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Community-associated methicillin-resistant *Staphylococcus aureus* causing diffuse xanthogranulomatous pyelonephritis in a neonate

Abdulnasir Al-Otaibi [a], Mohammad Al-Shaalan [a,*], Saud Al-Jadaan [b], Khaled O. Alsaad [c]

[a] Division of Infectious Diseases, Department of Pediatric, King Abdulaziz Medical City, King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia
[b] Division of Pediatric Surgery, Department of Surgery, King Abdulaziz Medical City, King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia
[c] Division of Anatomic Pathology, Department of Pathology and Laboratory Medicine, King Abdulaziz Medical City, King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia

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ABSTRACT

Xanthogranulomatous pyelonephritis (XGP) is an uncommon variant of chronic pyelonephritis; often associated with ipsilateral urological obstructive pathology and infection. It occurs rarely in the pediatric population and is caused usually by gram-negative bacteria. We herein present a case of a 6-week old male patient who presented with fever, gross hematuria and left flank tenderness. Urine and blood cultures were negative. Radiological investigations suggested an infiltrating malignant neoplasm of the kidney. There was no evidence of nephrolithiasis or obstructive pathology. A left radical nephrectomy was performed and histopathological examination revealed diffuse XGP. Microbiological culture of the perinephric purulent discharge proved positive for methicillin-resistant *Staphylococcus aureus* (MRSA). To the best of our knowledge, this is the first reported case of MRSA-induced XGP in a neonate emphasizing the expanding spectrum of disease secondary to community-associated MRSA.

Xanthogranulomatous pyelonephritis is a rare, severe, chronic form of pyelonephritis characterized by an exuberant, destructive infiltration of foamy macrophages with mixed inflammatory cells, multinucleated giant cell formation, and a granulomatous reaction. It is often associated with ipsilateral synchronous obstruction of the kidney with concomitant or superimposed infection by gram-negative bacteria; *Proteus mirabilis* and *Escherichia coli* being the most commonly implicated micro-organisms [1]. Xanthogranulomatous pyelonephritis is most often seen in middle-aged women, and typically found in patients with risk factors such as long standing nephrolithiasis or other urological obstructive conditions such as untreated urinary tract infections, diabetes, hyperlipidemia and immunosuppression [1,2]. It is uncommon in children and extremely rare in neonates and infants [3]. No single radiological feature has proven pathognomonic of XGP [4], and preoperative differentiation of XGP from other mass-forming renal pathologies, particularly malignant neoplasms, is either problematic or unachievable in most cases.

Methicillin-resistant *Staphylococcus aureus* is an important causative bacterium of nosocomial infections. However, *S. aureus* has rarely been reported as being an etiological micro-organism of XGP [5]; and more rarely, cases of MRSA-associated XGP [2,6,7]. We herein report a case of an XGP in a 6-week old male patient caused by community-associated MRSA (CA-MRSA), which is possibly the first reported case of CA-MRSA in this age group. We also reviewed pertinent cases in the literature.

1. Case report

A 6-week old boy was referred to our hospital for evaluation and management of a left renal mass. He was born normally at term following an uneventful pregnancy with normal antenatal ultrasound. He remained only a few hours in the nursery before discharged for home as a well-baby. The patient started to manifest occasional episodes of vomiting and tactile fever in his second week of life. At 20 days old, his mother noted gross blood in his urine, as he cried when pressure was applied to the left side of his abdomen. Physical examination revealed no fever, normal blood pressure for

* Corresponding author. Department of Pediatric, King Abdulaziz Medical City, P.O. Box 22490, Riyadh 11426, Saudi Arabia. Tel.: +966 11 801 1111x12576.
E-mail address: shaalanm1@ngha.med.sa (M. Al-Shaalan).

