Emphysematous pyelonephritis (EPN) was first described in 1898 as gas formation by uropathogens resulting in acute necrotizing and perirenal parenchymal infection [1]. The number of reported cases of EPN is <800 cases worldwide to date; however, the mortality rate of EPN ranges from 11% to 42% [2]. It is usually believed that antibiotic alone is usually ineffective in treating EPN; hence, surgical nephrectomy is necessary. However, several studies have found that the treatment of antibiotics alone can be effective [1]. Hemophagocytic lymphohistiocytosis (HLH) commonly occurs in children, and its occurrence in adults is rare. A retrospective study in Sweden reported an incidence of HLH-related malignancy in adults of 0.9% (8/887) [3]. Another cohort study revealed an average age of about 50 years for the majority of men (60%) [3]. In adults, the prevalence of HLH is estimated to be one in every 2000 adults hospitalized at tertiary health centers [4].

Here, we present the case of a 45-year-old woman who was diagnosed with EPN with a history of HLH, which is a rare case in a female adult, and who received medical therapy alone.

CASE REPORT

A 45-year-old woman presented to the emergency room complaining of right flank pain radiating to the lower right abdomen and a fever for 1 day. The patient had a previous history of right ureteric stenosis and had undergone ureteral dilatation. She has systemic lupus erythematosus (SLE), diabetes mellitus, chronic kidney disease, and HLH, which was diagnosed 1 year ago and was given methylprednisolone.

A general examination revealed a blood pressure of 120/80 mmHg, a heart rate of 112 ×/min, a respiratory rate of 20 ×/min, and an axial temperature of 38°C. Physical examination found anemic conjunctiva with right abdominal and lumbar tenderness. Examination of the kidneys revealed pain in the right costovertebral region.

Hematological examination showed Hb: 7.5 g/dL (12–14), Ht: 23% (37–43%), leukocytes: 14.700 10³/L (5.000–10.000), platelets: 268 10³/L (150–450), and GDS: 300 mg/dL (<200). Kidney function tests revealed urea at 107 mg/dL (10–50) and creatinine at 3.30 mg/dL (0.6–1.2). A complete urine examination showed pH 7 (5.0–7.5), leukocyte esterase 2+/125 cells/L, urine protein: trace/10 mg/dL, bacteria >100/HPF.

The patient was given intravenous fluids, ciprofloxacin, omeprazole, and insulin injections. 2 days later, an urinary tract ultrasound was performed, which discovered that the right kidney was difficult to assess in size because its lower pole was covered in lesions, which is a fluid collection with internal echo that...
appeared to contain an air component. In addition, the impression on the lower perirenal pole was approximately 13.9×7.2 cm. While the left kidney had a hyperchoic lesion with a small posterior acoustic shadow that measured 0.67 cm in diameter (Fig. 1). Then the patient was examined on computed tomography (CT) scan of the abdomen without contrast and found that the right kidney looked more hyperdense and a broad subcapsular fluid collection was seen with an air bubble; therefore, the right kidney was pushed ventromedial and the left kidney appeared to have a stone with a diameter of 0.84 cm (Fig. 2).

Based on an evaluation by a urologist, conservative management was necessary in the absence of urinary tract obstruction. On urine culture, *Klebsiella pneumoniae* bacteria were found with a total of >100000 CFU/mL. Antibiotic resistance tests showed that the bacteria were resistant to ampicillin, ampicillin-sulbactam, cotrimoxazole, gentamicin, amikacin, aztreonam, cefotaxime, ceftriaxone, piperacillin-tazobactam, ceftazidime, ciprofloxacin, and tigecycline. The bacteria were only sensitive to Meropenem and Ertpenem. The antibiotic ciprofloxacin was replaced by meropenem. 1 week later, the patient was re-examined for hematology and urinalysis, and there was an improvement. After 1 week of treatment, the patient had no complaints of pain and was discharged. The patient was followed up 3 days later.

**DISCUSSION**

EPN is a rare urological emergency condition. Generally, EPN is more prevalent in women than in men (ratio 6:1), with an average age of 55 years [5]. Common infectious causes are *Escherichia coli* and *K. pneumoniae* (69% and 29%, respectively) [6]. The number of cases in the left kidney is higher (67%) than in the right kidney (23%), while bilateral cases are the rarest, around 5–6% [5]. Risk factors for EPN generally occur in patients with uncontrolled diabetes mellitus. In non-diabetic cases, renal failure and immunosuppression are rare risk factors [7, 8]. Urinary tract obstruction is also one of the risk factors for the development of EPN [5]. In our case, the patient’s risk factors were uncontrolled diabetes mellitus, an autoimmune disease that required immunosuppressive drugs, and a history of right ureteral stenosis.

