Imaging in Ovarian Cancer

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INTRODUCTION

Majorities of ovarian cancers are epithelial tumours. Others include germ cell tumours, stromal-sex cord tumours and metastatic cancers from extra ovarian primary sites. Common tumours are serous and mucinous cyst adenocarcinomas. Others include endometroid, clear cell, brenner and undifferentiated tumors. Ovarian carcinoma predominantly occurs in postmenopausal women and upto 85% of them present with peritoneal spread[1] (stage III). Spread of the tumour is trans-coelomic and follows the pathways of peritoneal fluid circulation. Accordingly, deposits in right sub diaphragmatic region and para colic gutters occur early alongwith ascites. Eventually all peritoneal surfaces, omentum and mesentery may be involved. Metastases to the para aortic lymph nodes upto the renal hilum and pelvic lymph nodes also occur.

Ultrasonography

Ultrasonography is usually the first imaging modality to diagnose or confirm the clinically suspected adnexal mass. It is also used to characterize the adnexal masses based on their morphological features. Large, bilateral, complex solid-cystic masses are usually malignant. Cysts with thick walls, papillary nodules and irregular thick septations also favor malignancy. Presence of ascites, peritoneal deposits and lymph node enlargement are other supportive evidences. Transvaginal sonography is better than trans abdominal approach for assessment of morphological features of the adnexal masses.

Doppler studies are extremely important in evaluation of adnexal masses. Malignant tumours have abnormal neo vascularity and low resistance flow pattern. Low pulsatility index (1or less) and low resistive index (0.4 or less) suggest malignancy[2]. However, similar findings may also be seen rarely in benign tumours, inflammatory diseases and physiological cysts. Positive predictive value of 98% has been reported for ovarian malignancy using transvaginal colour Doppler[2]. It appears reasonable that a combined morphological and Doppler sonographic evaluation is the best approach in detection of ovarian cancer. The largest series using this combined approach has reported a sensitivity of 97.3 percent, specificity of 100 percent and accuracy of 99.4 percent for detection of ovarian carcinoma[3].

Ultrasonography has the potential to be used as a screening tool for ovarian cancer in high-risk group. These include women with family history or those with hereditary ovarian cancer syndrome (e.g. BRCA 1 or 2 gene positive). Combined approach, which includes bimanual pelvic examination, serum tumor markers (CA-125) and transvaginal sonography with Doppler studies, can be used for the screening[4]. The five year survival rates upto 90 percent for stage I cancers as compared to 15-20 percent in stage III or IV cancers and the fact that most patients present with advanced disease make screening important. However, the screening for ovarian cancer is yet to gain momentum like mammographic screening, even in developed countries. This is because of comparatively low incidence of ovarian cancer and high cost of the screening. In India the incidence is even lower and the resources are limited hence, regular screening programme for ovarian cancers is unlikely to be undertaken in near future.

CAT Scan

CAT is the main stay of preoperative evaluation of ovarian cancer. The CT features of ovarian cancer show varied morphological pattern: a multi locular cyst with thick internal septations and solid mural nodules, complex cystic-solid mass or lobulated papillary mass[5]. The solid components of the tumour enhance well with intravenous contrast. Solid looking areas

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that do not enhance may represent blood or mucinous fluid with high protein content. Calcification may also be present. Involvement of uterus, rectum, colon and small bowel by the tumour is well demonstrated. CT can also detect deposits on peritoneum, liver or bowel surfaces. Three most common sites to have peritoneal deposits are right sub diaphragmatic space, greater omentum and pouch of Douglas[6]. The sensitivity of CT in this regard is moderate, conventional CT scanners can detect only upto 50% of peritoneal deposits that are 5 mm or less in size. The helical and multi detector CT scanners have improved sensitivity in detection of small peritoneal deposits, especially in upper abdomen[1,7]. CT detection of peritoneal or liver surface deposits is facilitated by presence of ascites. Small foci of peritoneal calcifications may also represent deposits, especially, if it is a new finding.

Omental deposits are initially seen as multiple nodular lesions in omental fat. Later, they coalesce to form a solid 'omental cake', which is seen along the greater curvature of stomach or anterior to transverse colon or small bowel. Mesenteric metastases are seen as rounded, ill-defined soft tissue masses surrounded by small bowel loops or as thickening along the mesenteric vessels and lymphatics[1]. CT accurately detects para aortic and pelvic lymph node enlargement but later are uncommonly involved. Intra hepatic metastases are rare and occur late in the course of the disease. Ovarian cancer is one of the few primary cancers to have splenic metastases.