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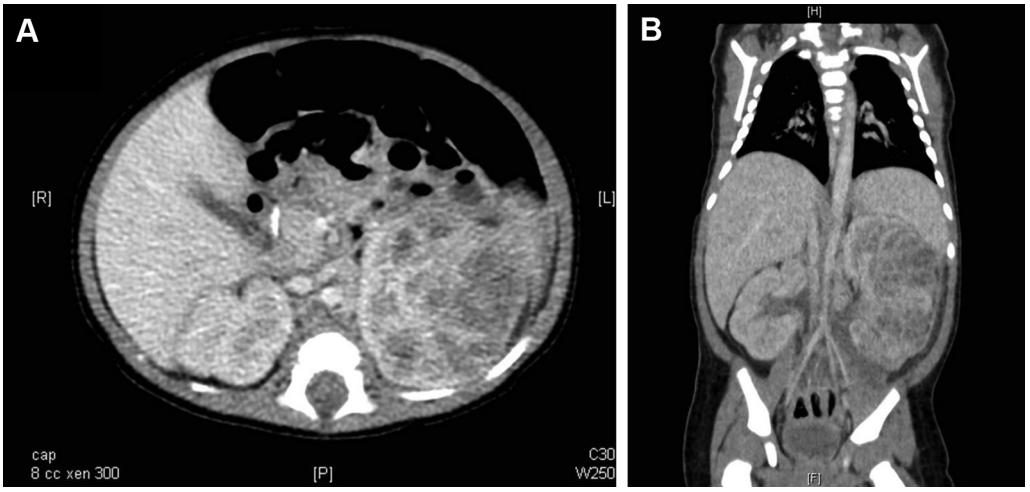

Fig. 1. (A and B) Computed tomography scan showing a large heterogeneous complex mass, involving most of the kidney parenchyma, and extending to the perinephric fat.

patient's age, but left flank fullness and tenderness. The remainder physical examination was normal. Blood tests showed a hemoglobin measurement of 96 gm/L and a leukocyte count of 20,000/mm^3. Serum electrolytes and renal function tests were normal. Urine and blood cultures were negative. Ultrasonographic and computer tomographic (CT) scans of the abdomen showed a large, heterogeneous complex mass involving most of the left kidney with extension into the perinephric fat radiographically (Fig. 1A and B). The radiological findings were highly suspicious of a malignant renal neoplasm. Accordingly, the patient underwent a nephrectomy procedure. Intra-operatively, the left kidney was adhered to the lateral abdominal wall and left colon. A purulent discharge, noted focally on the external surface of the kidney, was sampled and forwarded for microbiological analysis (Fig. 2A). Grossly, and after fixation in 10% buffered formalin, the kidney measured $9 \times 4 \times 3.5$ cm and weighted 100 g. Its external surface was grey and slightly nodular. The cut surfaces of the kidney revealed a cavitating lesion involving most of the renal cortex, medulla and renal pelvis measuring $7 \times 4 \times 3$ cm with nodular expansive boundaries, and containing a yellow-tan soft cheesy material (Fig. 2B). The lesion did not have a solid component. The renal pelvis was markedly distorted anatomically. Light microscopic examination revealed severe xanthogranulomatous pyelonephritis with a prominent focus of acute suppurative inflammation with numerous, variably-sized abscesses. The xanthogranulomatous inflammation was composed of sheets of foamy macrophages admixed with numerous lymphocytes, plasma cells, neutrophils and scattered eosinophils (Fig. 3A). The foamy macrophages expressed strong but diffuse immunostaining for CD68 (clone KP1, Dako, Carpinteria, California). Occasional multinucleated giant cells were noted (Fig. 3B). Foci of renal tubular neutrophilic microabscesses were seen; most evidently in the distal renal tubules. No well-defined epithelioid granulomas were seen. The inflammatory process extended into the perinephric adipose tissue, and renal pelvis. Special staining for acid fast bacilli (i.e., Ziehl-Neelsen stain) did not reveal mycobacteria. Periodic acid Schiff and Gomori's methenamine silver special stains were also negative for fungal elements. There was no evidence of malignancy.

The cultures from the perinephric purulent discharge grew MRSA, in accordance with the Center for Disease Control and Prevention criteria of CA-MRSA, and demonstrated a susceptibility to vancomycin, clindamycin, erythromycin and trimethoprim-sulfamethoxazole. The same organism was cultured from nares and nasopharyngeal aspirates of the patient. The patient's post-operative course was uneventful, and he was placed on parenteral vancomycin (60 mg/kg) for three weeks. A follow-up voiding cystourethrogram, to assess urine reflux was normal. The patient had shown no evidence of disease in the contralateral kidney three years post-surgery.

