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Patterns of SATB2 and p16 reactivity aid in the distinction of atypical polypoid adenomyoma from myoinvasive endometrioid carcinoma and benign adenomyomatous polyp on endometrial sampling

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Aims: Atypical polypoid adenomyoma (APAM) is an uncommon uterine lesion composed of complex endometrioid glands with frequent squamous morular metaplasia and fibromuscular stroma. On endometrial curettage, biopsy or polypectomy specimens, the admixture of endometrioid glands and smooth muscle raises the differential diagnosis of myoinvasive endometrioid carcinoma. Reproductive-age APAM patients may opt for fertility preservation, whereas myoinvasive carcinoma is treated surgically. One previous study reported an incidental finding that the stroma of APAM, in contrast to that of other polypoid lesions, was SATB2-positive. APAM has also been reported to show increased stromal p16 staining. We aimed to assess whether SATB2 and p16 are useful stains for the distinction of APAM from myoinvasive carcinoma and benign adenomyomatous polyps.

Methods and results: Cases of 'atypical polypoid adenomyoma' (n = 32), 'adenomyomatous polyp' (n = 39) and 'myoinvasive endometrioid carcinoma' (n = 30) were identified. Morphological features were assessed, along with the intensity and extent of SATB2 and p16 staining in the stromal component of each lesion. SATB2 expression was seen in the stromal components of 30 of 32 (94%) APAMs, versus none of 39 (0%) benign adenomyomatous polyps and five of 30 (17%) myoinvasive endometrioid carcinomas. Stromal p16 expression was seen in 31 of 31 (100%) APAMs, versus 20 of 39 (51%) benign adenomyomatous polyps and 12 of 30 (40%) myoinvasive endometrioid carcinomas.

Conclusions: Patchy to diffuse SATB2 and block-type p16 staining of fibromuscular stroma separating atypical endometrioid glands is more consistent with APAM than with myoinvasive endometrioid carcinoma. These stains are potentially useful adjuncts to careful morphological evaluation of endometrial biopsies/curettings.

Keywords: atypical polypoid adenomyoma, myoinvasive endometrioid carcinoma, p16, SATB2

Introduction

Atypical polypoid adenomyoma (APAM) is an uncommon uterine lesion composed of complex endometrioid glands with frequent squamous morular

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metaplasia in a background of smooth muscle stroma with short interlacing fascicles.[1] On endometrial curettage, biopsy or polypectomy specimens, the presence of endometrioid glands and smooth muscle stroma raises the differential diagnosis of myoinvasive endometrioid carcinoma.[2,3]

Accurate distinction between APAM and myoinvasive endometrioid carcinoma on endometrial biopsies or curettings can facilitate management decisions. APAM may be treated conservatively to allow for the preservation of fertility; approximately two-thirds of patients opt for local excision (polypectomy or curettage).[4,5] In contrast, myoinvasive endometrioid carcinoma is most commonly treated with hysterectomy. The vast majority of APAMs are considered to be benign, although recurrence is not uncommon. Endometrial carcinoma is detected in 8.8% of patients after treatment with curettage or polypectomy.[6] APAM is typically regarded as a localised form of endometrial intraepithelial neoplasia/complex atypical hyperplasia.[1]

In most cases, curettings of myoinvasive endometrioid carcinoma will show detached fragments of tumour in addition to fragments with myoinvasion.[1] Although many cases of APAM and carcinoma show only mild to moderate cytological atypia, marked cytological atypia favours a diagnosis of myoinvasive endometrioid carcinoma.[1] Short interlacing fascicles of muscle separating endometrial glands may favour a diagnosis of APAM, as normal myometrium shows more elongated fibres.[1] However, there is significant morphological overlap between these entities.

Various immunohistochemical stains have been studied in this context, owing to the subtle morphological distinctions between APAM and myoinvasive cancer. Ohishi *et al.* previously investigated the utility of CD10 immunohistochemistry for the diagnosis of APAM versus myoinvasive carcinoma.[3] In their cohort, one of seven APAMs showed focal weak staining of the stroma between glands, whereas all 19 myoinvasive carcinomas showed fringe-like positivity in the stroma immediately adjacent to a subset of myoinvasive neoplastic glands. Nonetheless, it is known that smooth muscle neoplasms and benign endometrial stroma (surface or adenomyosis) may both show areas of CD10 reactivity.[7] Horita *et al.* have reported that the APAM stroma is either negative or focally positive for h-caldesmon, but that infiltrated myometrium is diffusely positive for h-caldesmon (with the caveat that the stromal reaction may be negative or focally positive).[8] Travaglino *et al.* reported a case of APAM with fringe-like CD10 reactivity and stromal h-caldesmon reactivity that progressed to carcinoma.[9] McCluggage and Van de Vijver have reported an incidental finding that the stroma of APAM is positive for the nuclear marker SATB2, whereas the stromal components of other polypoid lesions are not.[10] Kihara *et al.* demonstrated increased stromal p16 reactivity in APAM as compared with myoinvasive endometrioid carcinoma.[11] The immunohistochemical features of each component of APAM have recently been documented in a review article by Travaglino *et al.*[12]

