Adenocarcinoma in situ & Microinvasive adenocarcinoma of cervix

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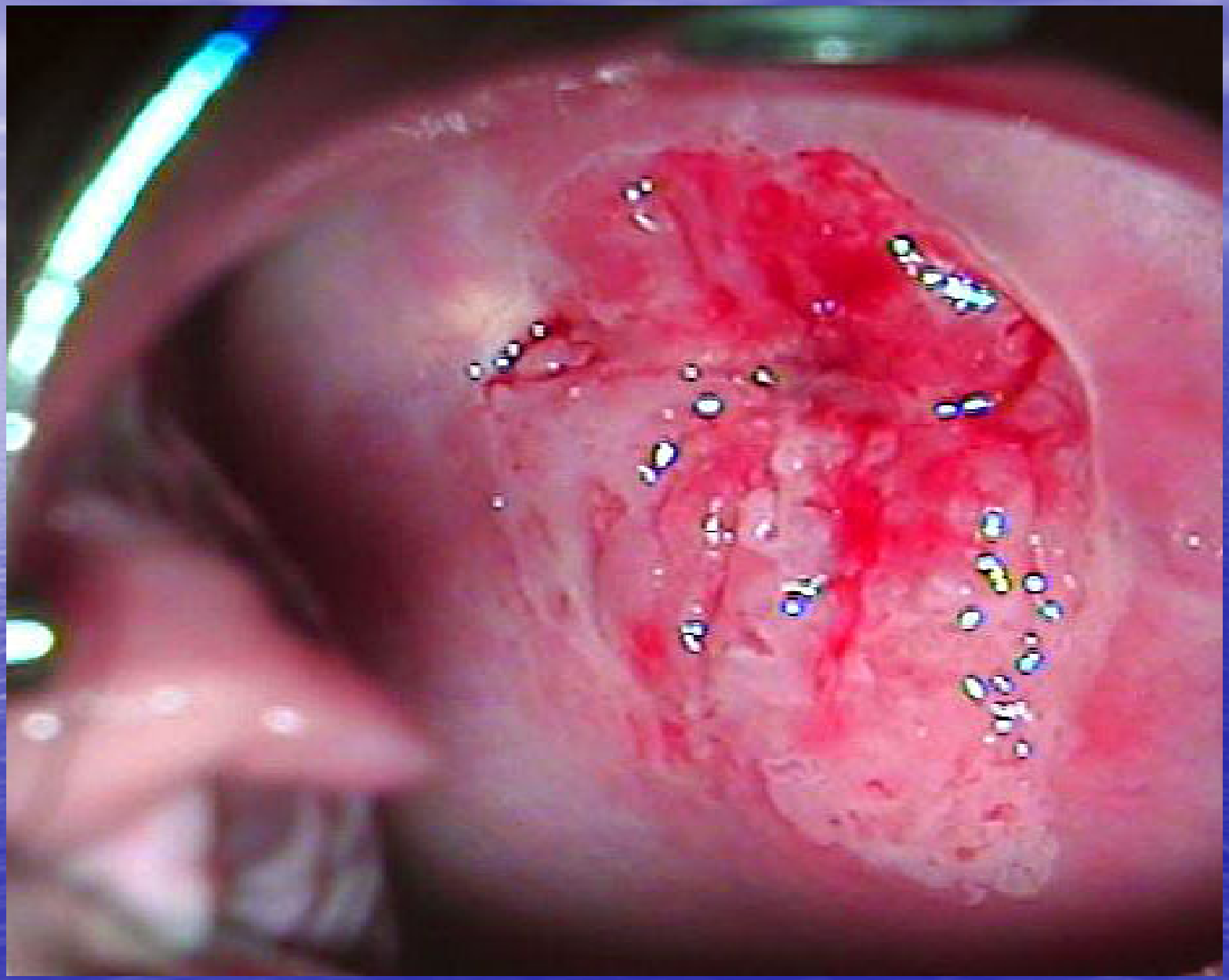
Case Summary

- Madam FCC, F/37
- Para 5, SVDs, 3TOPs, BTL done
- Good past health
- Presented in July 2001 with urinary stress incontinence and urgency, urodynamic study showed genuine stress incontinence, put on pelvic floor exercise and symptoms improved.

