

Review Article


Non-neoplastic lesions of the ovary – A review

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Abstract

Ovary is an important organ as it is concerned with the production of progeny. Ovary is the commonest site of neoplastic and non-neoplastic lesion, can present in childhood to postmenopausal age group and accounts for the most prevalent cause of hospital admissions. Non-neoplastic ovarian lesions are classified as inflammatory (infectious and non-infectious), non-inflammatory (cystic and non-cystic) and pregnancy related disorders.

Key words

Non-neoplastic lesions, Ovary, Pregnancy related disorders.

Introduction

Ovary is an important organ as it is concerned with the production of progeny. The ovary consists of sex cells and mesenchymal cells which are totipotential and multipotential respectively. Ovary is the commonest site of neoplastic and non-neoplastic lesion, can present in childhood to postmenopausal age group and accounts for the most prevalent cause of hospital admissions. Many of the non neoplastic lesions mimic ovarian neoplasms on clinical examination, at operation and even on pathological evaluation. Hence, their recognition is important from the view point of therapy and prognosis.

What is the need to diagnose all non neoplastic lesions?

In view of the diversity of ovarian lesions it is important to differentiate them preoperatively so as to avoid unnecessary surgical intervention. Ultrasonography is the primary imaging modality to identify and MRI has shown high accuracy [1]. Endovaginal ultrasonography with Doppler enhancement is the best imaging technique to establish the nature of cyst and to distinguish cysts suspicious for malignancy which require more invasive investigation [2].

Percutaneous ultrasound guided fine needle aspiration cytology is a useful tool in identifying the non-neoplastic cysts [3, 4]. Combined use of

ESR and C-reactive protein is more helpful in inflammatory conditions [5]. Quantitative serum β -hCG can rule out ectopic pregnancy and is a useful tumor marker as well.

Classification

Ovarian tumor and non-neoplastic lesions present a great challenge to Gynecological Oncologist. Certain non-neoplastic lesions of the ovary frequently form a pelvic mass and potentially mimic an ovarian neoplasm. Their proper recognition and classification is therefore important to allow appropriate therapy [6].

Inflammatory disorders: Infectious and Non infectious.

Non inflammatory disorders: Cystic and Non cystic.

Pregnancy related disorders.

Inflammatory disorders

Infectious

Pelvic inflammatory disease is a serious condition that can lead to abscess formation and the ultrasonographic finding of tubo-ovarian abscess are not specific [7]. Combined use of ESR and C-reactive protein is useful in assessing the severity of acute pelvic inflammatory disease [5]. Inflammatory disease of the ovary is part of PID of bacterial origin, most of the times, invariably secondary to salpingitis and classically presents as bilateral tubo-ovarian abscess [7]. It is a common serious complication of sexually transmitted pathogens like Neisseria gonorrhoeae and Chlamydia trachomatis. The usual sequelae are tubo-ovarian adhesion, tubo-ovarian cyst and changes similar to polycystic ovarian disease [8].

Only ovarian involvement without tube is very rare, usually results from direct of lymphatic spread from non gynaecological pelvic inflammatory process like diverticulitis, acute appendicitis, inflammatory bowel disease, post op pelvic infection and very uncommonly blood borne infection [9]. Only 10% of pelvic tuberculosis show ovarian involvement, invariably secondary to tubal disease. Cases of

raised CA125 levels in patients with tuberculosis have been reported [10, 11, 12].

Non infectious granulomas

Foreign material may evoke a granulomatous reaction on the ovaries and peritoneal surfaces mimicking metastatic lesion e.g. starch granules from surgical gloves, starch containing douche fluid or lubricants, talc and HSG contrast material.

Cystic lesions

Epithelial inclusion cyst

Usually epithelial inclusion cyst found in post menopausal women but can be present at any age. Arise from cortical invagination of surface epithelium that has lost their surface connection. Microscopically, cortical glands lined by columnar cells which may be ciliated are seen, psammoma bodies may be present within or around. Occasional arias stella reaction/dysplastic changes are known.

