NORTH SHORE PRIVATE HOSPITAL

NORTHERN SYDNEY CENTRAL COAST NSW HEALTH

Prophylactic Salpingo-oophorectomy The Northern Sydney Experience

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Introduction

- Ovarian cancer risk around 1:100, with around 1200 new cases per year diagnosed in Australia
- 5-10% of ovarian cancers involve inheritance of a mutated gene
- Risk of ovarian cancer if carrier up to age 75 of BRCA 1 10-60%, BRCA2 10-40%
- Commonly identified genes BRCA1, BRCA2, Tp53 (Li-Fraumeni syndrome) and MMR genes (HNPCC)

Screening

- Transvaginal Pelvic Ultrasound
- Serum CA125
- No proven value
- May lead to unnecessary investigation
- Interval cancers may occur
- Screening Trial results awaited with interest
  - UKTOCS
  - GOG 99 (High Risk Population)

Prevention strategies: prophylactic surgery

- Risk reduction for ovarian cancer 85-95%[1]
- Risk reduction for breast cancer after oophorectomy 56% for *BRCA1* carriers and 46% for *BRCA2* carriers[2]
- A reduction in overall mortality has been shown from prophylactic surgery HR 0.24, breast cancer mortality HR 0.10 and ovarian cancer mortality 0.23 [3]

1.Rebbeck et al NEJM 2002
2. Eisen et al JCO 2005
3. Domchek et al Lancet 2006

Cancer Risk

- Risk of primary peritoneal cancer following surgery 2-5% in BRCA1/ BRCA2 mutation carriers[1]
- Rates of occult cancer reported 2-10%
- Proportion of tumour recurrence due to occult tumour at the time of surgery remains yet to be determined

1. Finch et al JAMA 2006

Method

- Retrospective case series
- All women who underwent prophylactic surgery at RNSH and NSPH during the period 2004 - April 2008 with a single surgeon
- Information correlated with data from the familial cancer clinic on results of mutation screening

Northern Sydney Familial Cancer Clinic

- Established 2003 as a part time service
- Clinical geneticist and counselor
  - Gynaecologist, Breast Surgeon, Radiologist
- Family risk assessment and genetic testing
- Screening clinic for high risk breast/ovarian cancer families
- Patient referral via specialists, GPs, self/familial referral

Surgery

- For women with BRCA1, BRCA2 and inconclusive testing laparoscopic bilateral salpingo-oophorectomy was offered
- Fallopian tube is excised at the uterine cornu. The cornu is then ablated with bipolar diathermy.
- Women with HNPCC mutations were offered hysterectomy owing to the increased risk of uterine cancer

Histopathological Technique

- Entire ovary and fallopian tube embedded in case of ‘high risk’ patients
- The distal 2cm of the Fallopian tube was amputated from the rest of the tube. The fimbrial end was then sectioned longitudinally so that the maximum surface area of the fimbrial mucosa was available for histological examination
- The remaining fallopian tube was then cross-sectioned at 2-3mm intervals and embedded in total

Characteristic	Study participants
N	45
Mean Age	48.9 (28-76) years
BRCA 1	8/45 (18%)
BRCA 2	7/45 (16%)
HNPCC	5/45 (11%)
Inconclusive Strong family history (testing not done before surgery)*	19/45 (42%) 6/45 (13%)
Surgery performed	LBSO 37 TAHBSO 6 LAVH-BSO 2

*Family history of breast and/or ovarian cancer until 2005 (3/6), breast and ovarian cancer only after September 2005 (3/6)

