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Thoracic manifestations of Gynecological tumors: Airway and lung parenchymal involvement commoner in endometrial and ovarian cancers while pleural and interstitial involvement is predominant in cervix malignancies

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ABSTRACT

Introduction: The thorax is a frequent site of metastasis from numerous non-pulmonary cancers. Intrathoracic metastatic disease may manifest in a variety of forms, including solitary or multiple pulmonary nodules, endobronchial tumor, lymphangitic carcinomatosis, or a pleural effusion.

Materials and Methods: This is muticentric, observational study conducted in Pulmonary Medicine, MIMSR medical college & Venkatesh chest hospital and critical care center, Latur during June 2012 to November 2016 to observe various thoracic manifestations of gynecological malignancies. Total 2300 cases of various gynecological malignancies were screened and finally 330 cases showing various thoracic manifestations were enrolled after subjecting those cases to inclusion and exclusion criteria. All study cases were subjected to chest radiological investigations and histopathological investigations whenever necessary to diagnose metastatic disease. Hospital's ethical committee & IRB approval has been taken and written informed consent of patient was taken before enrollment.

Observations and Analysis: Screened total 2000 cases of gynecological malignancies (ovary, endometrium, cervix & benign ovarian tumors) and selected 330 cases with various metastatic thoracic manifestations. Malignant gynecological tumors including endometrial, cervical & ovarian cancers predominantly observed in above 50 years of age while benign ovarian and uterine tumors in below 50 years of age ($p<0.00001$). In study of 100 cases of ovarian cancer with thoracic manifestation, documented lung mass lesion as predominant involvement in 38% cases, pleural effusion in 19% cases & lymphangitic carcinomatosis in 11 % cases. In study of 100 cases of endometrial cancer with thoracic manifestation, documented lung mass lesion as predominant in 58% cases, endobronchial metastasis in 16% cases & lymphangitic carcinomatosis in 6 % cases. In study of 100 cases of cervical cancer with thoracic manifestation, documented lymphangitic carcinomatosis as predominant in 36 % cases, pleural effusion in 26% cases & endobronchial metastasis in 5 % cases. Lung metastasis and endobronchial involvement documented predominantly in ovarian and endometrial malignancies while pleural effusion and lymphangitic carcinomatosis documented predominantly in cervical malignancies ($p<0.00001$). Involvement of airway (endobronchial metastasis) and lung parenchymal mass lesion predominantly documented in endometrial malignancies; lung parenchymal (mass lesion) with lymphangitic carcinomatosis in ovarian malignancies and predominantly pleural involvement with lymphangitic carcinomatosis documented in cervical malignancies ($p<0.003$).

Conclusion: Thoracic metastatic manifestations of gynecological tumors are underdiagnosed & less reported in clinical practice because of lack of suspicion & use of modern radiological techniques to diagnose these lesions. Cases with gynecological tumors with respiratory symptoms should be evaluated with all possible conventional & advanced diagnostic methods to document metastatic manifestations of these tumors to have successful treatment outcome and longevity in survival.

Keywords: gynecological tumor's, thoracic metastasis, endometrial carcinoma, endometrial carcinoma, lymphangitic carcinomatosis

INTRODUCTION

Ovarian and cervical cancers are the most common gynecological cancers affecting women worldwide and in India. Cervical cancer is on a declining trend, but remains the second most common cancer in women after breast cancer. Every year in India, 122,844 women are diagnosed with cervical cancer and 67,477 die from this disease (1).

Uterine cancer, also known as endometrial cancer, is the most common malignancy of the female genital tract (2). Most cases of endometrial cancer show good prognosis, but in approximately 25% of cases appeared as extra-uterine

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disease (3). In distant metastasis, endometrial cancer is commonly spreading through pelvic lymph node and para-aortic lymph node or adnexa and pelvic viscera. Incidence of hematogenous metastasis is low in endometrial cancer. Pulmonary metastases represent a common site of extra-pelvic spread of disease but incidence is only 2.3%–4.6% (4, 5).

