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A Novel Prognostic Scoring System for Emphysematous Pyelonephritis

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Abstract

Introduction: Emphysematous pyelonephritis is an aggressive disease, the management of which has changed drastically over the past years. We present our experience of 128 cases of EPN managed in the Department of Urology, Govt. Stanley Medical College and Hospital, Chennai, during the period august 2015 - January 2019.

Aim of the study & objectives

1. To study the various prognostic factors involved in EPN
2. To device a scoring system to indicate the prognosis of the patient

Materials and Methods: The study design is both a retrospective & prospective analytical study, done during the period of august 2015-January 2019. All patients diagnosed to have EPN by CT were studied about their clinical and demographic information, laboratory findings, clinical features at initial presentation, imaging findings, type of management and patient outcomes were obtained from the medical charts.

Results: The overall survival rate was 92.18% (118/128) with only 10 patients requiring nephrectomy. On statistical analysis, the five independent variables (hypoalbuminemia, shock, bacteraemia, need for haemodialysis, thrombocytopenia) were significantly associated with poor prognosis. A Novel Scoring System called Stanley Scoring System was derived using the above five parameters. Stanley Score ≥ 4 indicated poor outcome with sensitivity 100%, specificity 93.10%, positive predictive value 86.67%, and negative predictive value 100%.

Conclusion: With the advancement in the field of radiology, newer antibiotics & better dialytic support, early diagnosis and effective conservative management of EPN has become possible. The patients presenting with Stanley score ≥ 4 needs to be aggressively managed.

Keywords: EPN; Prognostic factor; Scoring system

Introduction

Emphysematous pyelonephritis is a life-threatening disease that had a mortality of about 60 - 80% during the 1980s when managed by non- surgical means invariably resulting in nephrectomy. However, with the advent of radiological imaging and antimicrobials, the scenarios have changed with most of the cases being managed conservatively and mortality rates have dropped down 19 -40 %. We present our experience in the management of 128 cases of EPN at a tertiary care hospital.

Aim of the study

1. To study the various prognostic factors involved in EPN at Stanley Medical College from august 2015- January 2019.
2. To device a scoring system to indicate the prognosis of the patient.

Materials and Methods

The study design is both a retrospective & prospective analytical study, done during the period of august 2015- January 2019. 128 cases diagnosed to have EPN by radiological imaging (CT) were studied about their clinical and demographic informa-

tion, including age, sex, underlying medical conditions, laboratory findings, clinical features at initial presentation, imaging findings, type of management and patient outcomes were obtained from the medical charts. The clinical features included signs and symptoms at presentation and the patient's hemodynamic and mental status. The laboratory variables included HB, blood sugar, white blood cell count, LFT, platelet count, thrombocyte count, prothrombin time, C-reactive protein, albumin, sodium, HbA1c, and serum creatinine levels; and results of urinalysis, blood, wound, and urine cultures. All patients with suspected pyelonephritis (loin pain, fever, and vomiting) underwent a sonogram of the abdomen followed by computed tomography of the abdomen.

Definition

In accordance with the classification system of Huang and Tseng, which is based on the extent of air seen on CT, patients were divided into the following four types of EPN: class 1, gas in the collecting system only; class 2, gas in the renal parenchyma without extension to the extra renal space; class 3A, extension of gas or abscess to the perinephric space; class 3B, extension of gas or abscess to the Para renal space; and class 4, bilateral EPN or a solitary kidney with EPN .Thrombocytopenia was defined as a platelet count of less than 1,20,000/mL, hypoalbuminemia as serum albumin <3.0 g/dL and hyponatremia as serum Na <135 m Eq/L. The shock was defined as a systolic pressure less than 90 mmHg. Recurrent EPN was determined when both the clinical presentation of sepsis and progressive lesions disclosed on the imaging study were noted within 3 months after adequate treatment of EPN. A poor outcome was defined as death or recurrent EPN. A good outcome was defined as survival without recurrent disease.