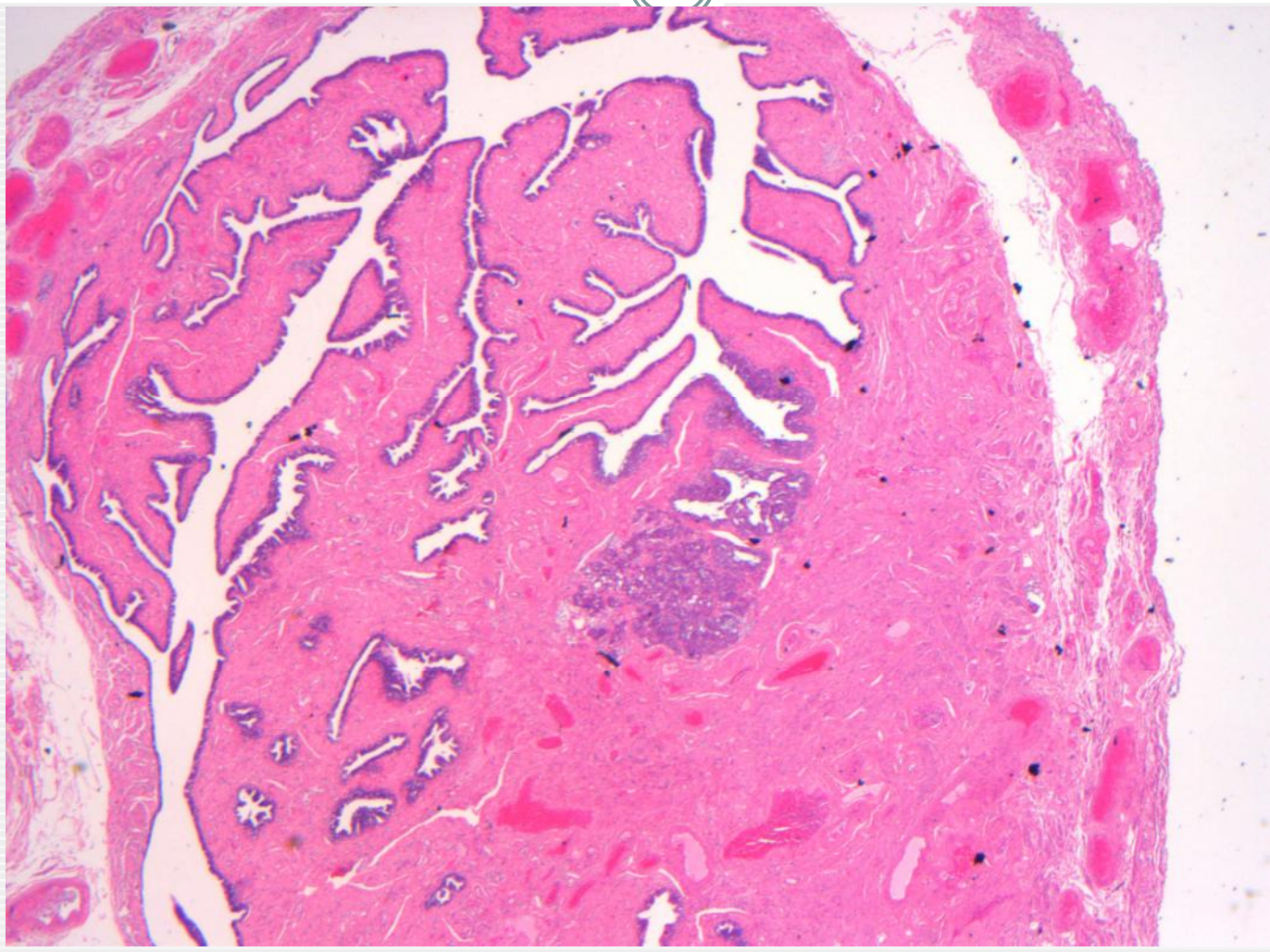
Characteristic	Number of patients
Histopathology: Negative	40/45 (88.9%)
Histopathology: Positive	5/45 (3 microinvasive tubal, 1 in situ tubal, 1 metastatic breast lesion) (11.1%)
Surgical complications	1/45 (inferior epigastric artery laceration recognised at surgery)
Recurrence/new cancer	1/45 (breast cancer)