Metastasis to the lung can take many forms. These include solitary and multiple parenchymal nodules, lymphangitic carcinomatosis, tumor emboli, endobronchial metastasis, and pleural effusion. These patterns can occur by direct extension or by systemic spread. In the case of systemic spread, tumor cells lodge in the lung as the vessel lumen narrows and grow into the parenchyma or along the pulmonary lymphatics. Venous blood is filtered by the lung, which makes it a frequent site of metastasis (6).

Parenchymal nodules are the most frequent representation of pulmonary metastasis. These nodules are usually multiple, peripheral, and basal in anatomic distribution and correspond with areas of increased blood flow in the lung (7). They may be symmetric, variable in size or miliary, or even present as large, well-defined cannonball-like masses. Symmetric, equally-sized nodules likely reflect a single embolic shower of tumor emboli, whereas nodules of variable size may reflect embolic events that occurred at different time periods (6). Solitary nodules represent a distinct form of pulmonary metastasis that is rare. In one study of solitary pulmonary nodules, 11% had an extrapulmonary source (8).

When tumor spreads by way of the lymphatic system, it does so in two ways. Tumor spread initially can be hematogenous and spread to the interstitial space and then the lymphatics or retrograde from the lymph node towards the periphery (9). Radiographically, lymphangitic carcinomatosis appears similar to interstitial edema with thickened bronchovascular markings and septal Kerley B lines (10). Lymphangitic carcinomatosis may be focal or diffuse. Approximately 40% of patients who have lymphangitic carcinomatosis have concomitant pleural effusion or mediastinal adenopathy (10). Bronchoscopy with transbronchial biopsy frequently is successful in making the diagnosis because of the proximity of lymphatic's to the peribronchial space (11).

Although endobronchial and tracheal metastases have been reported commonly in autopsy studies, clinically manifest disease is far less common (12). Metastasis to the airways occurs most often by direct extension from adjacent parenchymal or mediastinal tumor and rarely by hematogenous spread. Patients typically present with cough, dyspnea, wheeze, or hemoptysis (13). Radiographically, the lesions usually are occult on plain films, but may include atelectasis distal to the obstruction, focal air trapping (mosaic pattern), or post-obstructive pneumonia. CT scan can detect endobronchial disease with greater sensitivity than plain films (14).

Pleural effusion is a common finding in metastatic disease and can occur through a variety of mechanisms. It can occur by way of tumor spread along the peripheral lymphatics; in this situation, it frequently is associated with parenchymal disease. Pleural disease also can spread through the diaphragm by way of lymphatic channels (15). Exudative and bloody pleural effusion is much more likely to represent metastatic involvement (6). Pleural fluid cytology often can establish the presence of malignant cells within the pleural space, although the highest yield occurs with direct observation of the pleura at thoracoscopy.

Chest X-ray is shown to have less sensitivity and specificity than CT scanning in detection of pulmonary nodules. CXR fails to depict pulmonary metastatic lesions smaller than 7 mm, particularly those at the lung apices, bases, central locations adjacent to heart and mediastinum, pleural surfaces, and under the ribs. Of nodules smaller than 7 mm detected on CXR, 77% are calcified and are more likely to be granulomas (16, 17).

CT scanning is the modality of choice for detection and follow up of pulmonary metastasis, owing to its higher spatial, temporal, and contrast resolution and lack of superimposition of adjacent structures. It has been shown to have higher sensitivity than chest radiography (CXR) in the detection of pulmonary metastases. CT scanning is performed using a multi slice technique, and no intravenous contrast is required for the detection of pulmonary metastases. Contrast may be useful when a nodule is located adjacent to the hilum and mediastinum (18, 19).

When the nodules are numerous, they are distributed diffusely throughout the lungs in a random pattern without any specific anatomical distribution; when nodules are few, they are predominantly subpleural. Multiple pulmonary nodules in a patient with known malignancy are highly suggestive of metastasis. Of multiple pulmonary nodules detected with CT scanning, 73% are shown to be metastases (20).