2. Discussion

Xanthogranulomatous pyelonephritis is a rare, severe form of chronic pyelonephritis, which is typically associated with chronic

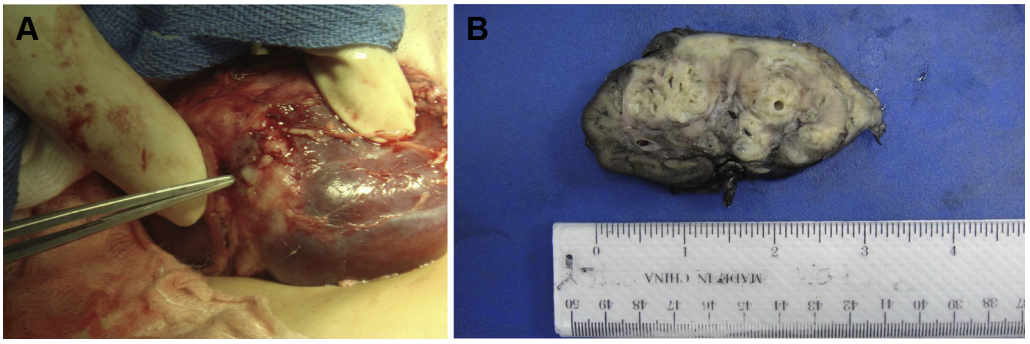

Fig. 2. A) Focal purulent discharge from the kidney was seen intraoperatively. B) Cut surface of the nephrectomy specimen demonstrating a vague tan-yellow nodular appearance of the lesion. The lesion significantly distorted the kidney and replaced most of its parenchyma.

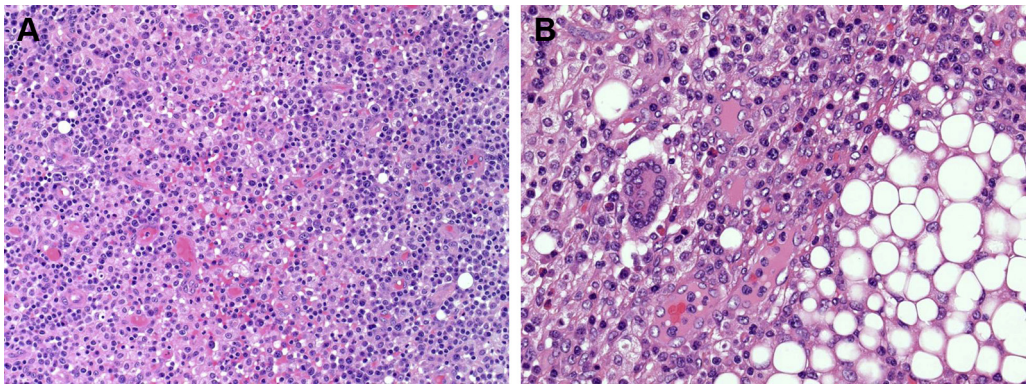

Fig. 3. A) Mixed inflammatory infiltrate with numerous foamy macrophages admixed with lymphoplasmacytic and neutrophilic inflammatory cell infiltrates was present [H&E ×200]. B) Scattered multinucleated giant cells were seen. Note the extension of the inflammatory process to the perinephric adipose tissue [H&E ×400].

obstructive uropathology with infection, and characterized by exuberant, commonly infiltrative xanthogranulomatous and suppurative inflammatory destruction of the renal parenchyma. Urinary tract obstruction due to calculi is implicated in the pathogenesis of most XGP cases [8]. Less frequently, non-calculus obstruction such as uretero-pelvic or vesico-ureteric obstruction can also be associated with XGP. The disease is often seen in middle-aged women particularly in those with long-standing obstructive uropathology, chronic depleting diseases and immunosuppression. Although XGP is uncommon in the pediatric age group, it occurs most frequently in patients under the age of eight without calculus obstructive pathology; despite the fact that XGP has been reported in all pediatric age ranges [2,9]. Rare cases of XGP have been described in neonates indicating possible prenatal origin of the disease [10] and in association with other etiological factors; such as altered immune response and disturbed leukocyte function; altered lipid metabolism; and lymphovascular or vascular obstruction [4].