Patient	Age	Mutation	Tumour site	FIGO stage
1	76	BRCA 2	Microinvasive serous papillary carcinoma fallopian tube	1A (suboptimal staging)
2	49	BRCA 1	In-situ serous papillary carinoma fallopian tube	0
3	52	BRCA 2	Microinvasive poorly differentiated serous carcinoma fallopian tube	1A
4	48	BRCA 1	Microinvasive fallopian tube carcinoma	1A
5	47	Inconclusive	Metastatic breast cancer	

Case 1

- 76 year old woman, known **BRCA 2 mutation**
- Personal history bilateral breast cancer
- Previous bilateral mastectomy
- Unremarkable pelvic ultrasound and CA125 13 u/mL
- Laparoscopic bilateral salpingo-oophorectomy performed
- Macroscopically normal uterus ovaries and tubes at time of surgery

Small area of microinvasive serous carcinoma (up to 0.3mm) with adjacent changes of insitu carcinoma towards the fimbrial end of the Fallopian tube



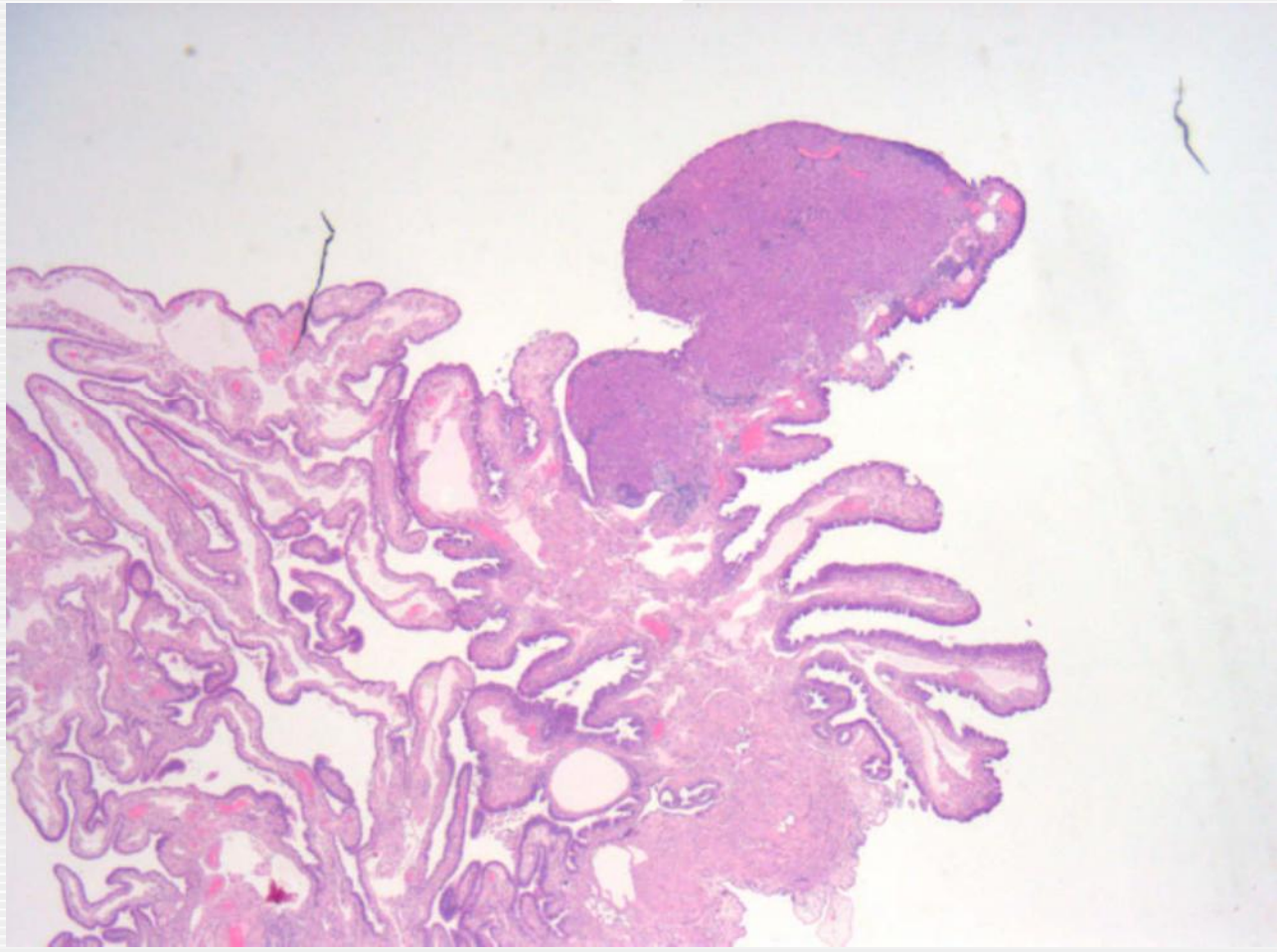
Patient progress

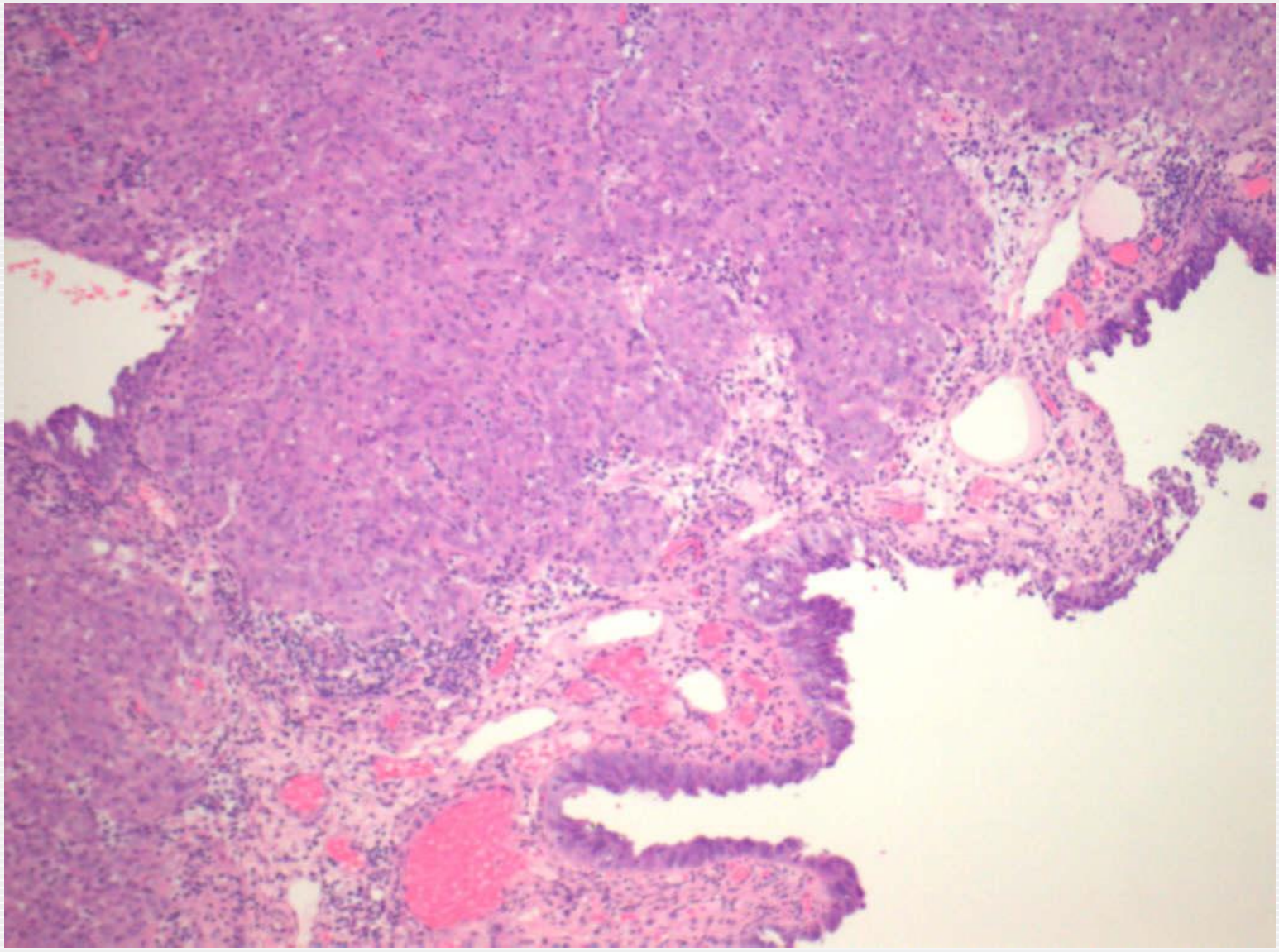
- After discussion with the patient, it was elected not to proceed with surgically staging
- Clinical and CA-125 monitoring at 18 months remains negative.