In this study, we predominantly screened all the cases of gynecological malignancies presented with respiratory problems and observed thoracic manifestations of these tumors.

MATERIALS AND METHODS

This is muticentric, observational study conducted in Department of Pulmonary medicine, MIMSR medical college, Latur & Venkatesh chest hospital and critical care center, Latur during June 2012 to November 2016 to observe various

thoracic manifestations of gynecological malignancies. Total 2300 cases of various gynecological malignancies were screened and finally 330 cases showing various thoracic manifestations were enrolled after subjecting those cases to inclusion and exclusion criteria. Hospital's ethical committee & IRB approval has been taken and written informed consent of patient was taken before enrollment.

Inclusion criteria:

1. Ovarian cancer cases having respiratory complaints like cough, shortness of breath, chest pain or hemoptysis
2. Cervix malignancies having respiratory complaints
3. Endometrial malignancies having respiratory complaints
4. Benign ovarian tumors having respiratory complaints
5. Cases with obvious lesion on chest radiograph with known case of gynecological malignancy
6. Cases referred for bronchoscopy with known case of gynecological malignancy

Exclusion criteria:

1. Cases not willing to participate or
2. terminally ill cases not giving valid written consent were excluded from study

All study cases were subjected to:

1. Chest x-ray
2. High resolution contrast tomography (HRCT) thorax for lung parenchymal lesions
3. CECT (contrast enhanced CT scan) of thorax for mediastinal metastatic lesions
4. Bronchoscopy in cases with lung parenchymal mass lesions, hilar lesions, suspected airway lesions or patients with hemoptysis.
5. USG Thorax in cases with suspected pleural effusion
6. Pleural fluid aspiration and analysis
7. Pleural fluid cytology assessment for malignant metastatic pleural effusion
8. Bronchoscopic forcep biopsy histological and cytological evaluation of bronchial wash for malignant cell evaluation.

All study cases were assessed in outdoor unit of pulmonary medicine and further proceed to other necessary evaluation like chest x-ray, HRCT as protocol.

Radiological lesions were categorized as (21):

1. Lung metastasis (mass lesion) - parenchymal mass lesions were further categorized as solitary or multiple mass lesions i.e. cannon ball type lesions. Coin lesions, para hilar lesions and air space consolidations also included in mass lesion category. In selected cases HRCT thorax is used to document exact nature of parenchymal lesions.
2. Lung mass plus pleural effusion- above mentioned criteria plus obliteration of costophrenic angles were included in this category. Ultrasound thorax evaluation done in all the cases with use of CECT thorax in selected cases.
3. Pleural effusion- obliteration of unilateral or bilateral costophrenic angles on chest radiograph without obvious parenchymal lesions on chest x-ray or CECT thorax in selected cases
4. Lymphangitic carcinomatosis- as many times chest x-ray is normal, HRCT is the crucial diagnostic modality in evaluating these lesions. Patients with unexplained breathlessness or normal chest radiograph with wheezing were having such type of abnormality.
5. Airway lesions- hilar opacity or patients with unexplained hemoptysis with normal chest radiograph were highly suspicious for airway or endobronchial lesions (22). Bronchoscopy has crucial role in evaluation these lesions.

During bronchoscopy we observed characteristic features of exophytic endobronchial lesions as cauliflower like, polypoid-like or nodular or multinodular endobronchial growth (23).

In selected cases, whenever necessary pleural fluid analysis in effusion cases and bronchoscopy in suspected airway lesions performed.

The statistical analysis was done by using chi-square test. Significant values of $\chi 2$ were seen from probability table for different degree of freedom required. *P* value was considered significant if it was below 0.05 and highly significant in case <0.001.