Although the pathogenesis of the disease remains unclear, superimposed infection with subsequent atypical forms of inflammatory response and tissue destruction are believed to comprise the sequence of events in the development of XGP. Various bacterial organisms have been identified by urine culture, but most commonly, gram-negative bacteria: *P. mirabilis* and *E. coli* [1]. Less frequently encountered bacteria are *Pseudomonas* spp, *Streptococcus faecalis* and *Klebsiella* spp [11]. *S. aureus* has rarely been reported as being the causative organism of XPG [7].

Methicillin-resistant *S. aureus* is a major causative micro-organism of nosocomial infections worldwide. The infection is considered community-associated namely if: acquired outside of a hospital setting; within 2 days of hospital admission; or if occurring in a person not hospitalized within a 2-year period prior to the date of MRSA isolation [12].

The number of reported CA-MRSA infections in the pediatric population has been increasing. The majority of CA-MRSA infections are typically resulting from mild skin and soft tissue infections; however, severe, oftentimes life-threatening invasive diseases such as sepsis, necrotizing pneumonia, pyomyositis and osteomyelitis do occur in children and adults with no risk factors [13,14].

Xanthogranulomatous pyelonephritis caused by MRSA is extremely rare, and only three cases have been documented in the literature; two in adults [6,7] and one in an adolescent [2]. The first patient with MRSA-induced XGP was a 41-year-old diabetic woman described by Treadwell et al. [6]. She developed a 4 cm XGP in the left kidney and had positive blood and urine cultures for MRSA. Despite appropriate antibiotic therapy, the patient had recurrent bacteremia, and nephrectomy was performed. Cultures from renal tissue also grew MRSA. In this particular patient, MRSA infection was thought to be acquired from a previous hospitalization (hospital-acquired MRSA) during an outbreak in the surgical service. Kempker et al. [7] reported the first case of XGP caused by CA-MRSA in a 52-year-old, Human Immunodeficiency Virus (HIV) infected woman. The patient's urine and blood cultures were negative, but abdominal CT scanning demonstrated a 17.5 × 12.8 cm mass in the right kidney. The risk factor for CA-MRSA infection in this patient was presumed to be intravenous drug use with hematogenous seeding to the kidney. Cultures from intra-renal purulent material and kidney tissue grew MRSA. Both these adult patients were African Americans and the diagnosis of XGP was established histopathologically from nephrectomy specimens.

Chalmers et al. [2] reported the initial case of MRSA-induced XGP in the pediatric population. The patient was a 16-year-old male who presented with febrile illness and a complex, cystic lesion in the left kidney and negative cultures. The source of infection in that case was considered to be hematogenous seeding from an unsterile tattooing procedure. Histopathological examination of the nephrectomy specimen revealed XGP and tissue culture grew MRSA.

Our case was unique in that it represented the likely first occurrence of neonatal XGP caused by MRSA, considered as being community-acquired, with negative urine and blood cultures, and our patient had no evidence of obstructive uropathology. Yet similar to most cases of XGP, the diagnosis was established histologically after nephrectomy, and MRSA was isolated from the perinephric purulent material. Transient bacteremia and hematogenous seeding of MRSA from nasopharyngeal colonization seemed to be the probable source of infection.

In conclusion, although XGP occurs in the pediatric age group, it is evidently rare in neonates. Methicillin-resistant *S. aureus* is an atypical causative organism of XGP, while CA-MRSA infection is a more unlikely etiological factor for XGP. To the best of our knowledge, this is the first report of a neonate who developed XGP caused by CA-MRSA infection. Invasive MRSA infection and XGP should be considered in neonates with fever, flank mass and hematuria even if blood and urine cultures are negative, and in the absence of risk factors commonly associated with the pathogenesis of XGP.

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