Patients were aggressively managed with fluid resuscitation, glycemic control with insulin and either third-generation cephalosporin or piperacillin-tazobactam. The patients were treated by the team of Urologists, Nephrologist and Intensivists. Further management of the patients was based upon the CT classification, the general condition of the patient and renal parameters. Dialysis was initiated according to the Nephrologist's opinion based on the general condition and serum creatinine. Surgical management included Double J Stenting of the ureter, percutaneous drainage, open drainage, and nephrectomy. All patients underwent CT 1 week after the first imaging to assess the treatment response.

Results

Variable	Survived(n=118)	Died (n=10)	p-value
Diabetes mellitus	106(89.83%)	10(100%)	0.62
Hypertension	38(32.20%)	5(50%)	0.593
Old CVA	13(11.01%)	0(0)	1
Liver cirrhosis	14(11.86%)	8(80%)	0.455
Leucocyte count(>10000/ml)	12.76	15.26	0.807
Obstructive uropathy	68(57.14%)	7(70%)	0.629
Urolithiasis	55(46.61%)	7(70%)	0.6
Platelet count(10000/ml)	227.5	120	0.117
Thrombocytopenia(<120000/ml)	43(36.44%)	10(100%)	0.003
Hypoalbuminemia(<3 gm/dl)	43(36.44%)	10(100%)	0.003
Shock	4(3.38%)	8(80%)	0.003
Bacteraemia	21(17.79%)	8(80%)	0.039
Need for hemodialysis	5(4.20%)	5(50%)	0.039
Acute kidney injury	47(39.83%)	8(80%)	0.295
Hyponatremia	18(15.25%)	5(50%)	0.159
Altered mental status	26(22.03%)	8(80%)	0.063
C- reactive protein	6.84	5.41	0.562
Pyuria	84(71.18%)	10(100%)	1
Haematuria	55(46.61%)	10(100%)	0.26
HbA1c((>8)	48(40.73%)	5(50%)	1
Polymicrobial infection	46(38.98%)	10(100%)	0.009
Alkaline phosphatise>120IU/ml	65(55.08%)	10(100%)	
HB <11 gm/dl	59(50%)	8(80%)	
Prolonged PT	78(66.10%)	8(80%)	

Table 1: Analysis of Demographic and clinical parameters in EPN.

Urine Culture	Wound/Pus Culture	Blood Culture	Overall
E. coli (37.25%)	P. mirabilis (12.5%)	E. coli (15.6%)	E. coli (43.6%)
Polymicrobial (21.9%)	E. coli (9.4%)	Polymicrobial (3.1%)	P. mirabilis (15.6%)
	P. aeruginosa (6.3%)		P. aeruginosa (12.5%)
	Polymicrobial (9.4%)		Enterococcus species (12.5%)
			K. pneumonia (9.4%)
			Candida species (9.4%)
			Polymicrobial (34.4%)

Table 2: Causative organisms from blood, urine wound/pus.

The mean age of the patients was 62 years (SD = 15.8). There were 87 women and 41 men. Female predominance was observed. A total of 116 patients (90.62%) had diabetes mellitus. Obstructive uropathy occurred in 58.59% of patients and urolithiasis occurred in 48.43% of patients. Other comorbidities included hypertension (43 patients, 33.59%), liver cirrhosis (22 patients, 17.18%), cerebrovascular accident (13 patients, 10.15%), and acquired immunodeficiency syndrome (4 patients, 3.1%). Seven patients had bilateral involvement. In the other patients, the left side was more frequently involved (69.53%) than the right side (25%).The shock occurred in 12 patients, and 34 patients had altered mental status on the initial presentation. Acute kidney injury was seen in 55 patients. 11 patients underwent emergency hemodialysis, and 5 of these patients died. The mean leukocyte count at admission was 12 600/μL. Thrombocytopenia and hypoalbuminemia were present in 53 out of128(41.40%) and 53 out of 128 (41.40%) patients, respectively. 31 patients had class 1, 42 patients had class 2, 25 had class 3A, 23 had class 3B, 7 had class 4 CT imaging findings. E. coli was the most common organism cultured from specimens of urine, blood, and wounds, and was present in 56 (43.75%) patients. The other organisms included Proteus mirabilis (15.6%), Pseudomonas aeruginosa (12.5%), Enterococcus species (12.5%), Klebsiella pneumonia (9.4%) and Candida species (9.4%). Urine culture was positive in 51 patients, and 46 patients had a polymicrobial infection. E. coli was the most common organism isolated from urine specimens (19 patients). Bacteraemia occurred in 31 patients (24.21%), with polymicrobial bacteraemia in 10 and E. coli in 16 patients. Culture of pus from the wound or percutaneous drainage was positive in 35 of 128 patients, with polymicrobial culture in 18, Proteus mirabilis in five, E. coli in 9 and Pseudomonas aeruginosa in three patients. Overall, the polymicrobial infection was found in 56 patients (43.75%) The overall survival rate was 92.18% (118/128). Hypoalbuminemia (P = 0.033), bacteraemia (P = 0.039), the need for emergency hemodialysis (P = 0.039), thrombocytopenia (P=0.003) shock on initial presentation (P = 0.003) were significantly more frequent in the non-survivors than in the survivors. There were no significant differences between the non-survivors and survivors with respect to age, history of diabetes mellitus, causative organisms, acute kidney injury, leukocyte count, and the presence of microscopic haematuria, pyuria, urinary tract obstruction, and urolithiasis. Recurrent EPN occurred in seventeen patients (28/128, 21.87%) and four finally patients died.