Observation and Analysis

Screened total 2000 cases of gynecological malignancies (ovary, endometrium, cervix & benign ovarian tumors) and selected 330 cases with various metastatic thoracic manifestations. Respiratory symptomatology of study cohort were Shortness of breath in 93% cases, cough in 85% cases, chest pain in 70% cases, wheezing in 52% cases & hemoptysis in

Table 1: *Age distribution of study cohort*

Type of malignancy	Age <50 yrs.	Age >50 yrs.
Ovarian malignancy (n=100)	14	86
Carcinoma of cervix (n=100)	28	72
Carcinoma of Endometrium (n=100)	32	68
Benign ovarian tumors (n=30)	24	6
Total	60	140

$\chi 2 = 48.55$, $df = 4$, $P < 0.00001$

Table 2: *Bar diagram showing thoracic manifestations of ovarian malignancies*

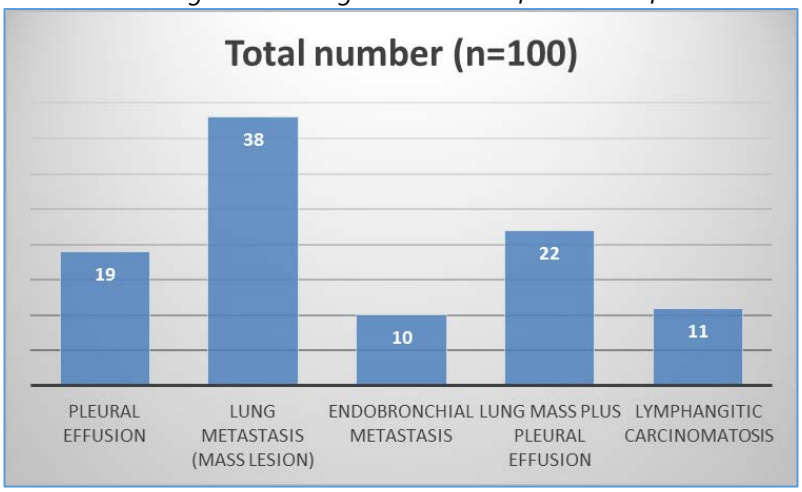
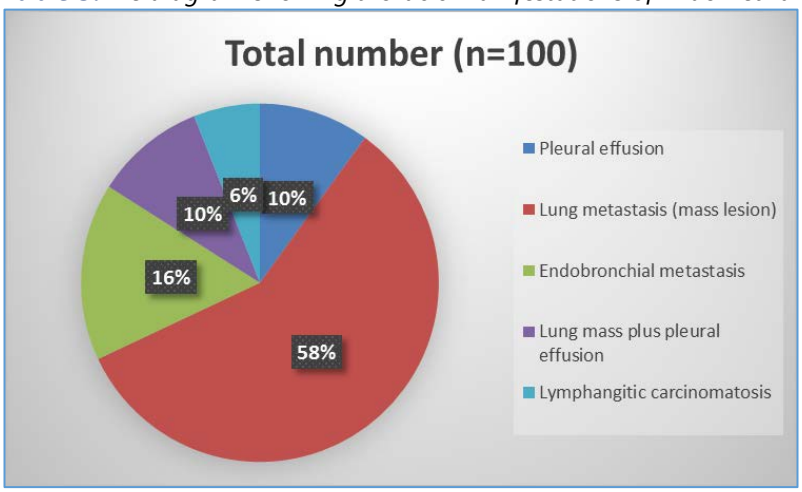


Table 3: *Pie diagram showing thoracic manifestations of Endometrial carcinoma*



31% cases. Of total 330 cases; endometrial, cervical and ovarian malignancy cases were 100 respectively and benign ovarian tumors were 30 cases.

Malignant gynecological tumors including Endometrial, cervical & ovarian cancers predominantly observed in above 50 years of age while benign ovarian and uterine tumors in below 50 years of age. ($p<0.00001$) Also propensity of malignant tumors below 50 years of age is increasing.

