Ovarian diseases

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Benign ovarian diseases
Ovarian Cysts

Prevalence

- 4% of women are admitted to hospital with an ovarian cyst / complication by the age of 65 years
- 25% of adnexal torsions occur in children
- 90% of all ovarian cysts are benign
- Risk of Ca in an ovarian cyst in a woman of:
  - Reproductive age: 0.4–0.8/100 000
  - Age 60–80 years : 60/100 000
Ovarian cyst events / complications

Rupture
• Asymptomatic / acute abdominal pain
• May follow sexual intercourse or physical activity
• Severity of pain depends on the type of fluid
  “Serous or mucinous/ sebaceous material/ Blood”

Haemorrhage into a cyst:
• Pain of variable degree. Usually mid cycle

Torsion
• Moderate-severe pain & of sudden onset
• Associated nausea and vomiting
• More pain than tenderness

Infection
• Pain, fever, peritoneal irritation ??PID
Clinical evaluation

History

• History of endometriosis/ PID/ known ovarian cysts
• Bowel / urinary symptoms
• Anticoagulants
• Progesterone only pills: develop recurrent ovarian cysts
• Pain may be referred down the cutaneous distribution of the Obturator nerve (inner thigh down to the knee)

Examination

• +/- low-grade fever. BP,PR: usually stable
• Abdominal tenderness
• Cervical excitation on vaginal examination
Investigations

- Pregnancy test
- Urinalysis and culture
- Full blood count, urea and electrolytes
- ? Coagulation screen
- Genital swabs for infection if PID is suspected
- CA-125 : Not as a routine
- Ultrasound examination
- Doppler blood flow of the cyst: Findings are variable and not diagnostic
D.Dx

In case of ovarian cyst complication, consider

- Ectopic pregnancy
- Pelvic inflammatory disease
- Pelvic abscess
- Fibroid degeneration
- Appendicitis
- Complications of diverticular disease
- Urinary tract infection
- Urinary calculi
- Renal colic
Management

• Expectant Mx: Haemorrhagic cysts and cyst rupture
  Analgesia and observation

• Repeat scan 6 wks

• Surgery: Laparoscopy / Laparoscopy if:
  o Haemodynamic compromise
  o Diagnostic uncertainty or likelihood of torsion
  o No relief of symptoms within 48 hours of presentation

• Consider COCPs for cyst formers
Special situation

Ovarian cysts in pregnancy

• Most common: Dermoid cysts (50%) then cystadenomas
• < 5% require intervention
• Conservative management is appropriate
• Indications for intervention:
  o Symptomatic relief
  o Suspicion of malignancy
Special situation

Ovarian tumours in children

• Ovarian ca represent 1.5% of childhood ca
• Most ovarian tumours are benign
• Types:
  o Most common: Epithelial cysts and teratoma
  o Most common ca: Germ cell tumours
• Most common complication: Torsion (33% of cases)
Malignant disease of the ovary and tubes
Malignant disease of the ovary

Ca ovary

- The second most common gynae ca after uterine ca
- 5th most common ca in women after breast, bowel, lung and uterine ca
- The majority of ovarian ca are epithelial
<table>
<thead>
<tr>
<th>Types of Ovarian cysts / tumors</th>
<th>Functional</th>
<th>Inflammatory</th>
<th>Benign tumours/cysts</th>
<th>Malignant /malignant potential</th>
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<tbody>
<tr>
<td></td>
<td>• Follicular cyst</td>
<td>• Tubo-ovarian abscess</td>
<td>• Endometriotic cyst</td>
<td>• Epithelia ovarian ca</td>
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<td></td>
<td>• Corpus luteum cyst</td>
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<td>• Brenner tumour</td>
<td>• Malignant teratoma</td>
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<td></td>
<td>• Theca lutein cyst</td>
<td></td>
<td>• Benign teratoma</td>
<td>• Endometrioid carcinoma</td>
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<td></td>
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<td>• Fibromia</td>
<td>• Dysgerminomia</td>
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<td>Inflammatory</td>
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<td>• Secondary ovarian tumor</td>
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<td>• Cystadenoma, cystadenocarcinoma</td>
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<td>• Granulosa cell tumor</td>
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<td>• Arrhenoblastoma</td>
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<td>• Theca cell tumor</td>
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</table>
Classification of ovarian tumours