Benign adenomyomatous polyps may also enter the differential diagnosis for APAM. Adenomyomatous polyps, although they are often not considered separately from other endometrial polyps, are endometrial polyps with myomatous stromal tissue.[13] Among 84 such cases reported by Strickland *et al.*, 55% were sessile polyps with vaguely fascicular myomatous stroma components admixed with glands, and 40% were pedunculated polyps with a stalk of disorganised smooth muscle extending towards the surface and entrapping benign glands. Distinction from APAM is based on the complexity of the glandular proliferation and degree of cytological atypia. The stromal components of benign adenomyomatous polyps are typically CD10-positive; the sessile polyps are typically caldesmon-negative, but the pedunculated polyps are caldesmon-positive.[13] Although SATB2 expression in benign adenomyomatous polyps has not been extensively studied, McCluggage and van de Vijver reported that the stromal components of five adenomyomatous polyps and of 11 of 12 endometrial polyps (with focal staining in one case) were SATB2-negative.[10] Moritani *et al.* reported that 89% of endometrial polyps showed stromal p16 expression, with a mean of 47% of cells being positive.[14]

In this study, we aimed to assess whether SATB2 and p16 are useful stains for the distinction of APAM from myoinvasive endometrioid carcinoma and benign adenomyomatous polyps on endometrial biopsies or curettings. To our knowledge, this is the first study to comprehensively evaluate SATB2 expression patterns in APAM, myoinvasive endometrioid carcinoma, and benign adenomyomatous polyps.

Materials and methods

With Institutional Review Board approval, the University of Michigan pathology and consultative archives were searched for cases of 'atypical polypoid adenomyoma' ($n = 32$), 'adenomyomatous polyp' [$n = 40$, including 39 benign adenomyomatous polyps and one adenomyomatous polyp (cannot rule

out atypical polypoid adenomyoma)] and 'myoinvasive endometrioid carcinoma' (n = 30) sampled between 1989 and 2020. Four of the myoinvasive endometrioid carcinoma specimens were biopsy or curettage specimens; the remainder were hysterectomy specimens. Study pathologists (H.I.W. and S.L.S.) reviewed all cases to confirm the diagnosis, assess the morphological features, and record available clinical follow-up information regarding recurrence and the development of carcinoma.

The morphological features assessed included the gland/stroma ratio, the presence of irregular endometrial gland contours, intraluminal complexity, the presence of cytological atypia, the presence of squamous metaplasia/differentiation, keratinisation, the mitotic rate, and the characteristics of the fibromuscular stroma.

Immunohistochemical staining for SATB2 (clone EP281, dilution 1:200; Cell Marque, Rocklin, CA, USA) was performed manually (Histoserv, Germantown, MD, USA). The intensity (weak, moderate, or strong) and extent (focal/patchy versus diffuse) of nuclear SATB2 staining in the epithelial and stromal components of each lesion were recorded. Immunohistochemical staining for p16 (clone E6H4, prediluted; Ventana, Roche, Basel, Switzerland) was performed with an automated immunostainer (Bench-Mark XT; Ventana, Roche), according to the manufacturer's protocol. The intensity (weak, moderate, or strong), extent (focal/patchy versus diffuse) and localisation (nuclear and/or cytoplasmic) of p16 staining in the stromal component of each lesion was recorded. Staining was considered to be diffuse when it was present in a majority (>50%) of cells. Block-type p16 positivity was defined as clusters of continuous cells with strong nuclear or nuclear and cytoplasmic staining.[15]

Results

In this cohort, the mean age of APAM patients was 41 years, as compared with 47 years for patients with benign adenomyomatous polyps, and 60 years for patients with myoinvasive endometrioid carcinoma. Ten APAM patients (31%) had concurrent cancer, but none developed new cancer after APAM diagnosis. Two patients with benign adenomyomatous polyps (5%) were subsequently diagnosed with hyperplasia (one with focal endometrial intraepithelial neoplasia, and one with benign hyperplasia), but neither developed cancer. The 47-year-old patient with an adenomyomatous polyp (cannot exclude APAM) was subsequently diagnosed with focal endometrial intraepithelial neoplasia/complex atypical hyperplasia. Demographics and clinical information are shown in Table 1.