- Incidentally cervical smear revealed HGSIL
- Cervical smears had been normal in 1996, 97, 98 in UCH
- Colposcopy showed entire transformation zone, coarse punctation at 4-5 o'clock
- After application of acetic acid, there was dense acetowhiteness at transformation zone at 4-9 o' clock
- Punch biopsies were taken at 4,5,7 o clock



- Cervical biopsy revealed at least CIN II, condyloma planum and adenocarcinoma in situ, no stromal invasion.
- In view of at least CIN II and adenocarcinoma in situ, cone biopsy was performed

- Pathology showed
  - 1. cervix diffusely involved by adenocarcinoma-in-situ
  - 2. microinvasive adenocarcinoma at 4 o’ clock, depth and horizontal distance 0.5mm
  - 3. CIN III at 8 o’ clock, CIN I at 9 o’clock, koilocytosis
  - 4. AIS focally involved the ectocervical margin at 8’o clock. The rest of resection margin were clear from microinvasive adenocarcinoma and CIN.
- Microinvasive adenocarcinmoa of cervix, FIGO stage 1A1, diffuse adenocarcinoma in situ, CIN I-III, condyloma planum

- In view of positive resection margin of cone biopsy specimen with AIS (MIAC resection margin clear), proceed to simple hysterectomy
- Laparoscopic assisted vaginal hysterectomy was performed uneventfully
- Hysterectomy specimen showed residual adenocarcinoma-in-situ in some endocervical glands over 5-6, 8-12 o’ clock. No evidence of microinvasion. Ectocervix unremarkable. No evidence of residual CIN or malignancy.

- She was then followed up and vault smears every 3 months were negative in 3 smears

Discussion

- Incidence of adenocarcinoma of cervix varies from 5.5% to 34%, increasing in young women
- natural history and aetiology of adenocarcinoma unclear
- Cervical intraepithelial glandular neoplasia: glandular atypia and adenocarcinoma in situ (AIS)

- Microinvasive adenocarcinoma of cervix exist as a separate entity
- 48-89% of cases associated with co-existent CIN
- HPV DNA can be detected in up to 85% of adenocarcinoma of cervix

Detection by cytology

- Features include nuclear pleomorphism, hyperchromasia, irregular chromatin distribution,prominent nucleoli, poorly-defined granular, finely vacuolated cytoplasm with indistinct cell borders, rosettes

- False negative smear common, up to 50%
  - sampling error (the use of Ayre spatula alone), *the use of endocervical brush in addition increase the detection of endocervical cells, odds ratio 3.33 (95% CI 3.05-3.63)* Cochrane review
  - glandular atypia situated in deeper glands, covered by normal columnar cells
  - co-existent squamous CIN, which have more clearly defined cytoplasm, more marked nuclear changes and glandular abnormality overlooked

- Interpretation error, small endometrioid AIS cells & AIS cells resembling reactive endocervical cells may be mistaken for benign cells, difficult to differentiate between AIS and microinvasive cells