In study of 100 cases of ovarian cancer with thoracic manifestation, documented lung mass lesion as predominant involvement in 38% cases, pleural effusion in 19% cases & lymphangitic carcinomatosis in 11 % cases.

In study of 100 cases of endometrial cancer with thoracic manifestation, documented lung mass lesion as predominant in 58% cases, endobronchial metastasis in 16% cases & lymphangitic carcinomatosis in 6 % cases.

Table 4: *Bar diagram showing thoracic manifestations of Cervix malignancies*

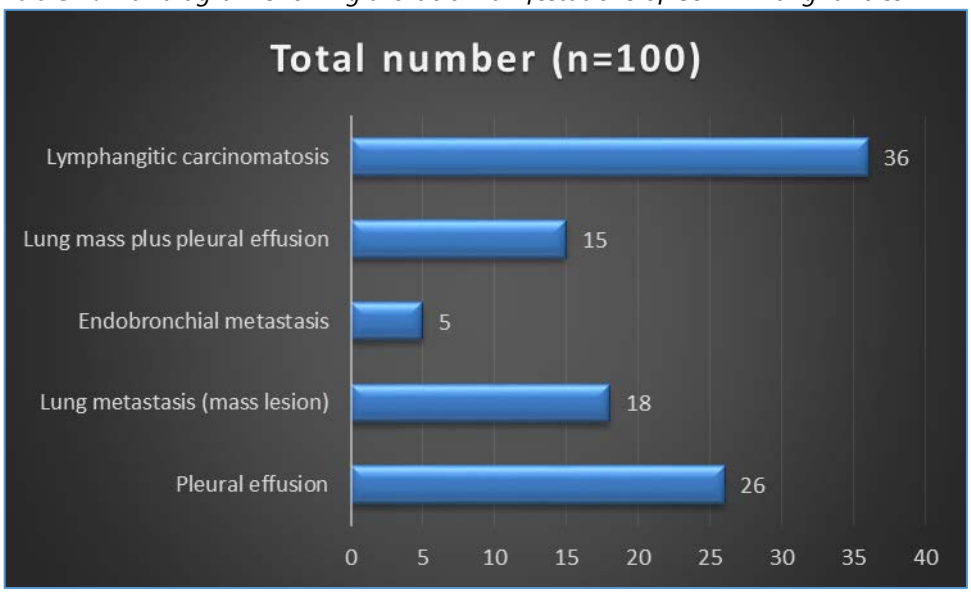


Table 5: *Thoracic manifestations of Endometrial, ovarian & Cervix malignancies*

Thoracic manifestation	Ovarian Malignancy (n=100)	Cervix malignancy (n=100)	Endometrial malignancy (n=100)
Pleural effusion	19	26	10
Lung metastasis (mass lesion)	38	18	58
Endobronchial metastasis	10	5	16
Lung mass plus pleural effusion	22	15	10
Lymphangitic carcinomatosis	11	36	6

$\chi 2 = 67.82$, $df = 8$, $P < 0.00001$

Table 6: *Airway, Lung parenchyma, Lung parenchyma plus pleura and isolated pleura involvement in gynecological malignancies*

Thoracic manifestation	Ovarian Malignancy (n=100)	Cervix malignancy (n=100)	Endometrial malignancy (n=100)
Airway (Endobronchial)	10	5	16
Lung Parenchymal (mass lesion+ Lymphangitic Carcinomatosis)	49	54	64
Lung Parenchymal plus pleura	22	15	10
Pleural effusion	19	26	10

$\chi 2 = 19.62$, $df = 6$, $P < 0.003$

In study of 100 cases of cervical cancer with thoracic manifestation, documented lymphangitic carcinomatosis as predominant in 36 % cases, pleural effusion in 26% cases & endobronchial metastasis in 5 % cases.

Lung metastasis and endobronchial involvement documented predominantly in ovarian and endometrial malignancies while pleural effusion and lymphangitic carcinomatosis documented predominantly in cervical malignancies. ($p<0.00001$).