- Ovarian tumors classified according to their origin, biological behavior or clinical manifestations

- WHO Classification:
  - Epithelial
  - Sex cord stromal
  - Germ cell
Epithelial tumours (80 - 90%)

Serous Tumors
- Benign/Borderline/ ca
- Can be bilateral
- Psammoma bodies
- BRCA 1 mutations

Mucinous Tumors
- Benign/Borderline/ ca
- Pseudomyxoma peritonei
- RT / CT resistant

Endometroid Tumors
- Malignant
- ? Endometriosis
- Ass. with endometrial ca

Clear Cell (Mesonephroid)
- Benign/Borderline/ ca
- Worst prognosis

Transitional cell (Brenner)
- Usually benign

Mixed epithelial tumours

Undifferentiated & unclassified
Germ Cell Tumours (10-15%)

Dysgerminoma
- Most commonly malignant
- Abnormal gonads/Turner
- Bilateral
- LDH
- Chemo/radiosensitive

Endodermal Sinus Tumors
(Yolk Sac Tumors)
- Young children < 4yrs
- 3rd decade
- Schiller-Duval bodies
- AFP

Teratomas
- Immature- can get malignant
- Mature
  - Solid
  - Cystic
  - Monodermal & highly specialized
    ▪ Struma ovarii
    ▪ Carcinoid
    ▪ Struma Ovarii & Carcinoma
    ▪ Mixed forms

GONADOBLASTOMA
- Pure
- Mixed with Dysgerminoma or other Form Germ Cell Tumors

Choriocarcinoma
- Malignant
- Cyto- & syncitiotrophoblast
- B-HCG
Sex Cord Stromal Tumours (5-10%)

**Granulosa-Stromal Cell Tumors**
- Granulosa cell
  - Any age
  - Inhibin A/B or Estradiol
  - Precocious puberty
  - Microscopic: Call-Exner bodies
- Tumours in the Thecoma-fibroma group

**Androblastomas**
- Sertoli-Leydig Cell Tumors
- Well /Intermediate/Poor differentiated
- Secretes androgen

**Fibromas**
- Associated with ascites & hydrothorax
  "Meigs syndrome"
Krukenberg tumour

- Secondary Ca of the ovary
- Metastasized classically from GIT and breast
- 80%: bilateral ovarian involvement
- “Signet ring cells”
Ovarian tumours

• Primary ovarian ca commonly: 40-60 yrs
• Teratomas and Sex Cord: mostly before puberty
• Borderline malignant: 30-50 yrs

Ovarian ca; a silent killer

• Asymptomatic in early stages
• 75% diagnosed with advanced stage disease
• Overall 5-year survival rate: 35%
• Most common cause of death from gynaecological cancer in UK
Ovarian ca; risk factors

Ovarian ca

- Most cases of EOC are sporadic
- The aetiology is unknown
- Most significant risk factor is genetic predisposition

Ovarian ca, a challenging disease

- Natural history not well understood
- No well-defined precursor lesion
- Length of time from localised tumor to dissemination is unknown
- No effective screening method for early detection yet
Risk factors: Heredity

- 10% of Epithelial ca cases are familial

- Familial syndromes:
  - Familial breast-ovarian cancer syndrome (BRCA I+II)
  - Cancer family syndrome (Lynch syndrome = HNPCC)

- Account for 90% of familial ovarian ca
Additional Risk Factors

• Age
  o Rare <30
  o Peak ≥ 60yrs
• Reproductive history
  o Early menarche
  o Nulliparity
  o Age >30 at first child-bearing
  o Late menopause
• Fertility drugs
• Personal history of breast cancer
• Talcum powder
Protective factors

• Multiparity
• First pregnancy before age of 30
• Oral contraceptives: 5 years of use decreases risk by 50%
• Tubal ligation
• Hysterectomy
• Lactation
• Bilateral oophrectomy
Diagnostic approach

History

- Abdominal bloating, increased girth, pressure
- Unusual fatigue
- GIT: nausea, indigestion, gas, constipation, diarrhea
- Urinary frequency or incontinence
- Unexplained weight loss or gain
- Shortness of breath