Follicular cysts

Follicular cysts are commonly seen in women in reproductive age group, particularly during early years after menarche and at around the time of menopause. Follicular cysts develop as a result of temporary pathologic variation of a normal physiological process. Ovarian enlargement results from non-rupture of dominant mature follicle or failure of an immature follicle to undergo the normal process of atresia. These cysts are unilocular thin walled several mm to 8 cm. Solitary follicular cysts are common and occur throughout life. Grossly, they present as unilocular, smooth surfaced, thin walled cysts with clear fluid, rarely exceeding 8 cm. These cysts are situated in the ovarian cortex, and sometimes they appear as translucent domes on the surface of the ovary. Microscopically, they are lined by an inner layer of granulosa cells and outer layer of theca interna cells.

The initial management of a suspected follicular cyst is conservative observation. The majority of follicular cysts disappear spontaneously by either

reabsorption of the cyst fluid or silent rupture within 4 to 8 weeks of initial diagnosis.

Corpus luteal cyst

Corpus luteal cysts are less prevalent than follicular cysts and mainly result from intracystic hemorrhage. Corpus luteum cysts may be associated with either normal endocrine function or prolonged secretion of progesterone. Grossly focal or circumferential yellow convoluted wall of unilocular cyst is seen. Histologically cyst wall is composed of an inner connective tissue layer, a middle layer of large luteinized granulosa cells and an outer layer of small luteinized theca interna cells. The fluid content is often bloody. If the cyst ruptures, hemorrhage into the peritoneal cavity occurs (sometimes over 500 ml), and an erroneous diagnosis of ruptured ectopic pregnancy may be made [13]. The treatment of unruptured corpus luteum cysts is conservative. However, if the cyst persists or intra-peritoneal bleeding occurs, necessitating operation, the treatment is cystectomy.

Polycystic ovaries (PCOS)

It is characterized by bilaterally enlarged polycystic ovaries, chronic anovulation and clinical manifestation due to secretion of excess androgens. It is believed to be due to hypothalamo-pituitary dysfunction leading to over-secretion of LH.

Various clinical syndromes may develop in patients with polycystic ovaries, including Stein–Leventhal syndrome which is characterized by amenorrhea and sterility, so-called ‘metropathia hemorrhagica’, and frank virilism. These syndromes tend to overlap considerably, as do the pathologic findings [14]. Grossly, both ovaries are enlarged with white surface, having cysts measuring less than 1 cm, just beneath the surface. The central portion of the ovary is composed stroma with few or no stigmata of ovulation. Histologically PCOs are characterized by multiple follicular cysts or cystic follicles with varying degrees of luteinization of the theca interna, covered by a dense fibrous capsule [15].

Theca lutein cysts

It is typically a self limited syndrome with asymptomatic bilateral enlargement of ovaries containing multiple theca lutein cysts due to excessive stimulation of the ovaries by B hCG [16]. On gross examination, multiple, almost invariably bilateral cysts, that result in moderate to massive ovarian enlargement up to 26 cm may be seen. Histologically both corpus luteum cysts and luteinized follicle cysts are seen with marked luteinization of theca interna cells, compared to granulosa cells. There is associated stromal edema and stromal luteinization.

Non cystic lesions

Stromal hyperplasia

This tumor is characterized by non-neoplastic proliferation of the ovarian stromal cells commonly seen in postmenopausal women. Always bilateral and may be associated with enlarged ovaries. Cut surface shows homogenous grey-white appearance. It is characterized by a diffuse or nodular proliferation of plump ovarian cortical stromal cells encroaching on the medulla [17].

Massive edema of ovary

Massive edema of ovary is typically seen in young, nulliparous women at an average age of 20 years, although cases have been reported in premenarchal girls [18]. Acute abdominal pain is a common presenting symptom. Irregular menstruation is seen more rarely. A palpable adnexal mass or virilisation can also be seen [19, 20, 21]. Unilateral cases make up to 85% and most are in the right ovary [22]. The most favoured hypothesis for the etiology is the development of massive edema as a result of disturbed venous and lymphatic circulation following complete or partial torsion of the ovary [23].

WHO defines it as an accumulation of edema fluid within ovarian stroma, separating normal follicular structure [24]. Grossly, ovary is enlarged ranging from 5 to 35 cm, soft, fluctuant and has a shiny, white smooth surface. The cut

surface shows a white, fibrotic and thickened superficial cortex, which appears like a capsule and a solid tan homogenous and gelatinous appearance. Microscopically, there is marked diffuse stromal edema that separates follicles and their derivatives with sparing of the superficial cortex. The histopathological differential diagnosis is fibroma and luteinized thecoma. The presence of signet ring cells or other epithelial cells in the stroma should be carefully evaluated to exclude krukensberg's tumor [25].