Case 2

- 49 year old teacher
- Personal history breast cancer 5 years earlier
- BRCA 2 identified in family and patient
- Mother pancreatic cancer, male cousin breast cancer.
- Unremarkable pelvic ultrasound, CA 125 6 IU/mL
- Laparoscopic bilateral salpingo-oophorectomy performed, at which time uterus, ovaries and tubes looked normal

2.5mm focus of poorly differentiated serous carcinoma at the fimbrial end of the Fallopian tube





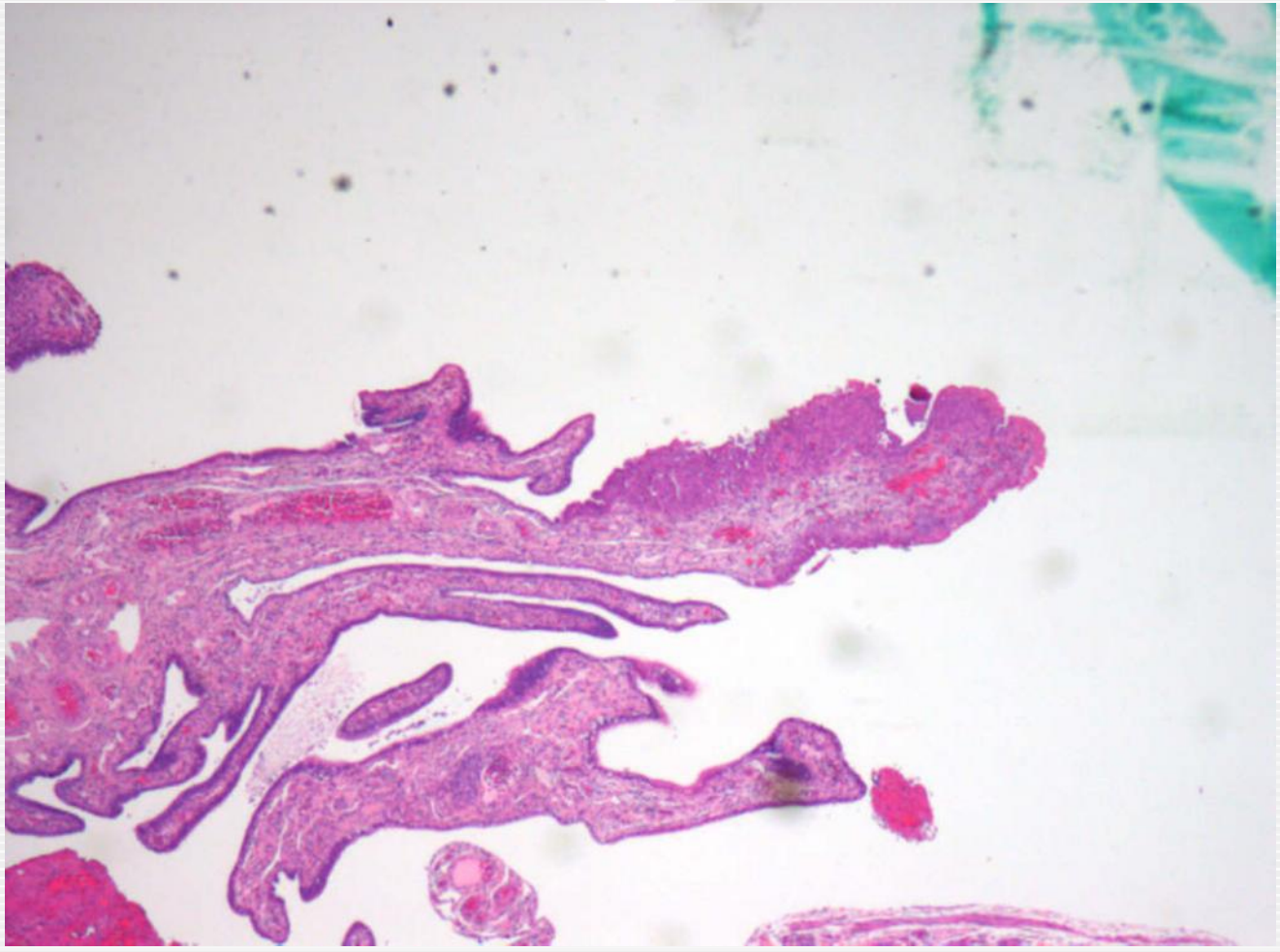
Progress

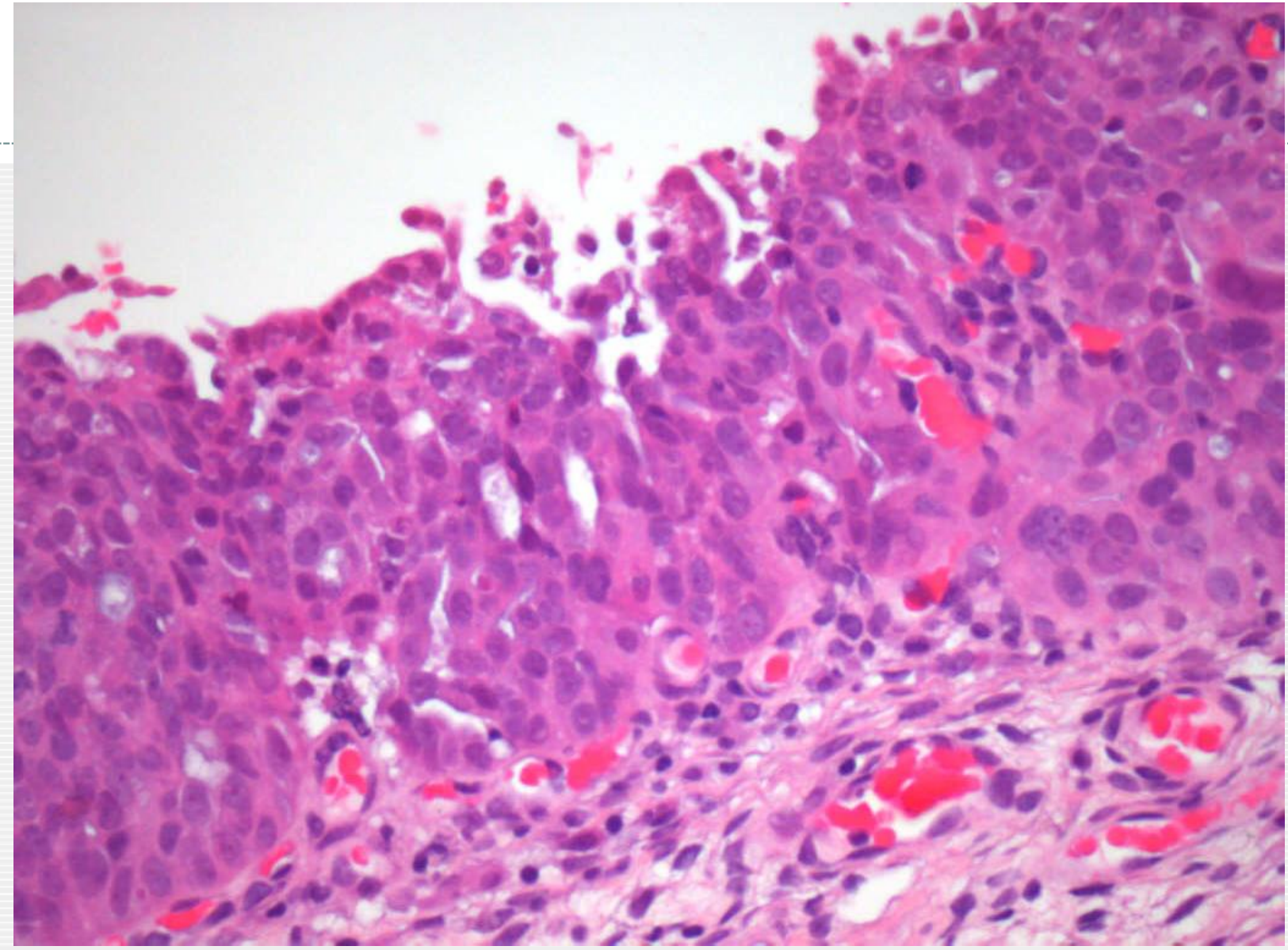
- Decision made to perform surgical staging
- Washings negative
- Para-aortic and pelvic nodes, appendix, omentum, uterus all negative for tumour.
- Patient remains well at 24 months with no signs of recurrence.

