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Eosinophilic Cystitis, Iatrogenic Bladder Rupture, Post Subtotal Cystectomy with Central Catheter Diversion, with Induced Pancytopenia

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Abstract

Eosinophilic cystitis (EC) is a rare disease. We describe two cases, where presentations of the disease were similar. 2 uneventful normal vaginal deliveries to highlight probable causes of the disease, symptoms, clinical findings, and treatment modalities, we reviewed 56 cases over a 10- year period. The most common symptoms were frequency, dysuria, urgency, pain, and hematuria. Common clinical findings were presence of bladder mass, peripheral eosinophilia, and thickened bladder wall. Recurrence of fever, dysuria, pyuria. Developed profound cytopenias with hematuria (Hb~7g/dl, TLC~200-300/uL, Plt~5-10K/uL). Was found to Klebsiella sepsis with UTI with septic encephalopathy and was and was managed with broad spectrum intravenous antibiotics. She also developed bladder clots, initially was kept on Foley's and no intervention was done due to cytopenias. Gradually cytopenia improved with growth factors (GCSF and Romiplostim). For persistent bladder symptoms, she underwent cystoscopy which revealed inflamed bladder mucosa, and during extraction of organized clot, she had an iatrogenic bladder rupture with extravasation of urine that required cystoplasty. She required ~20 PRBC and 12 SDAP's from February to May 2022. She developed a small capacity bladder that was leading to recurrent episodes of UTI and Bladder obstruction symptoms. A repeat marrow showed non-specific

changes. A variety of medical treatments were used, most frequently steroids, antibiotics, and antihistamines. Recurrence occurred in patients on tapering or discontinuing prednisone, among other reasons. There is no consensus about the treatment of EC, but in light of our findings in this review, the treatment of choice in our department was tapered prednisone over 6–8 weeks in combination with antihistamine.

Name: SP, 38/Female

R/O: Mandi, HP

Cr. No: 202202233898

Ad No: 2022048524 DOA:12/7/22

DOD: 28/7/22

Unit: Pulmonology (Prof ANA)

Clinical Discussant: Anil Batta

Medical Biochemistry: Prof Nandita Kakkar

Neurosurgeon: Dr Ravi Mohan

Hematology: Pulkit Rastogi

Radiology: Uma Debi

History: Had 2 uneventful normal vaginal deliveries.

June 2018: Patient had oral ulcers, diarrhea, and fever. Was evaluated and found to have leucopenia: HB: 10.9 g/dl, TLC: 1.7 x 109 /L, Plt:2.6x109 /L. Bone marrow was done that was variably cellular, mild increase in eosinophils. Received GCSF x 10 days, counts recovered, and she was fine for next 1 year.

July2019: Recurrence of oral ulcers, diarrhea, and fever, found to have Pancytopenia. Hb: 7.9g/dl, TLC:1.4x109 /L, Plt:1.72x109 /Repeat marrow was done: No evidence of dysplasia. Again, received GCSF counts normalized.

July2019-Dec2021: Asymptomatic

Jan-May2022: Recurrence of fever, dysuria, pyuria. Developed profound cytopenias with hematuria (Hb~7g/dl, TLC~200-300/uL, Plt~5-10K/uL). Was found to Klebsiella sepsis with UTI with septic encephalopathy and was managed with broad spectrum intravenous antibiotics. She also developed bladder clots, initially was kept on Foley's and no intervention was done due to cytopenias. Gradually cytopenia improved with growth factors (GCSF and Romiplostim). For persistent bladdersymptoms,she underwent cystoscopy which revealed inflamed bladder mucosa, and during extraction of organized clot, she had an iatrogenic bladder rupture with extravasation of urine that required cystoplasty. She required ~20 PRBC and 12 SDAP's from February to May 2022. She developed a small capacity bladder that was leading to recurrent episodes of UTI and Bladder obstruction symptoms. A repeat marrow showed non-specific changes.

First admission: 7/5/22-8/6/22: (Pvt ward under CHMO): Admitted with persistent hematuria, on and off fever and dysuria and leucopenia. Was diagnosed as MDR Klebsiella UTI and Pneumonia (BAL was negative for fungi and bacteria/MTB), received IV antibiotics Her leucopenia resolved with antibiotics, and she was discharged on oral antibiotics after a bladder biopsy with a diagnosis of infection associated cytopenias, UTI and Pneumonia.

Current admission: 2/7/22-28/7/22(Urology-RICU): Diagnosed as Eosinophilic cystitis, was admitted for Cystectomy with bladder reconstruction.

