High-grade urothelial cancer risk in patients with atypical urothelial cells: a hospital-based database

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Cyto-histologic results of patients with at least one AUC episode. Chronologic order. Clinicopathologic correlations and follow-up																							
Name/Fn Sex	Birth	Histo	y Date	Treatment	UC report	Date	Clin	Cysto/UUT	T	UR	UUT	Biopsi	es	Surg	Date	Significance	Histo	ology	UUT	Delay	Commentaries	Days	Age
		pT G							G Neg	pT G Neg	pTGN	leg pl	GN	eg	(months)	pT G	6 Neg	, (r	nonths)				
BEC-JO F	juil-21	a 1		TUR	Low grade	Feb-01	ND	Papill. lesion	X	2					Mar-01	Concordant	X 2			1		28621	78
BEC-JO		X 2	2	TUR	AUC	Apr-02	ND	Neg								56	IS 3	1					
BEC-JO		X	2	TUR	AUC	Nov-02	ND	Neg								49	IS 3	1					
BEC-JO		X	2	TUR	AUC	Nov-05	ND	Neg	IS	3					Dec-06	13	IS 3	1					
BEC-JO		IS 3	Dec-06	BCG	AUC	Jun-07	ND	Neg								23	IS 3	1					
BEC-JO		IS 3	3	BCG	AUC	Oct-07	ND	Neg								19	IS 3						
BEC-JO		IS 3	3	BCG	AUC	Mar-08	ND	Infl								14	IS 3	1					
BEC-JO		IS 3	3	BCG	AUC	Jun-08	ND	Neg								11	IS 3						
BEC-JO		IS 3	3	BCG	HG	Mar-09	ND	ND				IS 3			May-09	True pos.	IS 3			2	Diffuse CIS + pT1aG3 on stratified biopsies		
BEC-JO		IS 3	3	BCG	HG	Nov-10	Htu	Papill. lesion	2	3					Nov-10	True pos.	2 3	1		0	Refusal to surgery		
BEC-IO		2 1	Nov-10	BCG	HG	Mar-11	Htu	Docurr	2	3					Apr-11	True nee	2 3			1	• •		

Table 1. Example of patient's individual data. Cytological events (column 8: UC report) are chronologically ordered. The date (column 9: date) serves at calculating the delay between AUC report and the final diagnosis (see column 25: significance (months)). The date in column 24 (Date) is that of the histological control. In the example, the patient had a previous history of pTaG1 bladder tumour (columns 4 and 5) and presented with a papillay lesion at cystoscopy in Feb-01. Bladder TUR revealed a pTXG2 urothelial carcinoma. Later UC controls showed AUC-NOS (not otherwise specified) between Apr-02 (line 2) and Nov-05 (line 4). AUC appear 56 to 13 months (column 25: significance) before a high-grade pTIS tumour is diagnosed in Dec-06. Four additional AUC cases were reported, 23 to 11 months before high grade was documented both cytologically (columns 8: HG) and histologically (columns 12 and 13). Later, two recurrence episodes (pT2G3) were identified in Nov-10 and Apr-11 (True positive). The delay (months) in column 30 refers to the interval between UC (columns 9: date) and documented high grade (column 24: date). UC = urinary cytology ; HG = high grade ; Clin = clinical symptoms ; Cysto/UUT = cytoscopy and/or upper urinary tract findings ; TUR = bladder transurethral resection ; Surg = surgery, when performed.

Background:

Urine cytology (UC) is an accurate method in the search for high-grade urothelial carcinoma, with cyto-histologic correlation as high as 80-100%. Although an "atypical" or "suspicious' UC report carries a higher association with urothelial carcinoma in comparison with "reactive" or "negative" diagnoses, there remains great heterogeneity between the teams.

The Paris System for Reporting Urinary Cytology (PS-UC, see http://paris.soc.wisc.edu/) currently in progress aims at creating a reliable system to identify patients who need immediate cystoscopy vs. those who can be followed at an interval based upon risk stratification.

Aim:

To investigate whether atypical, non superficial urothelial cells (AUC) "of undetermined significance" and "cannot exclude high grade" (AUC-US and AUC-H, both candidates of the PS-UC, see Figure 1) might be associated with a) concomitant high-grade urothelial cancer and b) increased high-grade cancer risk in the follow-up period.

Methods:

A hospital-based patient Excel database to describe the diagnostic and prognostic values of AUC-US and AUC-H cases. Individual data were collected from the DIAMIC database (Infologic-Santé, Valence, France) of the pathology laboratory information system, and from the Easily information system developed by the Hospices Civils de Lyon.

Statistics included the BiostaTGV analysis software, Chi-2 square and Fischer's exact tests, Kaplan-Meier method and log rank test.

Overview and follow-up of data contents:

Demographic information including age, sex and birth date. Clinico-pathologic variables including cystoscopy, imaging techniques and histology. Treatment data (biopsies and TUR, bladder and upper tract surgery, BCG-, radio- and chemotherapy) including dates were recorded (see Table 1). Missing data being an issue, the database is regularly checked for data inconsistencies and completeness.

Inclusion period:

July 1999 to December 2013. Follow-up until May 2014 (at least 6 months). Cases from January 2014 were not recorded at the date of writing

Main results:

Before exclusion, there were 474 AUC cases representing 1.6% of all UC reports, which is in accordance with our previous reports. After 94 cases (19.8%) have been excluded, there remained 294 AUC-US and 86 AUC-H cases in 237 patients. The predictive value of AUC-H for urothelial carcinoma (all grades) was 83.7%, vs. 73.5% for AUC-US (p = 0.04)

Recurrence-free survival of patients with AUC-H was significantly shorter that that of patients with AUC-US (p = 0.005, see Figure 2).

Relevant work: example publications:

Cytopathology 2014; 25: 27-38

Acta Cytol. 57 (suppl 1), 11 (2013)

Ann. Pathol. 2011; 31: 11-17



Figure 1. Atypical urothelial cells, cannot exclude high grade (AUC-H), in a case of CIS previously treated by BCG immunotherapy with negative cystoscopy. Histological confirmation was obtained 6 months later. Non specific degene-rative features are present: eosinophilic cytoplasmic vacuoles (A), undefined cell borders (C and D), dense vitreous (A) or finely reticulated chromatin (D). Cells have increased N/C ratio with modified chromatin (C) or irregular nuclear shapes (A to D) with hyperchromatism (A to C). Papanicolaou, x400.





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