The pathophysiology of EPN involves the following five factors: (i) gas-producing bacteria; (ii) hyperglycemia (encourages rapid bacterial growth); (iii) tissue perfusion disturbances (regional oxygen transport in the kidney can be further hampered by diabetic nephropathy, leading to tissue ischemia, necrosis, and nitrogen retention on tissue necrosis); (iv) weakened immunological response as a result of vascular supply issues; and (v) obstruction of the urine outflow due to pathological, functional, or anatomical causes [5,8].

Clinical manifestations of EPN are non-specific, including fever, flank pain, nausea, vomiting, disturbance of consciousness, shock, acute kidney injury, and disseminated intravascular coagulation [8]. Leukocytosis, thrombocytopenia, acid-base and/or electrolyte imbalance, acute kidney disorder, hyperglycemia, hematuria, and proteinuria were found by laboratory study.

An abdominal X-ray commonly appears as a gas shadow over the affected kidney. Ultrasonography can show local echoes indicating the presence of intraparenchymal gas. The diagnostic imaging study of choice for determining the severity of an emphysematous process and assisting in therapeutic decision-making is CT [5]. Other than EPN, the differential diagnosis for gas in the renal parenchyma includes emphysematous pyelitis, localized renal abscess, perforated duodenal ulcer, unintentional or intentional injury to the kidney or bladder (through surgery, biopsy, urinary bladder catheterization, implantation of a nephrostomy tube, etc.), and enterorenal fistula [9, 10].

The treatments for EPN are medical management (MM), MM + endoscopic or percutaneous drainage, and emergency nephrectomy. According to Huang and Tseng, treatment can be

**Figure 1:** Ultrasonography of kidney. The white arrow indicated that the right kidney had a collection of fluid with internal echoes that appeared to contain an air component

**Figure 2:** CT scan urography. (a) Coronal view; (b) Axial view. The white arrow indicated that the right kidney had a large collection of subcapsular fluid seen with air bubbles
classified using a CT scan. Gas appears only in the renal collecting system, class (1). Gas appears only in the renal parenchyma without involving the extrarenal space is class (2). Expansion of gas or abscess occurs into the perinephric space is class 3A, whereas expansion of gas or abscess into the pararenal space is class 3B, and bilateral EPN or solitary kidney with EPN is class 4. All of the patients in either class 1 or 2 without obstruction are given MM [11]. In our case, from the results of the CT scan, it was class II and received medical treatment.

HLH is a rare and potentially fatal disease caused by uncontrolled immune cell activation and an excessive inflammatory response [12]. Based on the HLH-2004 criteria, the diagnostic criteria for HLH should include molecular diagnosis consistent with HLH or five of the eight HLH criteria, including fever (>38.5°C) for more than 7 days, pancytopenia (Hb <9.0 g/L, platelets count <100 × 10⁹/L, absolute neutrophil count <1.0 × 10⁹/L), splenomegaly, hemophagocytosis in the bone marrow or spleen or lymph node, hypertriglyceridemia (fasting triglycerides ≥265 mg/dL) and/or hypofibrinogenemia (fibrinogen ≤1.5 g/L), ferritin ≥500 μg/L, low or absent NK cell activity, and soluble CD25 (sIL-2 receptor) ≥2.400 U/mL [13]. HLH is divided into primary and secondary categories. Primary HLH, also known as familial HLH, is induced by genetic mutations. Secondary HLH, or acquired HLH, is caused by external triggers such as malignancy, infection, rheumatologic disease, drug hypersensitivity, post-allogeneic hematopoietic stem cell transplantation, or other underlying causes [14].

Infection is the most common trigger for secondary HLH, especially Epstein-Barr virus infection. Several studies suggest some microbes are associated with HLH in tropical areas, such as Mycobacterium, Hepatitis E, Plasmodium, Leptospira, Leishmania, etc. HLH triggered by staphylococcal UTI has been little explained [13]. Some studies show that negative-gram bacteria can also trigger HLH, such as K. pneumoniae, multidrug-resistant E. coli, and Pseudomonas aeruginosa [15]. In our case, urine culture showed multidrug-resistant K. pneumoniae infection, which might be the trigger of HLH. Infections can cause uncontrolled proliferation of lymphocytes and massive macrophage activation, which can lead to the release of inflammatory cytokines responsible for the clinical symptoms of HLH [12]. Whereas, in our case, the patient had been diagnosed with HLH and SLE and was undergoing immunosuppressant therapy. While undergoing immunosuppressant therapy, signs and symptoms of HLH were controlled, but the use of immunosuppressant drugs was a risk factor for developing EPN. In the literature, we did not find any association between HLH and EPN.

CONCLUSION

EPN is a rare and life-threatening disease. Clinical manifestations of EPN are non-specific, so it needs an imaging modality like a CT scan. Treating EPN is based on CT scan classification. Medical treatment was an option for these patients. There is no direct association between EPN and HLH; it is a challenging decision to treat patients presented with both. Besides the classification, the physician’s choice of treatment should also look up the other clinical conditions of the patient.

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