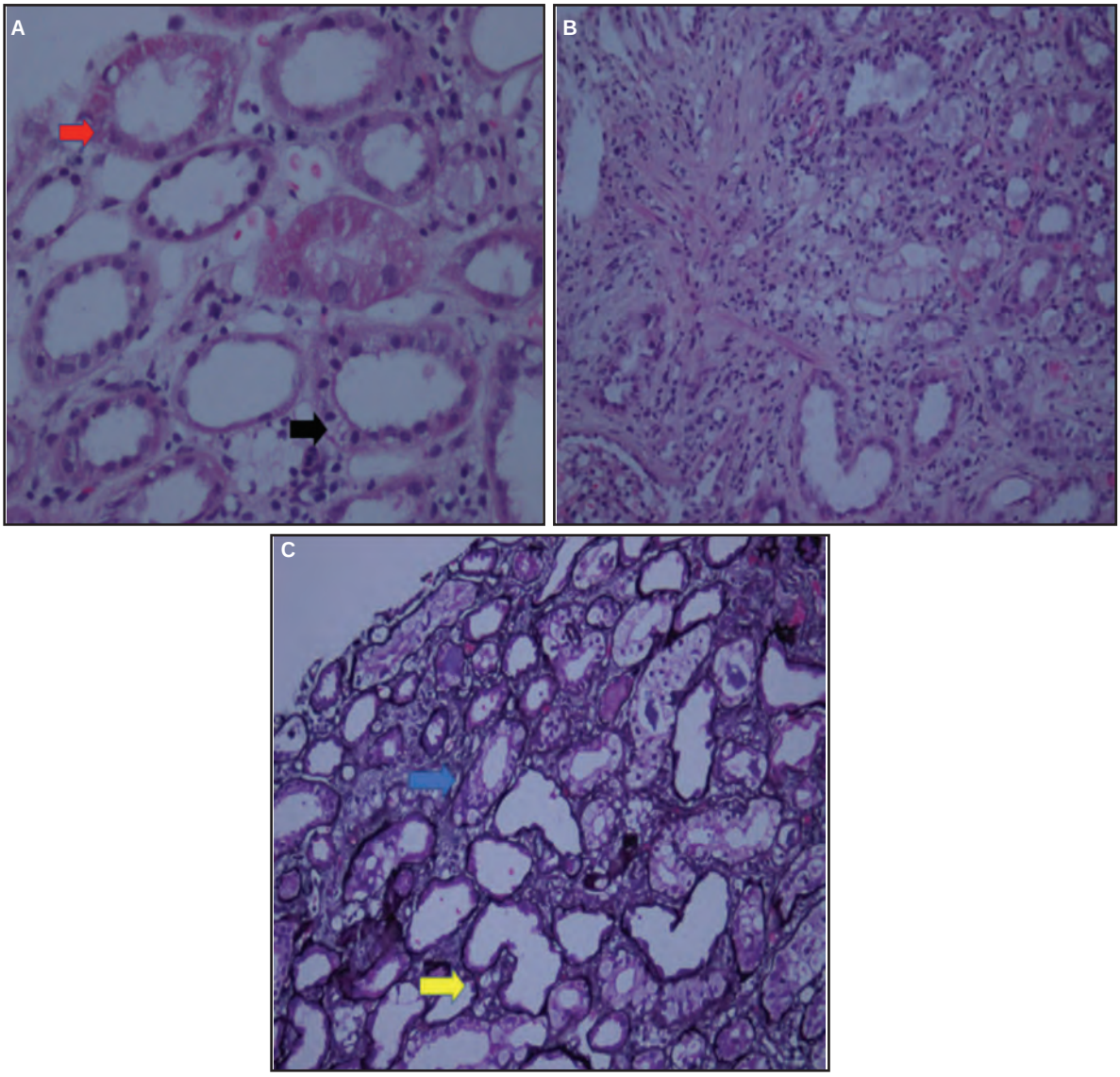

Fig. 1: Renal pathologic features associated with breast augmentation procedure in patient 4
(A) Tubular cell with loss of brush borders (red arrow) and presence of epithelial cells with cytoplasmic vacuolization (black arrow)
(B) Moderate inflammatory infiltrates in the interstitium
(C) Presence of dilated tubules (yellow arrow) and epithelial cell with vacuolization (blue arrow)

All images were obtained under polarized light microscopy. Images in A and B were stained under hematoxylin and eosin staining. Images in C was stained via silver stain

oliguric AKI with severe metabolic acidosis secondary to bilateral breast myonecrosis.