The average gland/stroma ratio was higher for the myoinvasive component of endometrioid carcinoma (3:1) than for APAM (1.5:1). In contrast, benign adenomyomatous polyps were stroma-predominant (1:2.5). Clear-cut lobular architecture was more often seen in APAM (34%) than in the myoinvasive components of endometrioid carcinoma (13%) or benign adenomyomatous polyps (3%). All APAMs showed at least focal areas with irregular outer contours of endometrial glands, as did 93% of myoinvasive endometrioid carcinomas and 92% of benign adenomyomatous polyps. Intraluminal complexity (cribriforming; epithelial bridging) was seen in all myoinvasive endometrioid carcinomas, in a subset of APAMs (38%), and in one benign adenomyomatous polyp (3%). At least mild cytological atypia was seen in most APAMs (97%) and myoinvasive endometrioid carcinomas (93%), but was only rarely seen in benign adenomyomatous polyps (5%, focal). Squamous morular metaplasia was seen in almost all APAMs (94%), whereas 57% of myoinvasive endometrioid carcinomas showed areas of squamous differentiation. Squamous metaplasia was not seen in any benign adenomyomatous polyp. Keratinisation was seen in 71% of myoinvasive endometrioid carcinomas with squamous differentiation, in contrast to 34% of APAMs with squamous metaplasia. The average mitotic rate was higher in myoinvasive endometrioid carcinomas [11 per 10 high-power fields (HPFs)] than in APAMs (6/10 HPFs), although

Table 1. Demographics and clinical information

Diagnosis	Age (years), mean (range)	Concurrent cancer, *n* (%)	Subsequent cancer, *n* (%)
Atypical polypoid adenomyoma	41 (17–71)	10 (31)	0 (0)
Myoinvasive endometrioid carcinoma	60 (37–77)	–	–
Benign adenomyomatous polyp	47 (18–76)	0 (0)	0 (0)
Adenomyomatous polyp (cannot rule out atypical polypoid adenomyoma)	47	0 (0)	0 (0)

the range overlapped between the two entities. The mitotic rate of benign adenomyomatous polyps was typically lower (1/10 HPFs; range, 0–14). Desmoplasia was more commonly seen in myoinvasive endometrioid carcinomas than in APAMs (60% versus 13%; Figure 1A,B). All APAMs and 97% of myoinvasive endometrioid carcinomas showed small muscle bundles separating endometrial glands (Figure 1C,D). In contrast, benign adenomyomatous polyps showed large muscle bundles and clusters of thick-walled blood vessels. Muscular stroma was seen beneath the surface endometrium in 19% of APAMs (Figure 1G,H) and in 10% of benign adenomyomatous polyps; the only myoinvasive carcinoma with this finding arose in a background of APAM. The morphological features are presented in Table 2.

SATB2 EXPRESSION IS MORE COMMONLY SEEN IN APAM THAN IN MYOINVASIVE ENDOMETRIOID CARCINOMA

Stromal SATB2 expression was seen in 94% (30/32) of APAMs (Figure 2A–D) versus 17% (5/30) of myoinvasive endometrioid carcinomas (Figure 2E,F).