Germ cell tumours

- Often present more acutely & at an earlier stage
- Typically:
  - Rapidly enlarging abdominal/pelvic mass
  - Acute severe lower abdominal pain due to tumour rupture, haemorrhage or torsion
Diagnostic approach

Examination
• Abdominal / pelvic: pelvic masses, ascites, hepatomegaly
• Chest: Pleural effusions, palpable lymph nodes

Imaging
• TA & TV scans: Detection of masses and its characters
• CT scan (Abdomen / chest): Assess spread to LN, pelvic & abdominal structures
• MRI: Best to distinguish malignant / benign tumors

Bloods: CBC, KFT, LFT, tumour marker
Diagnostic approach

Tumour markers

- Serous tumours: CA 125
- Mucinous: CA 19-9
- Granulosa: Inhibin
- Endodermal sinus: AFP
- Choriocarcinoma: HCG
- Dysgerminoma: LDH, Alkaline phosphatase
Diagnostic approach
Risk of malignancy index (RMI)

RMI:
• Gives an estimate of the risk of ovarian ca for women with adnexal masses
• Calculated using
  o Ultrasound findings (U)
  o Menopausal status (M)
  o CA-125 value (serum levels >30U/ml abnormal)
RMI

RMI = U x M x CA125

Ultrasound findings (U)

“Scored 1 point for each”

• Multi-locular cyst
• Evidence of solid areas
• Evidence of metastases
• Presence of ascites
• Bilateral Lesions

Menopausal status

• Postmenopausal status is graded M = 3
• Pre-menopausal status is graded M = 1

Ca-125

U:

• U = 0 (U/S score of 0)
• U = 1 (U/S score of 1)
• U = 3 (U/S score of 2 – 5)
<table>
<thead>
<tr>
<th>RISK</th>
<th>RMI</th>
<th>Risk of Cancer</th>
</tr>
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<tbody>
<tr>
<td>Low</td>
<td>&lt;25</td>
<td>&lt;3</td>
</tr>
<tr>
<td>Moderate</td>
<td>25-200</td>
<td>30</td>
</tr>
<tr>
<td>High</td>
<td>&gt;200</td>
<td>75</td>
</tr>
</tbody>
</table>
Ultrasound

- Both TA and TV (TVS has better resolution)
- Major limitations
  - Poor PPV in asymptomatic women
  - Inability to detect ca when ovaries are normal size
- Allows earlier stage detection
Benign vs Malignant Tumors
“Ultrasound & Doppler”

**Benign**
- More likely unilateral
- Unilocular
- Thin-walled
- No papillae
- No solid areas

**Malignant**
- More likely bilateral
- Multilocular
- Thick walls
- Papillae present
- Mixed echogenicity due to solid areas
- Greater Angiogenesis and Blood Flow
Benign ovarian cyst
Malignant ovarian mass
Spread of Ovarian malignancies

- **Direct seeding:** To peritoneum, omentum, tubes, ureters
- **Lymphatics:** To para-aortic nodes, umbilicus, diaphragm
- **Bloodstream:** To lower vagina and in the case of sarcomas and Teratomas to the lungs and else where
- **Direct spread:** To any neighboring organ or tissue
Ovarian ca: Staging
FIGO ovarian cancer staging: 2014 update
<table>
<thead>
<tr>
<th>Stage</th>
<th>Tumour confined to ovaries</th>
</tr>
</thead>
</table>
| I     | IA: Tumour limited to one ovary, capsule intact, no tumour on surface, negative washings  
       | IB: Tumour involves both ovaries otherwise similar to 1A  
       | IC: Tumour limited to one or both ovaries 1 Surgical spill, 2 Capsule rupture before surgery or tumour on ovarian surface  
       | 3 Malignant cells in the ascites or peritoneal washings |
|       | **Tumour involves one or both ovaries with pelvic extension (below the pelvic brim) or primary peritoneal cancer** |
| II    | IIA: Extension and/or implant on uterus and/or fallopian tubes  
       | IIB: Extension to other pelvic intraperitoneal tissues |
|       | **Tumour involves one or both ovaries with cytologically or histologically confirmed spread to the peritonium outside the pelvis and/or metastasis to the retroperitoneal lymph nodes** |
| III   | IIIA: Positive retroperitoneal lymph nodes and/or microscopic metastasis beyond the pelvis  
       | IIIA1: Positive retroperitoneal lymph nodes only  
       | IIIA1(i): Metastasis ≤10 mm  
       | IIIA1(ii): Metastasis >10 mm  
       | IIIA2: Microscopic, extrapelvic (above the brim) peritoneal involvement ± positive retroperitoneal lymph nodes  
       | IIIB: Macroscopic, extrapelvic, peritoneal metastasis ≤ 2 cm ± positive retroperitoneal lymph nodes  
       | IIIC: Macroscopic, extrapelvic, peritoneal metastasis > 2 cm ± positive retroperitoneal lymph nodes. Includes extension to capsule of liver/spleen without parenchymal involvement of either organ. |
| IV    | **Distant metastasis excluding peritoneal metastasis** |
|       | IVA: Pleural effusion with positive cytology  
       | IVB: Hepatic and/or splenic parenchymal metastasis, metastasis to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside of abdominal cavity) |
Ovarian ca: FIGO Grading