Detection by colposcopy

- Most authors believe there are no obvious colposcopic features
- Coppleson suggested that AIS lesions have a ‘stark acetowhiteness of either individual or fused villi in discrete patches of varying size at or near transformation zone. The presence of surface elevation with irregularity, ulcer, necrosis, abnormal vascular patterns suggest AIS or early adenocarcinoma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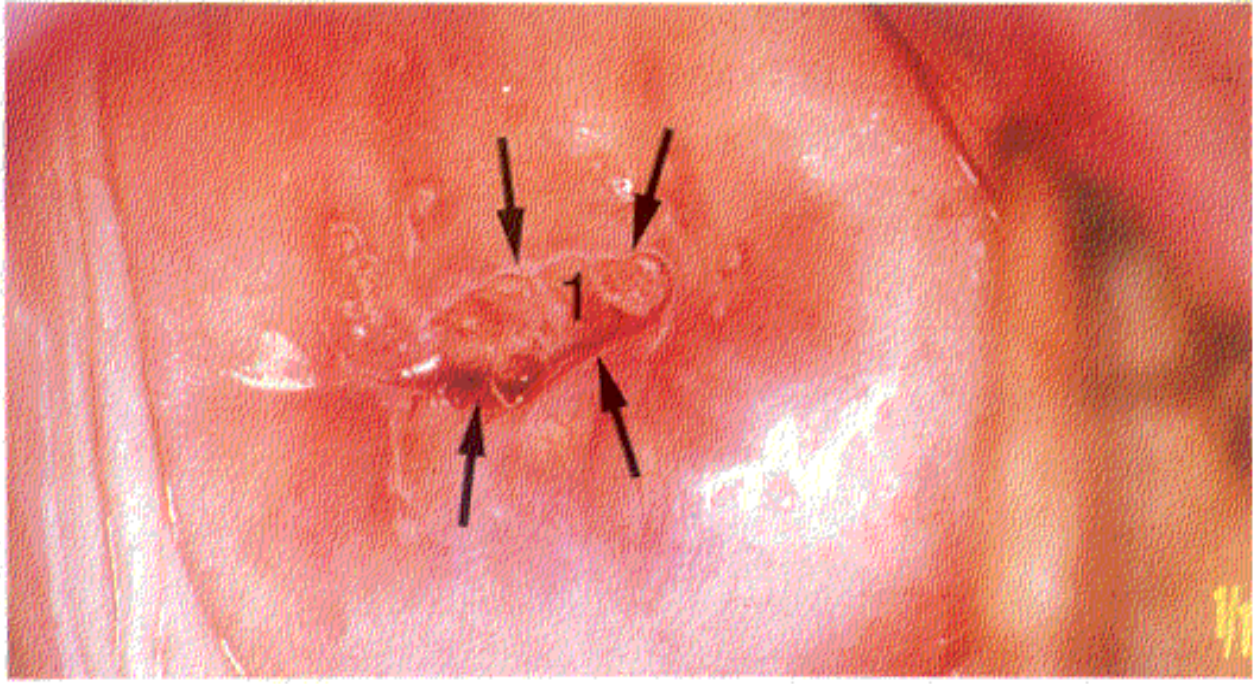
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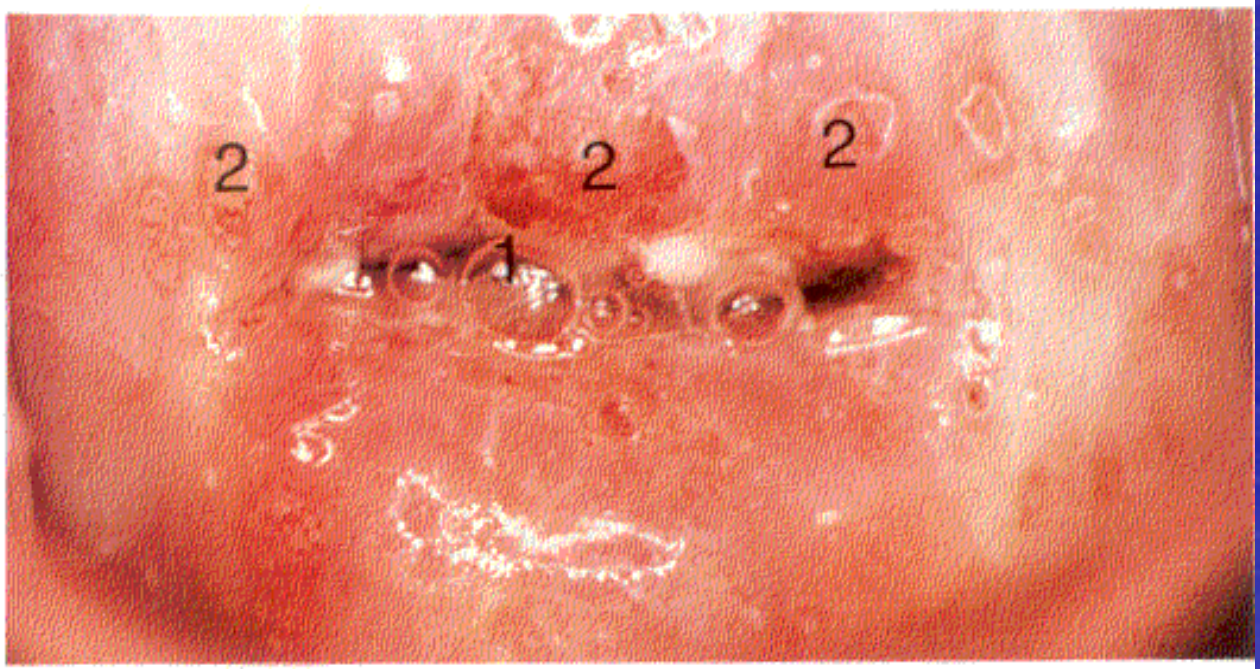
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- The glandular lesions may involve any part of endocervical canal with surface epithelium may appear normal (50%)
- review of colposcopic findings in our patient showed ? Acetowhiteness of villi

Detection by endocervical curettage

- Debatable
- Wolf et al 1996 reported only 35% of pre-conisation curettage were positive for AIS
- some suggest endocervical curettage after conisation to represent true sampling of tissue beyond surgical margins
- may have a role if cytology is equivocal, or suggestive of low grade glandular abnormality, but colposcopy normal