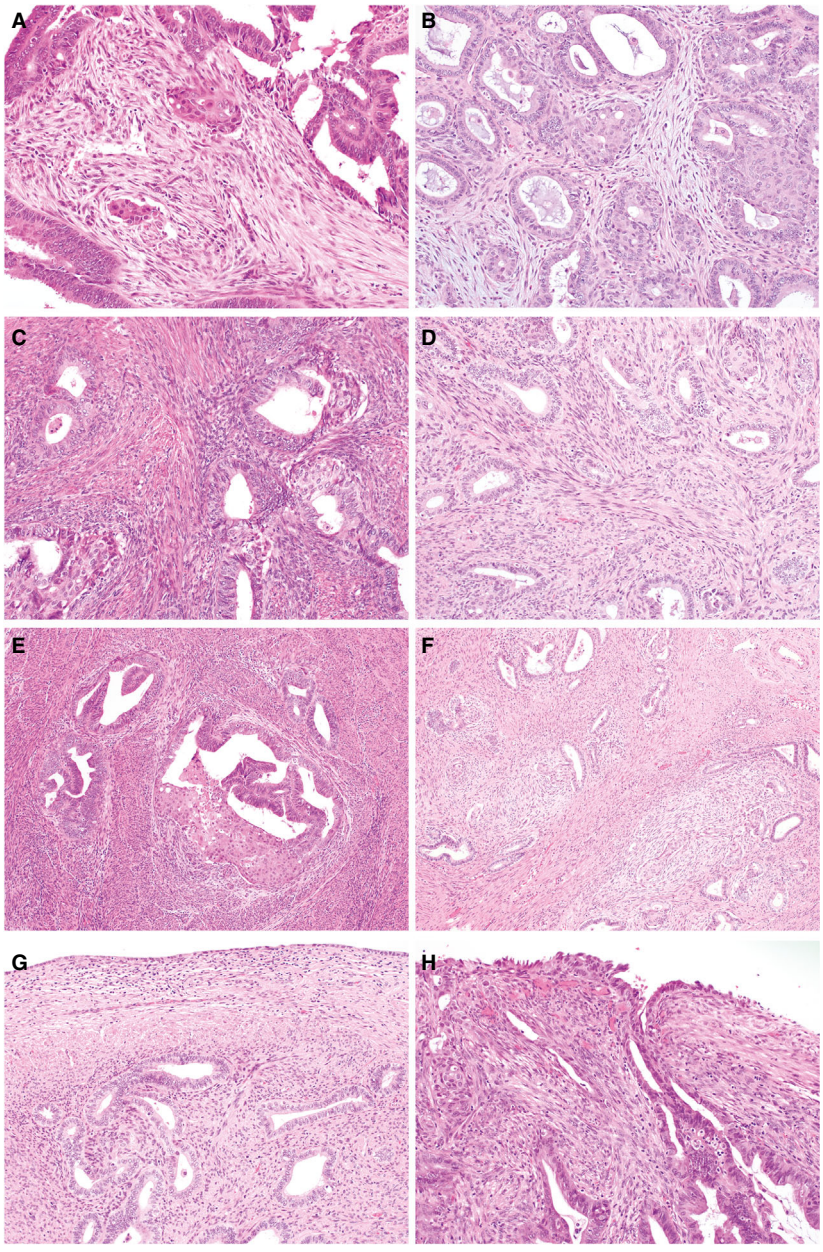

Figure 1. Atypical polypoid adenomyoma (APAM) and myoinvasive endometrioid carcinoma show significant morphological overlap. Although desmoplasia is considered to be essentially pathognomonic for invasive carcinoma [**A**, haematoxylin and eosin (H&E)], similar changes may be seen in the stroma of APAM (**B**, H&E). Small to medium-sized muscle bundles may be seen separating endometrial-type glands in both invasive endometrioid carcinoma (**C**, H&E) and APAM (**D**, H&E). Some myoinvasive endometrioid carcinomas show a lobulated, deceptively bland pattern of invasion (**E**, H&E), and sampled fragments may resemble the lobulated growth of glands in APAM (**F**, H&E). One feature that seems to be unique to APAM is the presence of muscle bundles beneath the surface endometrium (**G**,**H**, H&E).

Table 2. Morphological features

Diagnosis	Average gland/ stroma ratio	Clear-cut lobular architecture, *n* (%)	Irregular gland contours, *n* (%)	Intraluminal complexity, *n* (%)	Cytological atypia, *n* (%)	Squamous metaplasia/ differentiation, *n* (%)	Keratinising squamous metaplasia/ differentiation, *n* (%)	Mitotic rate (per 10 HPFs), mean (range)	Characteristics of fibromuscular stroma	Muscular stroma beneath surface endometrium, *n* (%)	Desmoplastic stroma, *n* (%)
Atypical polypoid adenomyoma	1.5:1	11 (34)	32 (100)*	12 (38)†	31 (97)	30 (94)†	11 (34)‡	6 (1–11)	Small muscle bundles separating glands	6 (19)	4 (13)
Myoinvasive endometrioid carcinoma	3:1	4 (13)	28 (93)	30 (100)	28 (93)	17 (57)	12 (71)‡	11 (1–41)	29 (97) with at least a few small to medium-sized muscle bundles between glands 7 (23) with pink fibrotic stroma between glands	1 (3)§	18 (60)¶
Benign adenomyomatous polyp	1:2.5	1 (3)	36 (92)**	1 (3)**	2 (5)**	0 (0)	0 (0)	1 (0–14)	Large muscle bundles and thick-walled vessels	4 (10)	0 (0)
Adenomyomatous polyp (cannot rule out atypical polypoid adenomyoma)	1:1	1 (100)	1 (100)	0 (0)	1 (100)	1 (100)	1 (100)	5	Small muscle bundles separating glands	0 (0)	0 (0)

HPF, High-power field.
*Three cases with a few irregular glands.
†Focal in one case.
‡Percentage represents the percentage of cases with squamous metaplasia/differentiation showing keratinisation.
§Carcinoma arising from atypical polypoid adenomyoma.
¶Focal in four cases.
**Nine cases with few irregular glands.
††Few papillae.
‡‡Mild, focal.