Endometriomas

Endometriosis corresponds to ectopic endometrial glands and stroma outside the uterus and is associated with pelvic pain and infertility [26]. The prevalence of endometriosis amongst female population is 6-10% [27] and in patients with adenomyosis the prevalence is as high as 90% [28].

Sampson's menstrual reflex theory is widely accepted as an explanation of endometriosis physio-pathology. It proposes five basic necessary processes to its development which include adhesion, invasion recruitment, angiogenesis and proliferation [29]. Endometriosis is reported to be more common on the left side as compared to the right and bilaterality is often seen [30]. One reason for increased left sided occurrence is decreased fluid movement on right side because of sigmoid colon [31]. Areas of ovarian endometriosis that become cystic are termed endometriomas. The size of ovarian endometriomas varies from small, superficial implants that are 1 to 5 mm in diameter to large, multiloculated, hemorrhagic cysts that may be 5 to 10 cm in diameter. The presence of small, sometimes dilated, capillaries within the endometriotic stromal component, sometimes associated with hemorrhage, can be clue to the diagnosis. Immunoreactivity of the stromal cells for CD10 can help confirm their endometriotic nature [32, 33]. Histological examination reveals typical endometriotic glands and stroma, although in some cases the glandular component is hyperplastic. The differential diagnosis in these cases is usually with

adenosacroma. Rarely, burnt-out foci of ovarian endometriosis can take the form of necrotic granulomatous nodules with neumerous foamy and pigmented histiocytes, diagnostic endometriotic glands and stroma are usually absent or sparse. Occasionally, endometriotic stroma, particularly in the walls of endometriotic cysts, can undergo striking smooth muscle metaplasia (endomyometriosis), sometimes with the formation of a uterus like mass .Cancer development has been estimated to occur in 0.7-5% of all cases of ovarian endometriosis [34]. According to one theory, there are indications of a defective local immune response in the pelvic cavity in women with endometriosis, which could play a role in cancer development.

Pregnancy related disorders

Pregnancy luteoma

Pregnancy luteoma have been typically encountered during cesarean section in multiparous women, sometimes accompanied by a mild degree of virilisation [32, 33]. They can be numerous, in 30 to 50 percent of cases they are bilateral.

It is described as a large solid mass, most frequently around 6-10 cm, but luteomas have been described from microscopic to 20 cm size. It typically has a multi nodular appearance of yellow or brownish yellow color, often with dark red hemorrhagic deposits characterised microscopically by groups of luteinised cells with large eosinophilic cytoplasm and regular nuclei. If these cysts are left undisturbed, they will regress after delivery [34].

Granulosa cell proliferation pregnancy

These microscopic proliferations resemble miniature sex cord stromal tumors, and although of no apparent clinical significance, they can be associated with diagnostic problems for the pathologists. Although their common association with pregnancy, microscopic size, multifocality, and confinement to atretic follicles suggest a non neoplastic hormonal response.

The proliferations are usually multiple and life within atretic follicles, which are typically enveloped by a thick layer of luteinized theca cells. The granulosa cells may be arranged in solid, insular, microfollicular, or trabecular patterns, and contain scanty cytoplasm and grooved nuclei. Another rare pattern is one in which the granulosa cells are arranged in nodules and are luteinized with variably sized, round, non grooved nuclei. The appearance resembles that of a pregnancy luteoma except for the origin from granulosa cells and the larger size of their cells.

Ectopic decidua

A decidual reaction within the ovary is usually a response to the hormonal milieu of pregnancy. It may occur as early as the ninth week of gestation, and is present in almost all ovaries at term. Ovarian decidua is usually an incidental microscopic finding, but careful inspection may reveal tan to often hemorrhagic, nodules on the ovarian surface and rarely large soft, hemorrhagic masses. The association of these cells with more typical decidual cells, their bland nuclear features, the absence of Cytoplasmic neutral mucin, and if necessary the cytokeratin negativity of the cells, lead to the correct diagnosis.

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