Epithelial tumours of the ovary are also sub-classified by histological grading

- Gx : Grade cannot be assessed
- G1 : Well differentiated
- G2 : Moderately differentiated
- G3 : Poorly differentiated
Treatment Options

- Surgery
- Chemotherapy
- Radiotherapy
Standard treatment for ca ovary

Surgery

Chemotherapy

- Platinum
- Taxol
Surgery
Types of Surgery

Aim of surgery
• Optimal cytoreduction: maximum residual tumour deposits no more than 1 cm
• May consider fertility preserving procedure should that be medically possible

Types of surgery
• TAH+BSO
• Unilateral salpingoophrectomy (if fertility has to be preserved)
• Cytoreductive or “debulking”
• Peritoneal metastasis reduction
• “Second look” laparotomy
Chemotherapy
Chemotherapy (CT)

- Ovarian ca is a chemo-sensitive
- Advanced disease “has progressed beyond the ovaries, stage 1c & above; require both surgery and CT

Types of chemotherapy
- **Adjuvant:** CT following surgery
- **Combination:** Several agents given simultaneously to enhance their effectiveness
- **Neo-adjuvant:** CT prior to surgery where Dx has been established by cytology of ascitic fluid or histology of a tissue biopsy
Chemotherapeutic Agents

- **Alkalyting agents:**
  Cyclophosphamide, Cisplatin, Carboplatin, Melphalan

- **Plant alkaloids:**
  Paclitaxel, Vincristine, Etoposide

- **Anticancer antibiotics:**
  Bleomycin, doxorubicin

- **Antimetabolites:**
  Fluorouracil, Gemcitabine
Side effects of chemotherapy

- Nausea and vomiting
- Fatigue
- Oral ulcerations
- Ototoxicity (cisplatin): hearing loss, tinnitus
- Peripheral neuritis
- Nephrotoxicity
- Myelosuppression
- Pulmonary toxicity (bleomycin). Any new-onset cough/shortness of breath should be investigated urgently to exclude pneumonitis or fibrosis.
Follow up after primary treatment

Follow up

• Provide reassurance
• Assess for early recurrence

Follow up

• Clinical
• CA-125
• MRI
Radiotherapy
RT; ca ovary

- Rarely used as the main Rx for ovarian ca
- Can be useful in treating areas where the cancer has spread, either near the main tumor or in a distant organ, like the brain or spinal cord
Primary fallopian tube carcinoma (FTC)

- 0.14% - 1.8% of female genital ca
- Only 1200 cases of primary FTC have been reported in the literature
- Aetiology is unknown but hormonal, reproductive & possibly genetic factors
- BRCA-1 and BRCA-2
- 90% of FTCs are serous papillary adenocarcinoma
Clinical manifestations & Rx

Presentation

• 40–60 years (median age 55 years)
• Symptoms are vague and non-specific, but are similar to ovarian ca

Latzko's triad of symptoms:
Present in 15% of the cases
  o Intermittent profuse serosanguinuous vaginal discharge
  o Colicky pain relieved by discharge
  o Abdominal or pelvic mass
• 0–10% are identified preoperatively

Treatment

• As epithelial ovarian ca