Management

Patients are managed depending on the severity as follows

- Antibiotics alone – 38
- Antibiotics +PCD – 28
- Antibiotics + URSL +DJ stenting – 26
- Antibiotics+ URS +DJ stenting – 27
- Emergency nephrectomy – 3
- Elective nephrectomy -- 6

Treatment with antibiotics alone was successful in 38 patients. Third-generation cephalosporin's were the most frequently used antibiotics and were used alone in 29 patients (for cases caused by E. coli or Proteus mirabilis). Treatment with percutaneous drainage with and without and antibiotics was successful in 24 of 28 patients; the other four patients died. 27 patients underwent emergency DJ stenting with antibiotics. Three patients underwent emergency nephrectomy and survived. An elective nephrectomy was carried out in 6 patients with a poorly functioning kidney to sum up, 38 patients received antibiotics alone, 28 patients experienced percutaneous drainage and antibiotics, 26 patients accepted ureteroscopic lithotripsy and Double-J stenting, 27 patients with URS & DJ stenting, 3 patients underwent emergency nephrectomy & 6 patients underwent elective nephrectomy. The Five independent variables (hypoalbuminemia, shock, bacteraemia, need for hemodialysis, thrombocytopenia) were significantly associated with poor prognosis in patients. Trend analysis showed that the

risk of death was directly associated with the number of prognostic factors (P = 0.002). The morbidity and mortality of the patients increased when 4 or more of the parameters mentioned (hypoalbuminemia, shock in the initial presentation, bacteraemia, thrombocytopenia, need for hemodialysis) were present. In Stanley medical college we developed a scoring system consisting of the above 5 factors (shock, hypoalbuminemia, bacteraemia, thrombocytopenia, need for HD) and applied for the above patients (42 patients out of total 128 patients, analysed retrospectively) & inferred the following results.

Factors	Point
Shock	1
Hypoalbuminemia	1
Bacteraemia	1
Thrombocytopenia	1
Need For Hd	1

Table 3: Stanley Scoring System for EPN.

Stanley Score ≥ 4 Indicates Poor Prognosis

Stanley Score≥4	Poor Outcome	Good outcome	Total No Of Patients
	+	-	
+	13	2	15
-	0	27	27
	13	29	42

Table 4: Development cohort.

Development Cohort

Sensitivity = 100%

Specificity = 93.10%

Positive predictive value = 86.67%

Negative predictive value = 100%

Regarding the outcome, after the management, 2 patients died within 24 hours of admission, and 2 patients died within 72 hours of admission in the hospital. Out of the remaining thirty-eight patients, 32 recovered completely while 6 patients developed chronic kidney disease (4 in Class III and 2 in Class II). The survival rate of our series was 90.47 %. The need for surgical intervention increased when the CT classification of EPN was of higher class. The above scoring system was implicated for prognosis in 86 patients out of 128 patients prospectively and the results obtained are:

Stanley score≥4	Poor outcome	Good outcome	Total no of patients
	+	-	
+	21	1	22
-	1	63	64
Total	22	64	86

Table 5: Validation Cohort.