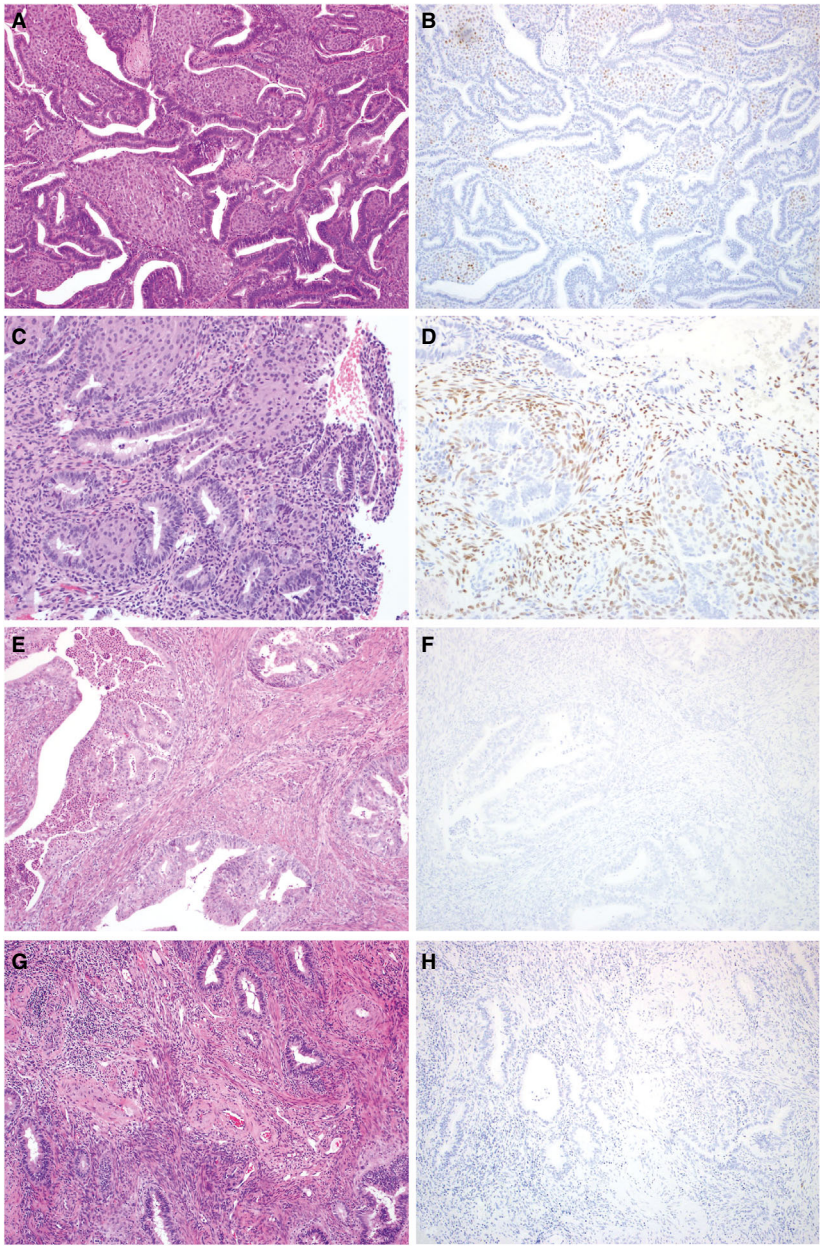

Figure 2. SATB2 expression is more frequently seen in atypical polypoid adenomyoma (APAM) than in benign adenomyomatous polyps and myoinvasive endometrioid carcinoma. SATB2 expression was most frequently observed in APAM [**A**,**C**, haematoxylin and eosin (H&E)], with nuclear staining in squamous morules [**B**, SATB2 immunohistochemistry (IHC)] and stroma (**D**, SATB2 IHC). In contrast, the fibromuscular stromata of myoinvasive carcinoma (**E**, H&E; **F**, SATB2 IHC) and benign adenomyomatous polyp (**G**, H&E; **H**, SATB2 IHC) were negative for SATB2.

SATB2 staining was diffuse in 28% (9/32) of APAMs, focal/patchy in 66% (21/32), and negative in 6% (2/32). Diffuse stromal SATB2 staining was not seen in any case of myoinvasive carcinoma. Three cases showed focal weak staining, one showed focal weak to moderate staining, and one showed patchy weak to moderate staining. Detailed SATB2 staining results are shown in Table 3.

