ATYPICAL ENDOMETRIAL HYPERPLASIA, LOW-GRADE: «MUCH ADO ABOUT NOTHING»

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Background

Atypical endometrial hyperplasia (AEH) is considered a precursor of endometrioid carcinoma. The 2014 World Health Organization (WHO) classification divides endometrial hyperplasia into two categories: hyperplasia without atypia and atypical hyperplasia/endometrioid intraepithelial neoplasia (EIN). However, this classification disregards the degree of nuclear atypia. The aim of this study is to show the importance of grading nuclear atypia and estimate the risk of developing endometrial carcinoma following a diagnosis of low-grade or high-grade AEH. In addition, we investigated the potential role of genes known to be involved in endometrial carcinogenesis such as *ARID1A*, *PIK3CA*, *PTEN*, *KRAS*, *CTNNB1* and mismatch repair genes.

Methods

We reviewed 91 biopsies of AEH from 91 patients who subsequently underwent hysterectomy within 1-year interval. The association between the grade of nuclear atypia at biopsy and the findings at hysterectomy was assessed via a Fisher's exact test. Targeted sequencing was performed in 26 cases of AEH and 4 samples of simple hyperplasia.

Table 1 Clinical and pathologic findings of 91 patients diagnosed of atypical endometrial hyperplasia (AEH) at biopsy who subsequently underwent hysterectomy within 1-year interval.

Biopsy		
	Low-grade AEH	High-grade AEH
N (%)	60 (66)	31 (34)
Age, ys (±SD)	49.0 (12.7)	60.1 (12.3)
P-value ^a	0.0002	
Hysterectomy (%)		
G0	27 (45)	0
G1	33 (55)	0
G2	0	9 (29)
G3	0	22 (71)
Total	60	31
P-value ^b	5.0 x 10 ⁻²⁵	

^a Mann-Whitney U test

^b Fisher's exact test

Results

The degree of nuclear atypia at biopsy was highly predictive of the findings at hysterectomy (P=5.0x10⁻²⁵). None of the patients with low-grade AEH had a diagnosis of high-grade AEH or carcinoma at hysterectomy; whereas 9 (29%) patients with high-grade AEH in the biopsy also had high-grade AEH in the uterus and 22 (71%) patients had FIGO grade-1 carcinoma. None of the genes tested showed a mutational load significantly associated with the degree of nuclear atypia

Conclusions

We conclude that in AEH is crucial to assess the degree of nuclear atypia. Our data strongly support that low-grade AEH is inconsequential and question the need of hysterectomy for such patients.

Low-grade AEH

High-grade AEH