

HISTOPATHOLOGICAL CHARACTERISTICS OF KETAMINE-ASSOCIATED UROPATHY AND THEIR CLINICAL ASSOCIATION

Hypothesis / aims of study

Previous studies revealed some bladder histopathologic characteristics in patients with ketamine associated uropathy (KU). However, comprehensive studies of the histopathological findings in KU and their association with the clinical disorder are lacking.

Study design, materials and methods

Thirty-eight patients with KU who had provided detailed clinical histories and had undergone video urodynamic studies were examined. Of them, 13 had clinically mild KU and underwent cystoscopic hydrodistention. The other 25 patients had severe KU and underwent enterocystoplasty with or without ureter reimplantation. Bladder and ureter specimens were obtained and stained with hematoxylin and eosin for histological examination. The mucosa, muscle and subserosal layers of bladder and ureter were examined respectively. The severity of the histopathological findings was graded on a 4-point scale (0: none, 1: mild, 2: mild, and 3: severe). The histopathology findings and grading were correlated with clinical parameters, including visual analogue scale for pain (VAS), cystometric bladder capacity (CBC) and maximal bladder capacity (MBC) under general anesthesia.

Results

Inflammatory cells infiltration and nerve hyperplasia were found in the mucosa, muscle, and subserosal layers of the bladder and ureters in patients with KU. In mild KU, lymphocyte infiltration predominated. In contrast, significant neutrophil, eosinophil, lymphocyte and plasma cell infiltrations were found in almost all severe KU bladders mucosa. Clinical severe KU was significantly correlated with severe to moderate lymphocytes, plasma cells, neutrophils, eosinophils infiltration and nerve hyperplasia in bladder mucosa. The chi-square test showed statistically significant association between severe bladder pain ($VAS \geq 6$) and moderate to severe histopathological findings (Table 1). On the other aspect, independent T test revealed KU patients with moderate to severe neutrophils or lymphocytes infiltration in the bladder mucosa had significantly higher VAS pain score, smaller CBC and MBC (Table 2).

Interpretation of results

The histopathology findings of KU revealed a pancystitis with possible ureter involvement, it was similar to eosinophilic cystitis rather than interstitial cystitis. In early or mild KU, only lymphocyte infiltration was found in the bladder mucosa. In contrast, eosinophil, neutrophil, plasma cells involved the inflammation in the late or severe KU bladder. The inflammatory cells infiltrations were significantly correlated with clinical symptoms in KU, including bladder pain and capacity. Severe inflammatory cells infiltration was associated with more severe bladder pain and smaller bladder capacity.

Concluding message

In patients with KU, the histological findings showed whole-layer inflammation and nerve hyperplasia in the bladder and ureter. The severity of inflammatory cell infiltration in the bladder mucosa is associated with clinical symptoms. A histopathological examination is a useful tool to evaluate KU severity.

Table 1. Bladder mucosal histopathology findings in KU patients with different symptom severity

*: $p < 0.05$ in chi-square test

		Patients characteristics					
		VAS<6 N=15	VAS≥6 N=23	CBC<100ml N=12	CBC≥100m N=26	MBC<300ml N=14	MBC≥ 300ml N=24
Neutrophil	None or mild	15	11	11	15	12	14
	Moderate or severe	0	12	1	11	2	10
	p-value	<0.001*		0.060	0.147		
Eosinophil	None or mild	12	9	8	13	9	12
	Moderate or severe	3	14	4	13	5	12
	p-value	0.020*		0.486	0.506		
Lymphocyte	None or mild	10	4	8	6	9	5
	Moderate or severe	5	19	4	20	5	19
	p-value	0.005		0.014*	0.014*		
Plasma cell	None or mild	15	17	11	21	14	18
	Moderate or severe	0	6	1	5	1	5
	p-value	0.044*		0.643	0.376		
Nerve hyperplasia	None or mild	13	8	9	12	11	10
	Moderate or severe	2	15	3	14	3	14*
	p-value	0.002*		0.161	0.043*		

Table 2. Clinical parameters in KU patients with different severity of histopathological findings

		VAS	CBC (ml)	MBC (ml)
Neutrophil	None or mild (n=26)	4.27±2.96	104.045±56.22	267.61±142.01
	Moderate or severe (n=12)	8.54±1.29	49.125±13.11	108.75±41.89
	P-value	<0.001*	0.002*	0.001*
Eosinophil	None or mild (n=12)	4.44±3.29	99.93±50.67	255.29±151.82
	Moderate or severe (n=17)	7.02±2.15	77.35±57.47	179.16±117.66
	P-value	0.032*	0.390	0.121
lymphocyte	None or mild (n=14)	4.07±3.27	123.41±65.05	283.84±172.45
	Moderate or severe (n=24)	6.75±2.80*	66.72±30.27	175.00±89.44
	P-value	0.020*	0.027*	0.048*
Plasma cell	None or mild (n=32)	5.25±3.36	91.65±55.13	237.60±147.26
	Moderate or severe (n=6)	7.66±1.50*	74.75±52.5	137.50±47.87
	P-value	0.017*	0.309	0.003*
Nerve hyperplasia	None or mild (n=21)	5.92±3.30	93.00±61.51	247.85±170.93
	Moderate or severe (n=17)	7.10±2.42	78.75±57.56	153.33±81.64
	P-value	0.012*	0.180	0.010*

*: p<0.05 in independent T test

Disclosures

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