Date	Symptoms	Hb (g/L)	TLC/ANC ($x10^9$/L)	Plt ($x10^9$/L)	Rx
JUNE'18	Oralulcers, fever,	109	1.7	2.7	GCSF
JULY'19	Oralulcers, fever,	79	1.4	1.72L	GCSF
JAN'22	UTI, Hematuria	65	1.2/0.6	6	GCSF, Romiplostim
MAY'22	Fever, Hematuria	73	1.3	70K	Recoveryspontaneous

Examination: Conscious and oriented to time/place/person

Vitals: 110/70 mm hg, PR: 88 bpm, RR: 18/min, spo2: 98% at room air, Temp: Febrile

Pallor Emaciated, Pallor Present, Nail and Skin Pigmentation, Foley's Catheter in situ.

Systemic Examination: Respiratory: B/L NVBS CVS: S1 S2 normal. No murmur heard.

	May (Beginning) Pvtward	May	June	July Pre-Op	July PostOpD5	July PostOpD10
Hemoglobin(g/L)	**73**	**81**	**82**	**96**	**89**	**81**
WBC($x10^9$/L)	**2.1(N51/L21)**	**1000 (N20L70)**	**5500 (N60L20)**	**8500 (N68L21)**	**400**	**100**
ANC($x10^9$/L)	**1.1**	**200**	**3800**	**5500**	**240**	**20**
MCV/MCHC/Retic						**100/32/0.1**
PBF						**Noatypia, normocytictomacrocyticcells**
Platelet($x10^9$/L)	**175**	**211**	**169**	**111**	**77**	**5**
Sodium/Potassium	141/4.1	140/3.2				**150/3.92**
Urea/Cret	22/0.61	34/0.9	22/0.8	16/0.52	34/0.37	**72/0.9**
Calcium/Phosphate	7.8/4.1	8.8/3/3				
PT/INR/aPTT/PTI/Fib	14/1.1/28/4.1/-	WNL		WNL	30/2.1/45/45%	
T.Bilirubin/Direct Bilirubin	**2.92**/0.88	1.04/0.81			**3/2.2**	**10/9.1**
TotalProtein/Albumin	6.3/2.22	6.4/3.5		6.3/2.8	4.5/2.2	**4.4/1.7**
AST/ALT/ALP	30/13	22/11		22/26/120	37/19/118	**14/16/127**
LDH	161	290				
ETAspirate C/S						***ACB,KPneu***
BloodCulture						***ACB***
UrineCultures	***KPneu***	***KPneu***		Sterile		
PusCulture					***KPneumo***	***EColi***
Beta D Glucan/Galactomannan	-	**Neg**				
BALWUp/ BAL G-man	-	**Neg**				

P/A: soft, no organomegaly. bowel sounds present CNS: E4V5M6 Pupils: bilaterally normally reactive to light. Sensory system: Normal Investigations **Pancytopenia Work Up:** Bone Marrow: Variably cellular, mild dymega karyopoiesis. Inherited Marrow Failure Syndrome Next Generation Sequencing Gene Panel: Neg, MDS Gene Mutation Panel: Neg, FISH for MDS: Negative, Conventional Karyotype: Normal PNH FCM: Neg Immunoglobulin Profile: Normal, Chronic Granulomatous Disease Work Up (NBT Test): Negative DCT: NegHIV/HBsAg/AntiHCV: neg ANA/dsDNA/ANCA: Neg :

Positive (Collected Postmortem), COVID PCR: Negative S-14885/22: Bladder Biopsy: Eosinophilic cystitis.

Arterial Blood Gas

Date	21/7/22	23/7/22	25/7/22	27/7/22
PH	7.3	7.4	7.4	**7.11**
PO2	40	25	91	**55.4**
PCO2	30	28	26	**48**
HCO3	14	18	18	**15**
LACTATE	0.91	1.7	1.55	**6.6**
MODE OF VENTILATION	**CMV**	**CMV**	**CMV**	**CMV**

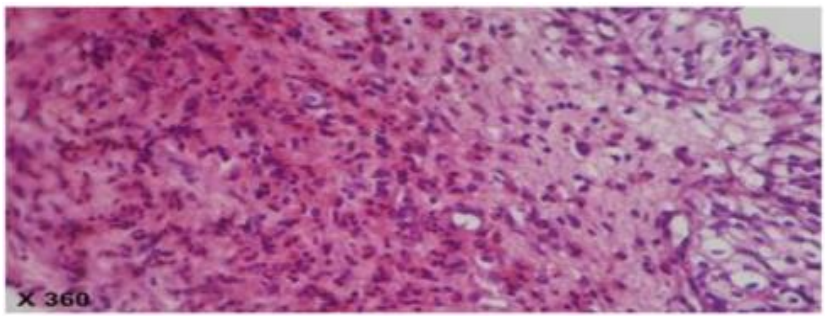

Figure 1: Histopathology image showing abundant eosinophils infiltrating the mucosa and lamina propria.