It is of note that three myoinvasive endometrioid carcinomas showed focal weak to moderate SATB2 staining in normal endometrial stromal cells (in surface endometrium or adenomyosis). Two myoinvasive endometrioid carcinomas showed weak to moderate nuclear or cytoplasmic SATB2 staining in deep myometrial bundles, although no staining was seen in the fibromuscular stroma immediately surrounding invasive glands. Weak to moderate nuclear SATB2 staining was occasionally seen in vessel walls (focal), lipoleiomyomas, and rare glandular cells with tubal metaplasia. Squamous morules showed frequent SATB2 staining, regardless of the entity in which they were seen (26 of 30 APAMs with squamous morules, and nine of 14 myoinvasive endometrioid carcinomas with squamous morules); therefore, care

Table 3. SATB2 staining

Staining pattern	Atypical polypoid adenomyoma, *n* (%)	Myoinvasive endometrioid carcinom, *n* (%)	Benign adenomyomatous polyp, *n* (%)	Adenomyomatous polyp (cannot rule out atypical polypoid adenomyoma), *n* (%)
Diffuse	9 (28)	0 (0)	0 (0)	0 (0)
Focal/patchy	21 (66)	5 (17)	0 (0)	1 (100)
Negative	2 (6)	25 (83)	39 (100)	0 (0)

Table 4. p16 staining

Staining pattern	Atypical polypoid adenomyoma, *n* (%)	Myoinvasive endometrioid carcinoma, *n* (%)	Benign adenomyomatous polyp, *n* (%)	Adenomyomatous polyp (cannot rule out atypical polypoid adenomyoma), *n* (%)
Block-type	14 (45)	0 (0)	4 (10)	0 (0)
Diffuse	13 (42)	0 (0)	0 (0)	0 (0)
Focal/patchy	18 (58)	12 (40)	25 (64)	1 (100)
Negative	0 (0)	18 (60)	14 (36)	0 (0)

should be taken to distinguish staining of squamous morules from staining of the stroma.

SATB2 EXPRESSION IS MARKEDLY INCREASED IN APAMS AS COMPARED WITH BENIGN ADENOMYOMATOUS POLYPS

Stromal SATB2 expression was seen in 94% (30/32) of APAMs, as compared with 0% (0/39) of benign adenomyomatous polyps. Focal moderate SATB2 staining was seen in the one adenomyomatous polyp for which a diagnosis of APAM could not be ruled out. Importantly, SATB2 staining was not seen in the stromal components of definitively benign adenomyomatous polyps (Figure 2G,H).

STROMAL P16 EXPRESSION IS NOT UNCOMMON IN APAM, BENIGN ADENOMYOMATOUS POLYPS, OR MYOINVASIVE ENDOMETRIOID CARCINOMA

For one APAM, further material was not available for p16 staining. Increased nuclear and cytoplasmic p16 staining was seen in the fibromuscular stroma in 100% (31/31) of APAMs, in 51% (20/39) of benign adenomyomatous polyps, and in 40% (12/30) of myoinvasive endometrioid carcinomas, as well as in the adenomyomatous polyp for which a diagnosis of APAM could not be ruled out. Importantly, inflammatory cells often showed moderate nuclear and cytoplasmic p16 staining, which often made interpretation challenging in cases of myoinvasive endometrioid carcinoma (particularly those with the 'microcystic, elongated and fragmented' pattern of invasion). Rounded cells in the surface endometrial stroma or areas of adenomyosis can show p16 staining. Detailed staining results for p16 are shown in Table 4, and representative photomicrographs of stained slides are shown in Figure 3A–H.

STROMAL BLOCK-TYPE P16 EXPRESSION IS MORE SPECIFIC, BUT LESS SENSITIVE, FOR APAM

Block-type p16 staining was seen in 45% (14/31) of APAMs, in 10% (4/39) of benign adenomyomatous polyps, and in 0% (0/30) of myoinvasive endometrioid carcinomas, but was not seen in the adenomyomatous polyp for which a diagnosis of APAM could not be ruled out. Although stromal block-type p16 staining can be seen in benign adenomyomatous polyps as well, it is more highly associated with APAM ($P = 0.0019$).

Of the 10 APAMs with concurrent endometrioid carcinoma, stromal SATB2 staining was focal/patchy in nine (90%). Stromal p16 staining was seen in all nine stained APAMs with concurrent non-myoinvasive endometrioid carcinoma (focal/patchy in eight cases and diffuse in one, with three showing areas of block-type staining).