Involvement of airway (endobronchial metastasis) and lung parenchymal mass lesion predominantly documented in endometrial malignancies; lung parenchymal (mass lesion) with lymphangitic carcinomatosis in ovarian malignancies and predominantly pleural involvement with lymphangitic carcinomatosis documented in cervical malignancies. ($p<0.003$).

DISCUSSION

Does Age at Presentation will help in Predicting Malignant Type from Benign Type?

In our study, we observed that malignant gynecological tumors including endometrial, cervical & ovarian cancers predominantly observed in above 50 years of age while benign ovarian and uterine tumors in below 50 years of age. ($p<0.00001$) Also propensity of malignant tumors below 50 years of age is increasing. Agarwal et al (24) observed cervix was the commonest site affected accounting for 71.47% of cases. The mean age of patients with cervical cancer was 50.1 ± 12.9 years (median = 50 years; range = 14 to 90 years). Patients between 45 and 49 years of age constituted the

commonest age group affected. Ovarian malignancies constituted 15.11% of all gynecologic malignancies reported, with a median age of 45 years (range 4 to 93 years) (24).

A comparative evaluation of our data with that from SEER Program revealed significantly lesser percentage of cervical malignancies in our cohort of patients in 20-34 yrs.; whereas a higher percentage was noted in 45-64 year age group. This may be a manifestation of better screening programs in the US where cervical malignancy is detected in younger patients at a localized stage (25).

Among uterine malignancies also, significantly higher incidence was noted in 45-54 years of age. A similar trend has been reported from Asian registries where uterine cancer occurs a decade earlier than in the West (26). On the contrary higher percentage of ovarian malignancies in children and young adults (birth to 44 years) was noted. Above 75 years of age cervical, uterine and ovarian malignancies were significantly lesser in our cohort of patients presumably due to a lower life expectancy in our country (24).

As previously thought, benign tumors common in early ages and malignant trend increases proportional to age at presentation, this dictum is not universal now and many gynecological tumors have diagnosed and presented below 50 years of age. This change may be because of changing lifestyle, dietary change, hormonal exposures and familial trends. Cervix malignancy showing bimodal peak.

Thoracic Manifestations of Cervix Malignancies in this Study

In study of 100 cases of cervical cancer with thoracic manifestation, documented lymphangitic carcinomatosis as predominant in 36 % cases, pleural effusion in 26% cases, lung metastasis (mass lesion) in 18%, lung mass plus pleural effusion in 15% cases & endobronchial metastasis in 5 % cases.

Pulmonary involvement is associated with cancer stage and tissue histology. Although squamous cell is the most common cell type, adenocarcinoma and poorly differentiated carcinoma have a much higher likelihood of lung involvement (27, 28). The most common thoracic manifestation consists of multiple pulmonary nodules; however, mediastinal disease and pleural effusions are not infrequent (27, 29, 33). Lymphangitic carcinomatosis, solitary pulmonary nodules, and endobronchial disease occur rarely (27, 29, 30).

In this study, we observed pleural effusion in 15% cases with it is second most common manifestation of thoracic metastasis due to cervix malignancies. In studies by Imachi et al (27), Sostman et al (28) and Shin et al (29) observed Pleural effusions represent a significant proportion of thoracic metastasis in cervical carcinoma. Early autopsy studies reported pleural metastasis in 11% of cases. The incidence of pleural effusion in patients who had newly-diagnosed cervical carcinoma or in those who were followed over several years has ranged from 9% to 44% (27, 28, 29). Sostman and Matthay (28) found that pleural effusions were related to histology; squamous cell carcinoma was associated more commonly with a pleural effusion than adenocarcinoma. It is rare for a pleural effusion to be the sole manifestation of metastatic disease (28, 29).