Course and Management

Current Admission

Urology stays (12/7/22-21/7/22): For her persistent dysuria and pain after all clearances, she underwent partial cystectomy with bladder reconstruction with central catheter drainage on 16/7/22. Post-surgery on day 4, she developed hypoxia (20/7/22 1:30 pm) associated with orthopnea and worsening cytopenias. She was evaluated for PTE, her DVT screening and cardiac markers (SOB kit) came negative. She was managed with PRBCS, Platelets. She received diuretics for fluid overload and was shifted to RICU from the private ward.

RICU stay (21/7/22-28/7/22): She continued to have worsening hypoxia, hypotension and altered sensorium that required mechanical ventilation.

Repeat 2D Echo was s/o cardiomyopathy, global hypokinesia (EF 30-35%). Her pus swab from surgical site yielded Klebsiella for which she was given colistin. She also had features suggestive of necrotizing enterocolitis and worsening jaundice for which she was kept NPO. She was given Filgrastim, Amphotericin, Metronidazole and Vancomycin along with cardio-respiratory and hemodynamic vasopressor support. However, she succumbed to worsening shock on 28/7/22. Her ET gs/cs and drain c/s reports were available postmortem which showed growth of ACB and E. coli, respectively.

Discussion

Peripheral eosinophilia is detected in about 43% of cases [2], more than half of cases without significantly elevation of peripheral eosinophilia. Eosinophils are rarely shed and degrade rapidly in urine; therefore, urinalysis usually reveals proteinuria, microscopic hematuria, pyuria [3], only rare cases with eosinophilia. Bladder irritation was the main manifestation of most EC patients, with frequency (67%) and dysuria (62%) [2]. The main manifestation of our patient was right lumbago and dysuria, which may own to the huge follicle-like mass lesion on the right portion wall and the neck of the bladder. It is suggested that not all bladder irritation or abnormal urinalysis could be found in EC cases. Imaging examinations are not helpful in determining those present as diffuse or irregular thickening of the bladder wall, or as nodular or huge masses. There were no characteristic manifestations with EC. Tumor-mimicking masses, polyps, follicles, ulcers, mucosal edema, hyperemia and erythema have all been reported. The large tumor-mimicking masses like our case was relatively rare and easily misdiagnosed. Eventually, pathological biopsy is needed, more than 25 eosinophils per high power field of view can be diagnosed with EC [4]. Significantly elevation of peripheral eosinophilia with the mucosa and submucosa was seriously involved in acute stage of EC, chronic mucosal inflammation was usually observed in chronic stage [4], which may the reason why cystoscopic biopsy affirmed the chronic mucosal inflammation of bladder with no eosinophilia founded in this patient. Few literatures were reported on EC complicated with other disease. We report herein the case of large mass-forming EC complicated with CG diagnosed by biopsy. CG is a inflammatory disease with a low incidence, which characterized by the Brunn nests existed in the lamina propria of bladder stimulated by inflammation, obstruction and stone [3]. CG with large-area follicle-like and papillomatoid changes was classified as high-risk type, which with the risk of malignant transformation [4]. For patients with tumor-like masses, we speculate that EC and CG may mutually aggravate the progression of the disease, but whether EC would complicate with CG or malignancy tumor is unknown. There is no consensus on the treatment of EC, medical treatments such as glucocorticoids, antihistamines, and antibiotics can be regarded as the initial treatment [5]. The recurrence of those patient who treated with medicine was 17%, whereas that was only 2.6% who treated with surgery [2]. For our patient, diagnostic transurethral resection of the bladder was performed, after that, antibiotics, glucocorticoids, and antihistamines were treated. Surgery is recommended for the treatment of those with large tumor-like or follicle-like lesions [1]. The patient recovered uneventfully without evidence of recurrence, which revealed that surgical treatment was preferred for large tumor-like EC complicated with CG. Taken together, large tumor-like eosinophilic

cystitis complicated with cystitis glandularis is rare, malignant tumors need to be ruled out. We deem that prompt biopsy led to the exact diagnosis; appropriate treatment led to better prognosis.

Final Diagnosis

Eosinophilic Cystitis, Iatrogenic Bladder rupture, post subtotal cystectomy with central catheter diversion, with sepsis induced pancytopenia (Gram Negative [K Pneumoniae, Acinetobacter, E Coli])

Cause of death

Refractory Septic Shock

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