

HISTOPATHOLOGICAL CHARACTERISTICS OF KETAMINE-ASSOCIATED UROPATHY AND THEIR CLINICAL ASSOCIATION

Hueih-Ling Ong¹, Jia-Fong Jhang¹, Yung-Hsiang Hsu², Hann-Chorng Kuo¹

Department of Urology¹, Buddhist Tzu Chi General Hospital and Tzu Chi University, Hualien, Taiwan

Department of Pathology², Buddhist Tzu Chi General Hospital and Tzu Chi University, Hualien, Taiwan

Introduction

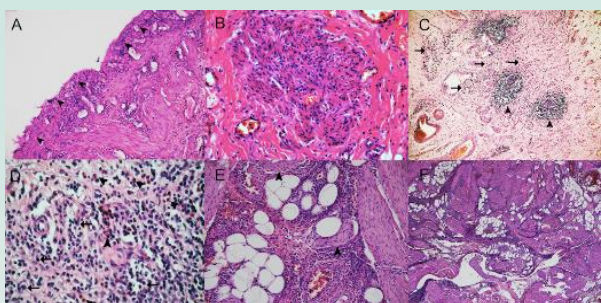
Urothelial denudation, submucosal lymphocyte and eosinophil infiltration was noted in bladder biopsy specimens in ketamine associated uropathy (KU) in previous case series [1]. However, comprehensive studies of the **histopathological findings** in entire bladder and ureters in KU and their correlation with the severity associated **symptoms** are scanty.

Methods

38 KU patients were enrolled in this study with provided detailed clinical histories and video urodynamic studies parameters. 13 of them was classified as clinically mild KU, undergone cystoscopic hydrodistention; whereas another 25 patients was classified as severe KU, undergone enterocystoplasty with or without ureter reimplantation [2]. Bladder and ureter specimens were obtained and stained with hematoxylin, eosin and immunohistochemical stain S100 for nerve hyperplasia distribution. 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), and it was correlated with clinical parameters, including visual analogue scale for pain (VAS), cystometric bladder capacity (CBC) and maximal bladder capacity (MBC) under general anesthesia.

Results

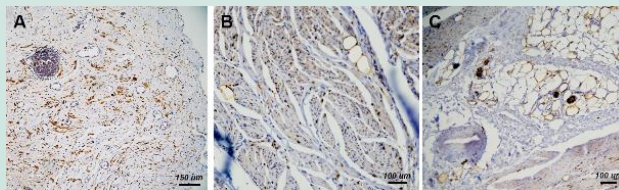
Inflammatory cells infiltration and nerve hyperplasia were found in the mucosa, muscle, and subserosal layers of the bladder and ureters in patients with KU. In mild KU, lymphocyte infiltration predominated. However, in severe KU, significant neutrophil, eosinophil, lymphocyte and plasma cell infiltrations were found in bladder mucosa.



(A) denuded epithelium (arrow head) with lymphocytes infiltration (100X) in mucosa, (B) nerve hyperplasia in mucosa (arrow head) (100X), (C) numerous neutrophil (arrow head) in mucosa (40X), (D) eosinophil (arrow head) and plasma cells (arrow) infiltration in mucosa (400X), (E) inflammatory cells infiltration and nerve hyperplasia in muscle layer (100X) and (F) inflammatory cells infiltration in serosal layers (40X)

Results (Continued)

Figure 2. Histopathology findings in KU ureter



KU ureter revealed: (A) inflammatory cells infiltration in all ureter layers (40X), (B) epithelium denudation (arrow) with mixed inflammatory cells in ureter mucosa (100X), and (C) nerve hyperplasia (arrow) in ureter mucosa (100X).

Table 3. Bladder mucosal histopathology findings in patients with KU by symptom severity

		Patients characteristics					
		VAS<6 N=15	VAS≥6 N=23	CBC≥100ml N=12	CBC<100ml 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	

VAS: Visual Analogue Scale for bladder pain; CBC: cystometric bladder capacity; MBC: maximal bladder capacity
*: p<0.05 in chi-square test

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	104.04±56.22	267.61±142.01
	Moderate or severe (n=12)	8.54±1.29	49.12±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

Conclusion

Whole-layer nerve hyperplasia and inflammatory cell infiltration, including neutrophils, eosinophils, lymphocytes, and plasma cells were seen in KU patients. **Moderate to severe neutrophil or lymphocyte** infiltration in the bladder mucosa were associated **more severe bladder pain and smaller bladder capacity**. Histopathological examination is a useful tool to evaluate KU severity.

References

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Disclosures Statement: None