Case 3

- 51 year old nulliparous woman, known BRCA 1 carrier
- Breast cancer aged 29 and 45, bilateral mastectomy
- Sister breast cancer at age 42 and ovarian cancer aged 45, another sister ovarian cancer 47
- Normal CA 125 and pelvic ultrasounds every 6 months
- Laparoscopic bilateral salpingo-oopherectomy performed, all pelvic organs appeared normal

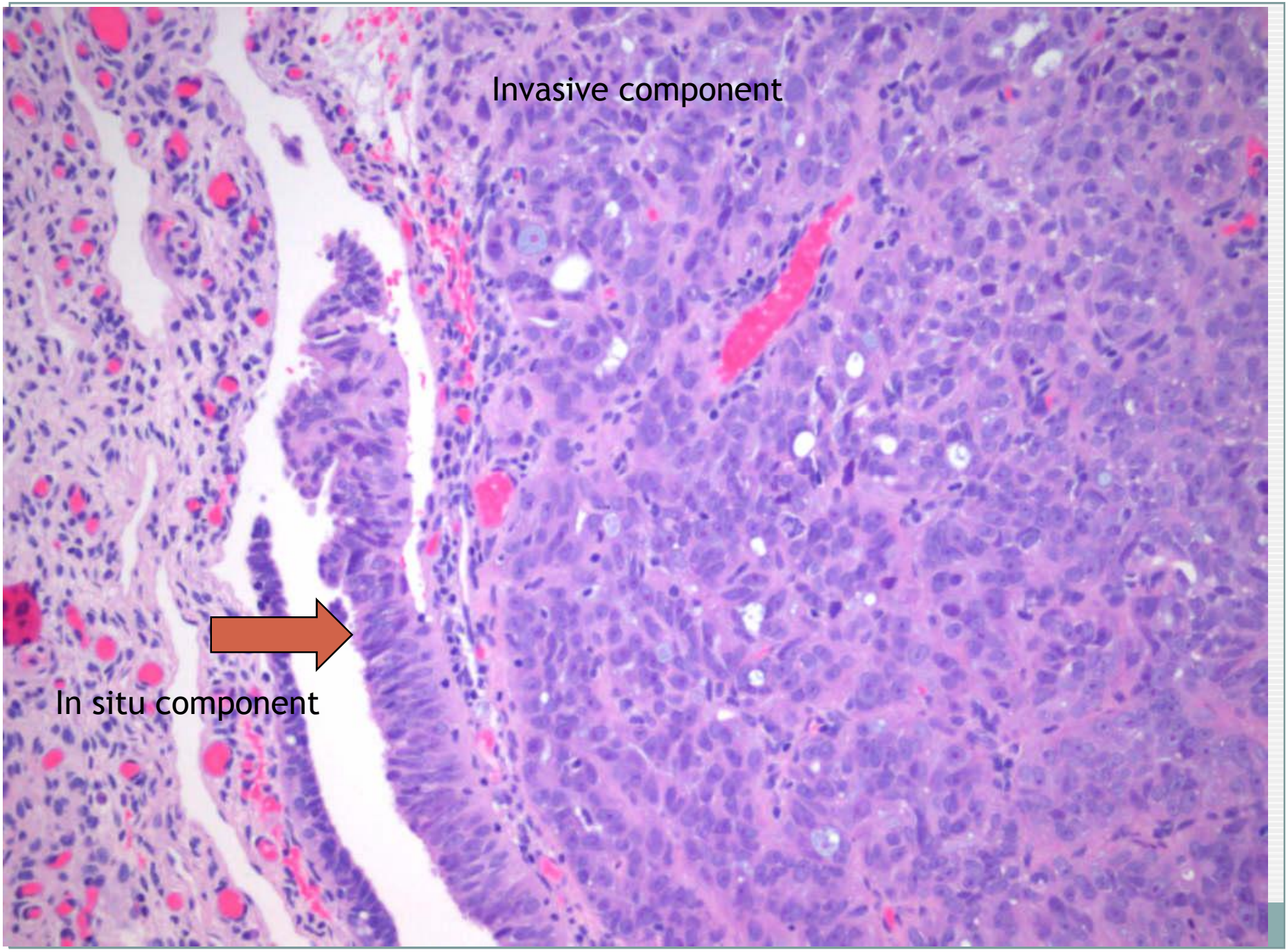
Fallopian tube showed a single 1mm focus of insitu serous papillary carcinoma. No invasive malignancy was seen.