Pseudomyxoma pertonii occurs due to rupture of mucin secreting tumors into the peritoneal cavity leading to gelatinous deposits throughout the peritoneum[1]. On CT, locules of high-density fluid are seen on peritoneal and serosal surfaces that frequently indent the adjacent structures.

MRI

T1W fat suppressed, T2W and gadolinium enhanced T1W sequences are important in ovarian cancer. The morphological features of ovarian cancer on MRI are similar to those seen on sonography or CT, but because of excellent soft tissue contrast, the details are better demonstrated. Most tumours are low or intermediate in signal intensity on T1W and high in signal intensity on T2W images. Contrast enhancement helps to differentiate solid and necrotic areas. MRI is better than other modalities in determining the origin of a pelvic mass. It is also more accurate in classification of adnexal masses into benign and malignant[1]. MRI features favoring malignancy are: size more than 4 cm, large solid component, wall or septal thickness of more than 3 mm, nodularity or vegetations and necrosis. Ancillary features supporting the diagnosis of malignancy include involvement of other pelvic structures, peritoneal deposits, ascites and lymphadenopathy. These features have specificity of 95% in characterization of malignant ovarian tumour [8].

MRI is also accurate in demonstration of direct involvement of other pelvic structures by the ovarian tumour. The peritoneal and lymph nodal spread detection by MRI is comparable to the CT[9]. Long imaging time required for MRI evaluation of entire abdomen and pelvis makes it unsuitable and more expensive for routine study in ovarian cancer. Longer imaging time also affects the detection of small peritoneal deposits in upper abdomen. However, newer sequences like breath-hold, HASTE and fast spin echo may overcome time and cost limitations of MRI[1].

Role of Imaging

Role of imaging in ovarian cancer is to detect and characterize adnexal masses, recognize unusual findings that may suggest atypical or alternative diagnosis, demonstrate metastases in order to prevent surgical understaging and detect specific sites of the disease that may be unresectable[6].

Ultrasonography is usually the first imaging modality in evaluation of patients suspected to have adnexal mass. Transvaginal sonography and Doppler Studies in combination with clinical and laboratory findings (tumour markers) are fairly satisfactory for characterization of adnexal masses. Sonography is unsuitable for evaluation of peritoneal spread of the ovarian cancer.

CT is the imaging modality of choice for evaluation of ovarian cancer. The staging of ovarian cancer is surgical. In standard surgical procedure both staging as well as therapeutic resection of the tumour are combined. The complete surgical procedure includes total abdominal hysterectomy with bilateral salpingo-oophorectomy, omentectomy, retroperitoneal lymph node sampling, peritoneal biopsies and cytology of peritoneal washings.

Although the staging is always surgical, preoperative CT is recommended and it is now becoming popular. Demonstration of GIT and urinary tract involvement helps to modify the surgical plan[6]. Preoperative CT can accurately predict the surgical outcome and hence has important role in deciding the management of ovarian cancer[10]. Non resectable disease such as those with large deposits at porta hepatis, root of the mesentery, diaphragm and retroperitoneum can be spared of surgery and put on neo-adjuvent chemotherapy, as optimal debulking of the disease is unlikely to be achieved in these patients[6,10].

MRI is superior to sonography or CT in the diagnosis of ovarian malignancy, particularly when physical examination and sonography findings are equivocal. For pre-operative staging, MRI is predominantly used as a problem solving modality at present[11].

TREATMENT AND FOLLOW-UP

Although only 10-15% patients present with early stage diseases, high cure rate is achieved with surgery with or without post-operative chemotherapy[1]. Patients with advanced diseases are rarely cured with surgery. Neo adjuvent (pre-operative) and adjuvent (post-operative) combination chemotherapy is effective in these patients.

Recurrence rate is high in ovarian cancer even after complete remission. The patients are followed up with pelvic examination, serum tumour markers (CA-125), and CT of abdomen and pelvis every 3-4 months for 2 years[11]. Less frequent follow-up is required after that. After completion of the treatment, a surgical exploration of the asymptomatic patient (second look laparotomy - SLL) was the standard procedure to document pathological complete remission. This procedure is now uncommonly performed, as CT with tumour markers is adequate for majority of the patients. However, SLL is still indicated for patients with normal CT examination but high clinical suspicion of having persistent disease or recurrence.