She received CVVHDF with slow kidney function recovery necessitated IHD for three weeks. Multiple wound debridement sessions were conducted with cultures revealing Candida and Aspergillus species. Antifungal treatment was administered in stages.

A kidney biopsy was performed in the fourth week of hospitalization revealed features of acute interstitial nephritis (AIN) and acute tubular injury. Inflammatory cell infiltrates were present, mainly consisting of lymphocytes with scattered neutrophils and occasional eosinophils. Glomeruli appeared normal.

In the fourth week of her hospital stay, the patient showed improved urine output and kidney function recovery. Follow-up assessments indicated healing breast wounds and improving kidney function over the subsequent weeks and months. Creatinine 232 mcmol/L at 6 months post discharge.

DISCUSSION

Within a span of four weeks in November 2021, four unusual young females with acute kidney injury admitted to four different hospitals in the southern state of Johor, Malaysia. The cases were collaborated on with in-house nephrologists, using clinical information derived from medical case notes.

We have summarized the findings, including patient characteristics, comorbidities, chronic kidney disease status, admission and peak serum creatinine levels, vasopressor use at the time of AKI, risk factors for AKI, dialysis initiation in the hospital, and patient outcomes as in Table I. The average age of the patients was 37 years, with minimal or no premorbid history. Among the four patients, all had severe AKI requiring kidney replacement therapy, and the mortality rate was 25%. Symptomatology and signs are provided in Table II, while Figure 1 shows the serial clinical data of the patients.

These four cases of AKI were caused by unlicensed and unsupervised injections of HA. Presently, neither the Food and Drug Administration nor the National Pharmaceutical Regulatory Agency has authorized any of the above liquid injectable substances for cosmetic use.

HA is a glycosaminoglycan polymer composed of repeating disaccharides (glucuronic acid and N-acetyl-glucosamine). It is naturally found and produced in cells and tissues such as joints, basement membranes and the vitreous of the eye. It provides structural and mechanical support.[3] Studies have postulated that HA interacts with CD44, leading to increased formation of fibrotic molecules and subsequent tubular damage.[4,5] These findings support the plausibility of HA as a contributor to the AKI observed in these cases.

Furthermore, ischemia-reperfusion injury is a well-known cause of AKI, involving hemodynamic changes, inflammation, and tubular injury.[5] Recent studies have hypothesized that HA may promote a pro-inflammatory environment during ischemia-reperfusion, leading to AKI. While the molecular weight of HA involved in this process remains uncertain, our presented cases prompt further exploration of its potential role in ischemic renal damage.

The above case series also reported other minor adverse events associated with cosmetic hyaluronic injections, such as swelling, hematoma, and pain.[6] Infections can occur as a result of a breach of the skin's surface integrity by injectable fillers, with infectious agents ranging from fungal, bacterial to viral.6 Severe infections were described in the above cases, leading to multi-organ failure, as evidenced by imaging, inflammatory markers, and positive cultures. In the renal biopsy of case 4, we saw AIN and acute tubular injury, with potential etiologies of infections and ischemia of the kidneys. Unsupervised cosmetic procedures performed by unqualified practitioners may compromise sterility and result in severe complications, as evidenced by our reported cases. The presence of Candida and Aspergillus in case four raises concerns about the risk of infections associated with injectable fillers.[6] This aligns with existing literature that highlights the potential for infections, including fungal, bacterial, or viral, to occur following cosmetic filler injections.[6]

Furthermore, the severity of the injury and poor outcomes linked to AKI worsen when there is a delay in recognition and subsequent treatment.[7] This is clearly illustrated in cases 3 and 4, where both patients delayed seeking treatment, resulting in severe kidney damage with a higher risk of mortality and morbidity.