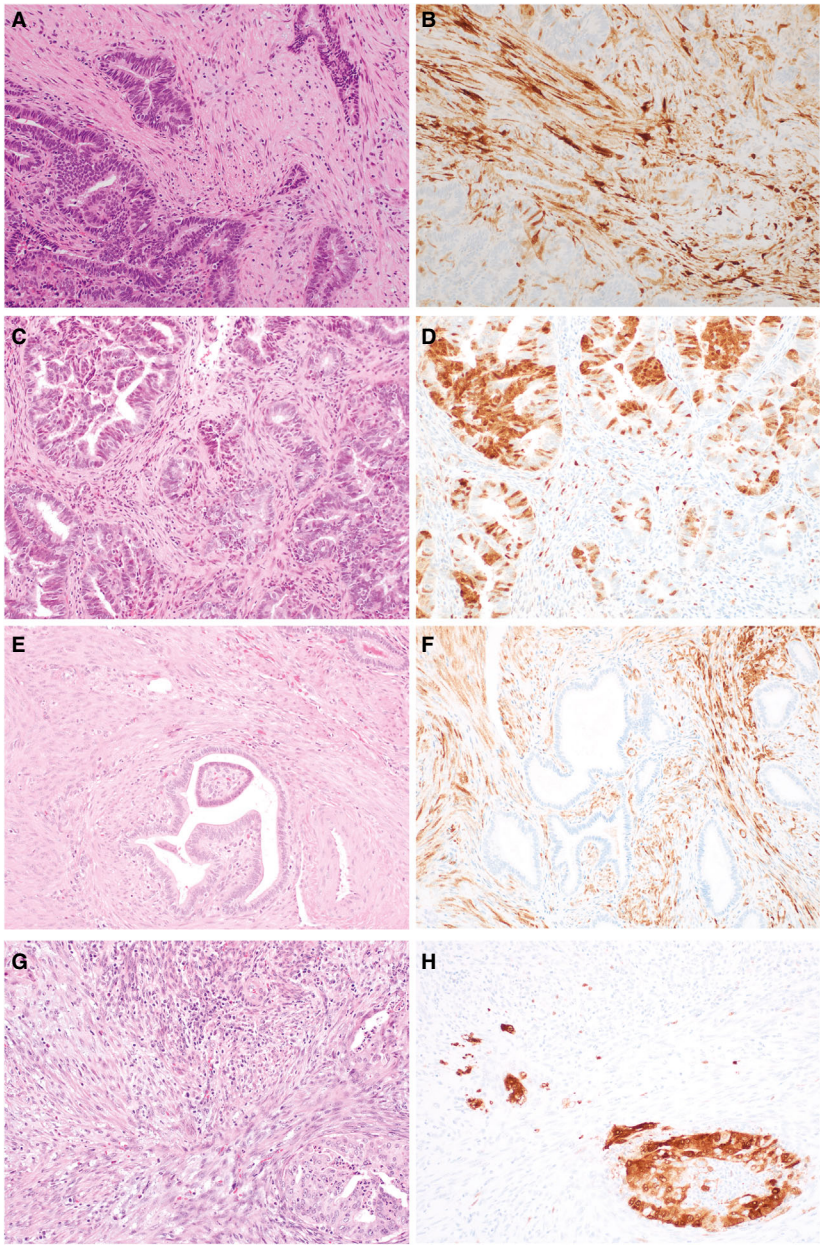

Figure 3. p16 expression can be seen in stromal tissue associated with atypical polypoid adenomyoma (APAM), benign adenomyomatous polyps, or myoinvasive endometrioid carcinoma, but is increased in APAM. A large subset of APAMs showed diffuse stromal p16 staining [**A**, haematoxylin and eosin (H&E); **B**, p16 immunohistochemistry (IHC)], but 10% showed only focal stromal p16 staining (**C**, H&E; **D**, p16 IHC). Whereas p16 was negative in the stromal components of 36% of benign adenomyomatous polyps in our cohort, many benign adenomyomatous polyps (**E**, H&E) showed at least patchy p16 staining (**F**, p16 IHC). p16 staining, if present at all, was typically focal in the stromal components of myoinvasive endometrioid carcinomas; however, inflammatory cells often showed moderate staining (**G**, H&E; **H**, p16 IHC).

Discussion

Despite the significant morphological overlap that can be seen in biopsies and curettings of APAM and myoinvasive endometrioid carcinoma, there are nuanced morphological and immunohistochemical features that can facilitate distinction of these two entities. The stromal staining patterns of SATB2 and, to a lesser extent, p16 may facilitate accurate classification.