Validation Cohort

Sensitivity -95.45%

Specificity-98.43%

Positive predictive value-95.45%

Negative predictive value-98.43%

Regarding the outcome, after the management, 4 patients died within 24 hours of admission, and 2 patients died within 72 hours of admission in the hospital. Out of the remaining 80 patients, 66 recovered completely while 14 patients developed chronic kidney disease (8 in Class III and 6 in Class II).

Discussion

Our study is a single institutional case series, included cases studied over three years of which 42 patients were analysed retrospectively and 86 patients were followed and analysed prospectively. Patients with EPN require immediate attention because of the life-threatening nature of the associated septic complications. [1]. The present study sought to identify factors that were predictive of high mortality and poor outcome and to device a scoring system to indicate the prognosis of the patients. It was found that the persons with 4 or more of the factors in the scoring system had a poor outcome compared with others which were confirmed by the statistical analysis. Diabetes mellitus appeared to be the most common risk factor for EPN. All the patients diagnosed to have EPN by computed tomography were managed by either antibiotic alone (38 patients) or surgical interventions in addition to antibiotics (90 patients). Similar to other series the bilateral EPN was uncommon; only 7 patients had bilateral disease. The most common organism isolated from the urine culture in the study was E. coli and Klebsiella similar to other studies. [2].

The results summarised above shows except for 10 patients, the remaining 118 survived and out of the 118, 20 ended up in chronic kidney disease. The 6 patients who died on the day of admission had Class III EPN, altered sensorium, shock, elevated creatinine, and thrombocytopenia. The patients died despite aggres-

sive resuscitation and PCD. The surgical intervention was done based upon (I) the presence of hydroureteronephrosis (Double J stenting of the ureter), (II) PCD based upon CT findings (Class III), (III) not responding to conservative management and (iv) an extensive disease. Only four patients required open drainage since the patient didn't improve after PCD. Nephrectomy was done in three patients after 72 hours again due to the patient not responding to conservative management. The literature shows that patients managed with antibiotics and PCD had low mortality (13.5%) as against 25 percent when managed with nephrectomy. As proposed by Huang and Tseng, higher the grade in CT classification of EPN, morbidity, and mortality increased ($p = 0.046$). The triad of thrombocytopenia, altered mentation, the shock is associated with poor prognosis [3-7]. Our series reflected the same (altered sensorium $p = 0.063$, shock $p = 0.003$,). In addition, our study detected that hypoalbuminemia ($p=0.003$), thrombocytopenia($p=0.003$), bacteraemia ($p=0.039$), need for HD ($p=0.039$) was associated with poor prognosis and outcome. Falagas ME et al in his meta-analysis had shown overall mortality of 25%, however, our study had very little mortality (7.81%). Unlike in the past era when the mortality was about 50% to 60%, [8] with the advent of imaging studies and effective conservative management most of the patients are being saved. All patients presenting with urosepsis especially diabetic population should be evaluated radiologically to rule out EPN and aggressively managed.

Limitations

It is a retrospective analysis and the number of cases was too small to analyse other risk factors. The small number of patients could account for the lack of significance of some of the factors analysed. Second, several comorbidities, such as liver cirrhosis, might be associated with risk factors, such as thrombocytopenia. Third, we did not definitively designate a specific follow-up period. However, in our patients, the longest time to recurrent EPN was 3 months from the initial medical treatment. Therefore, we believe that a 6-month follow-up period is sufficient to demonstrate the trends of the disease outcomes. There were no laboratory or clinical features that strongly predicted the need for nephrectomy. Larger prospective studies are required to corroborate the present results

Conclusion

The management of EPN has drastically changed, with most of the cases being managed conservatively while in the past it was invariably nephrectomy. The advancement in the field of radiology, with the newer antibiotics and better dialytic support, early diagnosis and effective conservative management have become possible. Nephrectomy is indicated when patient not responding to conservative management or when there is an extensive disease which will not respond to conservative management. The patients presenting with Stanley score ≥ 4 needs to be aggressively managed.

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