The recurrences are most common at the site of previous lesions hence, preoperative CT scans must be reviewed while evaluating the follow-up CT scans. Careful search for the recurrences should be made at these sites. Both CT and MRI are useful in detection of macroscopic recurrences, however, in absence of effective second line treatment, cost effectiveness of routine CT and MRI follow-up is questionable[12]. Germ cell tumours (GCT) of the ovary are rare and constitute only 5-15% of ovarian malignancies. These affect young and adolescent women. GCT is commonest ovarian tumor in pediatric age group. Commonest of these tumours is dysgerminoma. Others include immature teratoma, embryonal tumour, endodermal sinus (yolk sac) tumor, chorio-carcinoma and mixed germ cell tumours.

Patients present with abdominal pain, mass or with acute abdomen because of torsion, rupture or hemorrhage in the tumour mass. Tumour markers such as AFP, HCG and LDH may be elevated. Staging of GCT according FIGO guidelines is similar to that for epithelial ovarian carcinoma.

On cross sectional imaging, germ cell tumours are usually unilateral, solid and well defined, however cystic, necrotic or hemorrhagic areas within these are frequently seen. These tumours are often quite large on presentation because of their aggressive nature. Dysgerminoma is seen as multi lobulated solid mass with fibro-vascular septa between the lobules. Prominent arterial flow may be demonstrated in these septae on colour Doppler[13]. Sonographic appearance of immature teratoma and yolk sac tumours is similar to that of dysger-

minoma. Calcifications may be seen in dysgerminoma and teratoma.

Spreads of germ cell tumours occur by direct extension into adjacent organs and/ or by lymphatic or hematogenous dissemination. Metastases to the lymph nodes, liver and lungs are more common with germ cell tumours than with epithelial carcinomas.

Most patients present early in the course of the disease and hence, prognosis is usually good. Surgery with unilateral salpingo-oophorectomy and preservation of uterus and contralateral ovary can be performed in most patients, thus preserving the fertility. Advanced diseases are treated with surgery and chemotherapy. Dysgerminoma, like seminoma, are radiosensitive and can be treated with radiotherapy if preservation of fertility is not the main concern. Patients are followed with periodic physical examination, serum tumour markers and ultrasonography. CT scan is performed if sonographic examination is equivocal or tumour markers are rising. Functional ovarian cyst are often seen in normal ovary after fertility preserving surgery and these evoke anxiety and fear of recurrent disease, however, these can be safely followed-up. Recurrences after complete remission of GCTs are uncommon and occur in 10-20% of patients. Most of these occur in first two years and late relapses are extremely rare.

Stromal-sex cord tumours

Neoplasms arising from sex cord or stromal cells constitute 3-6% of ovarian malignancies. Commonest of these is granulosa cell tumour, which is almost always malignant, while fibromas, thecomas and sertoli-leydig cell tumours, which usually behave in benign fashion. Histology of stromal-sex cord tumours can not accurately predict the clinical behavior and actual grade of malignancy can not be defined. These tumours occur either in postmenopausal women or in pre-pubertal girls. These secret estrogen and hence cause sexual precocity in girls and resumption of menses in postmenopausal women.

On cross sectional imaging, these tumours vary in appearance from homogeneously solid to multicystic masses. Granulosa cell tumours are seen as predominantly solid and multilobulated adnexal masses. Heterogenous enhancement may be seen after intravenous contrast on CT or MRI. They have high propensity for local invasion and sacral involvement is frequently seen[1].

Metastatic Ovarian Tumours

About 15% of ovarian malignancies are metastatic in nature. Common primary sites are stomach, colon and breast. Uncommon primary sites include lung, gall bladder and pancreas. 'Krukenberg tumour' is the term used for specific histological pattern of mucin secreting signet cells with sarcomatous stroma, usually from a gastric primary. Clinical presentation in metastatic ovarian tumours is variable. About one third of the patients present with pelvic mass and not with the symptoms of primary site. Metastases from breast cancer are commonly seen at autopsy but often they are not apparent clinically or radiologicaly. Melanoma usually secondarily involves ovaries, however, primary malignant melanoma of the ovary also occurs[14].

On cross sectional imaging, ovarian metastases are usually bilateral large and lobulated. These are often indistinguishable from primary ovarian carcinoma[1]. Ascites, peritoneal nodules and omental deposits are seen in both primary and metastatic ovarian tumours. Hematogenous spread to liver is rare with primary ovarian carcinoma but common with metastatic ovarian disease. Hence presence of intra hepatic metastases should warrant a search for primary tumour in stomach or colon. Possibility of metastatic ovarian tumour must be considered in any patient with ovarian mass if there is a known extra ovarian primary cancer or liver metastases. Ovarian lymphoma is usually a part of disseminated non-Hodgkin's lymphoma. Most of these are seen as bilateral large adnexal masses. Ovary is the commonest organ of female genital tract to be involved in leukemia.

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