In addition, vascular occlusion following filler injections is a recognized major complication, causing skin necrosis through localized obstruction or blindness or cerebral ischemic events due to distant obstruction.[6] Studies have postulated that high filler injection pressure could trigger embolization to the retinal circulation, causing loss of vision or into the intracranial circulation, causing cerebral ischemic events.[8]

According to the HA Safety profile document, there were rare but serious events included partial or complete vision loss following upper face injections, as well as brain infarcts or hemorrhage. The overall quality of evidence is moderate.[9]

Hearing issues are frequently mentioned in the context of surgical breast implant procedures, with hearing loss and tinnitus being the most prevalent complaints. The link between breast implants and hearing problems is thought to be associated with autoimmune or inflammatory responses triggered by adjuvants.[10] There are reports indicating substantial symptom improvement, partly with self-reported tinnitus, after the removal of breast implants.[10] Further research involving larger cohorts of women with breast implants is essential to confirm the presence of hearing impairments in this population.

Alternative options to hyaluronic acid injections include autologous fat transfer, which uses the patient's own fat harvested through liposuction to augment breast volume; however, it carries risks such as fat necrosis and cyst formation.[6] Breast implants use silicone gel but carry risks of capsular rupture and rare cases of implant-associated anaplastic large cell lymphoma.[6]

Our case series has several limitations. The limited number of kidney biopsies performed restricts the generalizability of our findings. Consent issues, patient choices, and the severity of illness prevented two patients from undergoing kidney biopsy, which may confirm various types of kidney injuries. Additionally, alternative inflammatory biomarkers were unavailable, which might have provided more insight into distinguishing inflammation from infection.

Crucial information of the specific components such as the concentration of HA derivatives and details about the injection and sterility techniques, were unavailable in most cases. This lack of information may impact the interpretation of our results and conclusions. Moreover, since there is no clear data on the total number of people undergoing BA in Malaysia, we cannot establish a clear incidence rate of such acute kidney injuries following BA procedures. Furthermore, the relatively short follow-up period and limited number of patients in our study prevented us from identifying specific patient characteristics or clinical features associated with more severe presentations, slower recovery or the need for dialysis.

Despite these limitations, our case series provided important insights into the potential risks and adverse effects associated with HA injections for BA. These cases also underscore the need for stringent regulation and licensing of practitioners administering cosmetic injections. Public awareness campaigns regarding the risks associated with seeking cosmetic treatments from non-licensed individuals are essential to promote informed decision-making by patients. Proper education on the potential hazards of unregulated procedures can empower patients to prioritize their safety and seek treatment from qualified medical professionals. We have reported to the enforcement unit of the State Health Department of Johor, Malaysia to tighten the policing of such malpractices. Since then, we are pleased that no such complications were seen over the subsequent two years.

CONCLUSION

This report highlights the troubling cases of four adult females who developed acute kidney injury (AKI) following breast augmentation with hyaluronic acid injections administered by unlicensed personnel. The outcomes varied, with one patient achieving full recovery, another succumbing to her condition, and a third progressing to chronic kidney disease. These findings emphasize the urgent need to raise awareness about the serious risks and potential toxic effects associated with unauthorized HA injections. We stress the critical importance of seeking cosmetic treatments exclusively from licensed and qualified medical professionals operating in regulated and hygienic facilities. The awareness generated from this report can play a pivotal role in safeguarding patient health and well-being when undergoing cosmetic procedures involving injectable substances like HA.

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DECLARATION

It is hereby affirmed that consent for publication has been obtained from the patient or their caregiver. Furthermore, it is declared that the Medical Research and Ethics Committee (MREC) of the Ministry of Health Malaysia (MOH) has determined that this study, being a case series, does not require MREC review or approval. The authors declared that there was no fund applicable for this study. The authors declare that there are no conflicts of interest regarding the publication of this paper.

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