Management of AIS

- AIS is well known for multifocal lesions/skip lesions present high in endocervical canal

Hysterectomy for AIS

- Some advocate hysterectomy as primary treatment of AIS, because of skip lesions, and to exclude invasive disease
- Nicklin, reviewed the incidence of residual disease following cone biopsy for AIS with uninvolved margins, found an overall incidence of 10.2%

- Azodi, a retrospective review, 40 patients, found residual AIS in 31% of cases with negative margins in cone biopsy and in 56% of cases with positive margins
- difficult to follow up with cytology and colposcopy

Cone biopsy for AIS

- For women want to preserve fertility, cone biopsy accepted as an alternative to hysterectomy, also less morbidity
- the depth of conisation should be at least 25mm, as the abnormal glands seldom extend further than 25mm
- If cone biopsy resection margins were involved with AIS, proceed to repeated cone biopsy or simple hysterectomy

- Negative resection margins did not reliably predict the absence of residual disease. They should be followed up closely with cervical cytology, endocervical curettage and colposcopy
- The cumulative rate of histologically proven recurrence after conservative management was 4.3% at one year and 15% at 4 years

- In those cases with clear margins in cone biopsy, 16.7% will require further treatment after 4 years. *Soutter et al BJOG 2001*

LLETZ

- Azodi et al, LLETZ were significantly more likely to have positive endocervical margins than cold knife cone biopsy (75% vs 24%)
- little evidence available to support the use of LLETZ as treatment for AIS

Management of microinvasive adenocarcinoma of cervix

- Controversial
- Prognosis depends on depth of invasion, tumor volume, lymph-vascular space invasion
- radical surgery (radical hysterectomy, +/- adnexectomy +/- node dissection) vs more conservative surgery (cone biopsy +/- node dissection, simple hysterectomy)

- 77 women with microinvasive adenocarcinoma of cervix, stage 1A1 & 1A2
- 16 women treated with cold-knife conisation, combined with pelvic-node dissection in 4, other had some types of hysterectomy
- none of 26 women who had radical hysterectomy had parametrial spread, none of 48 who had pelvic-node dissection or 23 in whom adnexa removed had metastases
  Andrew et al Obs & Gynae 1997

- 21 women with microinvasive adenocarcinoma, FIGO stage 1A1
- Median follow-up 76 months
- Underwent radical hysterectomy or simple hysterectomy
- No evidence of parametrial invasion or lymph node metastases in any patients with radical hysterectomy, no disease recurrence
- Conclusion: cone biopsy or simple hysterectomy might offer them definitive treatment
- Schorge Obs & Gynecol 1999

- 301 microinvasive adenocarcinoma, 131 stage IA1, 170 IA2
- Simple hysterectomy in 54 women with IA1, 64 with IA2
- Radical hysterectomy in 50 women with IA1, 83 with IA2
- Only 1 patient with stage 1A2 positive pelvic lymph node
- Survival rate was 99.2% for IA1, 98.2% for IA2
- Mean follow up 46.5 months
- Webb et al Obs & Gynecol 2001

- 5 women, FIGO stage IA1, women expressed strong wish to preserve fertility
- cone biopsy alone as the treatment, negative resection margins
- no recurrent disease after 6-20 months of follow-up
- need long-term follow up, and larger study

Schorge et a Gynae Oncol 2000

- First case report of bilateral pelvic lymph node metastases in a case of FIGO stage 1A1, who underwent simple hysterectomy,bilateral salpingo-oophorectomy, pelvic lymph node dissection
- *Nagarsheth et al Gynae Oncol 2000*

Follow-up

- Requires long-term follow up with cytology (both Ayres' spatula and endocervical brush smears, ?use of liquid based cytology) and colposcopy, although their effectiveness are questionable
  - *use of liquid based cytology improved the diagnosis of low grade and high grade squamous CIN but the number of studies available for atypical glandular cells of undetermined significance evaluation was too small to have a conclusion Bernstein et al, Am J O&G*

- invasive glandular disease had been reported after hysterectomy for AIS
- optimal interval between follow-up smears and length of follow up unknown

Summary

- The incidence of AIS and adenocarcinoma is increasing
- Both cytology and colposcopy are not very sensitive in detecting glandular lesions
- Treatment is controversial, but tends to be less radical for AIS and microinvasive adenocarcinoma
- requires long-term follow up after treatment for any recurrence

Thank You!