Case 4

- 48 year old multiparous woman
- Strong family history breast and ovarian cancer: mother died of ovarian cancer age 62, maternal grandmother died ovarian cancer age 52, 3 1st cousins breast cancer
- Cousin confirmed BRCA1 mutation, awaiting mutation testing
- Past history peritonitis (uncertain cause)
- Normal CA 125 and ultrasound
- Laparoscopic bilateral salpingo-oophorectomy was performed



Progress

- Patient underwent surgical staging
- Adjuvant chemotherapy not offered
- All pathological specimens and cytology negative
- Currently alive without disease 18 months following surgery.

Summary

- Rate of occult cancer in entire group 11%
- Rate of occult cancer in confirmed BRCA mutation carriers 26%
- In BRCA group all occult neoplasia found in the Fallopian tubes
- All preoperative investigations were negative

Author	Year	N=	Occult cancer	Fallopian tube	Ovary
Powell et al	2005	67	10.4%	4	3
Lu et al	2000	33	12.1%	0	4
Colgen et al	2001	60	8.3%	Not specified	
Scheuer et al	2002	90	2.2%	1	1
Leeper et al	2002	30	13.3%	3	1 (+1 PP)
Kauff et al	2002	98	3.1%	1	2
Rebbeck et al	2002	259	2.3%	0	6
Finch et al	2006	159	4.4%	6	1
Finch et al	2006	490	2.2%	3	7 (+1 PP)
Olivier et al	2004	58	8.6%	2	2
Callahan et al	2007	122	5.7%	7	0
Lamb et al	2006	113	6.2%	5	1 (+1 PP)
Carcangiu	2003	26	7.7%	2	0

Risk Factors for Occult Cancer

- Age
- BRCA 1> BRCA2
- Rigour of pathological examination, particularly of Fallopian tubes
- Potential importance of Fallopian tube as being the site of genesis of cancer in BRCA 1 & 2 mutation carriers
- This case series predictably confirms a lack of reliability of the CA 125 and transvaginal ultrasound in diagnosing micro-invasive disease.

Conclusion:

- Small series, but confirms value of prophylactic surgery and rigorous pathological sectioning
- High rate of occult malignancy in BRCA group raises question as to optimal age to perform surgery