In our cohort, the fibromuscular stroma surrounding myoinvasive endometrioid carcinoma was often a close mimic of the fibromuscular stroma of APAM. The gland/stroma ratio was often higher in the myoinvasive component of endometrioid carcinoma than in APAM; however, some myoinvasive endometrioid carcinomas show atypical glands with smooth outer contours and lower gland/stroma ratios. Lu *et al.* reported that 72% (26/36) of their APAMs showed fibromuscular branches separating glands into vague lobules, with fibromuscular bundles being present beneath surface epithelium in 86% (31/36).[16] This feature was seen less frequently in our cohort, and was only identified in APAMs.

Squamous morules were common in APAMs, as has been previously reported; keratinising squamous differentiation is more common in endometrioid carcinoma.[2,16] Although desmoplasia has been described as a feature supportive of myoinvasion,[16] two APAMs in our cohort showed desmoplastic stroma despite the absence of carcinoma. Lu *et al.* reported seeing no more than two mitotic figures per 10 HPFs in their APAMs[16]; however, the mean mitotic rate in our cohort was 6/10 HPFs. On the basis of these features, it is not surprising that fragmented samples of APAM may be misdiagnosed as myoinvasive carcinoma. On the other hand, some myoinvasive endometrioid carcinomas show vague lobular architecture and insignificant cytological atypia, leading to misinterpretation as APAM.[16]

Overall, stromal expression of SATB2 and of p16 appear to be supportive of a diagnosis of APAM. Stromal SATB2 staining was seen in 94% of APAMs, as compared with 17% of myoinvasive endometrioid carcinomas and 0% of benign adenomyomatous polyps. In three myoinvasive endometrioid carcinomas, stromal SATB2 staining was seen in the fibromuscular stroma of the endometrial mass and the myometrium/reactive stroma surrounding myoinvasive glands. Focal weak to moderate SATB2 staining is non-specific; however, patchy or diffuse moderate stromal staining was seen much more commonly in APAMs (50%) than in myoinvasive carcinomas (3%). As previously reported by McCluggage and van de Vijver, squamous morules were frequently positive for SATB2 in our cohort.[10]

Although increased stromal p16 staining was more often seen in APAMs than in myoinvasive endometrioid carcinomas or benign adenomyomatous polyps, it was seen fairly commonly in all three entities. Block-type stromal p16 staining was not seen in myoinvasive carcinoma, but this finding has limited sensitivity, as it was present in only 45% of APAMs. Some benign adenomyomatous polyps in our cohort showed block-type p16 staining; this finding is consistent with previous reports of stromal p16 staining in endometrial polyps.[14] Occasional block-type p16 staining in the stroma of benign adenomyomatous polyps may also be expected, as Strickland *et al.* reported that a subset of benign adenomyomatous polyps show an immunoprofile similar to that of APAM.[13] A major benefit of using p16 is that many laboratories already have access to this antibody, whereas they may not have an in-house SATB2 stain. No myoinvasive carcinomas showed diffuse stromal SATB2 or p16 staining.

The strengths of this study include the comprehensive evaluation of 32 APAMs, given the rarity of the neoplasm. The spectrum of immunohistochemical findings for each diagnostic entity was recorded, and potential pitfalls were described. One significant limitation of this study is the inclusion of only four myoinvasive endometrioid carcinoma samples from endometrial biopsies or curettings, given the suggestion that these stains may be useful in that setting. However, the use of sections from hysterectomy specimens increases confidence in the diagnosis of APAM rather than myoinvasive endometrioid carcinoma.

In summary, the APAMs and myoinvasive endometrioid carcinomas in our cohort showed significant morphological overlap, and the entities that we studied more reliably showed distinct SATB2 expression patterns than p16 expression patterns. On the basis of our data, patchy to diffuse SATB2 staining and block-type p16 staining in the fibromuscular stroma separating atypical endometrioid glands are more commonly seen in APAMs than in myoinvasive endometrioid carcinomas. Evaluation for specific SATB2 and p16 immunohistochemical staining patterns, in addition to careful morphological examination, can increase our confidence in the accurate classification of APAM and myoinvasive carcinoma in endometrial biopsies or curettings.

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Author contributions

All authors were involved in study design, interpretation of stains, and analysis of results. S. L. Skala and H. I. Worrell took photographs of cases. S. L. Skala and H. I. Worrell wrote the initial draft of the manuscript, with A. P. Sciallis providing helpful suggestions.

Conflict of interest

The authors state that they have no conflicts of interest.

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