In this study, we observed lymphangitic carcinomatosis in 36 % cases & is the most common thoracic manifestation due to cervix malignancies. Studies by Kennedy et al (30), Sawin et al (31) & Perez et al (32) documented lymphangitic carcinomatosis and endobronchial metastasis in cervical carcinoma are rare, with only a handful of case reports in the literature. Shin et al (29) reviewed squamous cell cervical carcinoma metastatic to the lung and found that lymphangitic carcinomatosis or endobronchial obstruction was present in only 3% to 5% of cases. By contrast Sostman and Matthay (29) and Tellis and Beechler (33) found no cases of either. Imachi et al (27) reported that in the few patients who had lymphangitic carcinomatosis, many had positive sputum cytology.

In this study, we observed lung metastasis (mass lesion) in 18%, lung mass plus pleural effusion in 15% cases & it is third most common manifestation of thoracic metastasis due to cervix malignancies. Most studies that have evaluated the incidence and pattern of lung metastasis in cervical carcinoma have been retrospective in nature. Accordingly, the incidence and type of thoracic metastasis in these studies is affected by the method in which the patients were screened for advanced disease. Most studies relied on screening CXRs or specific respiratory symptoms. Imachi et al (27) observed multiple pulmonary nodules were present in 46% of patients who had thoracic metastasis. In this same study, a pneumonia-type pattern favored adenocarcinoma, whereas a reticular pattern was more commonly representative of squamous squamous cell carcinoma. Tellis et al (33) also reported that 13 of 22 patients (59%) exhibited multiple pulmonary nodules as the main radiographic finding. Another study reviewed patients who had squamous cell cervical carcinoma who died with evidence of thoracic metastases. Shin et al (29) observed multiple pulmonary nodules was the most typical pattern and was seen in 71% of patients. Nodules ranged in size from 0.5 cm to 7.0 cm and a significant

percentage showed cavitation. Other studies demonstrated that cavitating nodules frequently are a part of the spectrum of metastatic disease in cervical carcinoma. Sostman et al (28) found that adenocarcinoma was associated solely with multiple nodules, whereas squamous cell carcinoma had pulmonary nodules in 67% of cases of metastatic disease.

Thoracic Manifestations of Ovarian Malignancies in this Study

In study of 100 cases of ovarian cancer with thoracic manifestation, documented lung mass lesion as predominant involvement in 38% cases, lung mass plus pleural effusion in 22% cases, pleural effusion in 19% cases & lymphangitic carcinomatosis in 11 % cases & endobronchial metastasis in 10 % cases.

Studies by smith et al (34) & Kerr et al (35) observed that the frequency of pulmonary involvement in patients who were diagnosed with ovarian cancer ranged from 21% to 45% and is as high as 70% in autopsy studies. Studies by smith et al (34), Kerr et al (35) & Mateo et al (36) observed that patients with ovarian cancer with metastasis typically have pleural involvement, but parenchymal, endobronchial, and embolic phenomena have been described. Patients typically have pleural involvement, but parenchymal, endobronchial, and embolic phenomena have been described (34, 35, 36). Right-sided ovarian cancer was more likely to produce thoracic metastases. Many studies have highlighted the lack of symptoms, particularly respiratory, in patients who present with advanced disease (34, 35). In one study of patients who had pulmonary involvement, only 3% had respiratory symptoms (35).

In this study, we observed lung mass lesion is the 38% cases & is most common thoracic manifestation in due to ovarian malignancies. Studies by Kerr et al (35), Akahira et al (37) & Fuller et al (38) Parenchymal disease represents the second most frequent presentation of thoracic metastasis in ovarian cancer. Solid parenchymal disease has been reported in 3% to 10% of extraperitoneal malignancies. Despite the lack of evidence for a survival advantage in patients who have solid parenchymal disease, resection for discrete lesions was performed in patients who had recurrent ovarian cancer (38) Multi-nodular lung disease and alveolar hemorrhage also have been reported in patients who had nonepithelial ovarian carcinoma (39, 40). Nodal involvement is part of the spectrum of thoracic involvement; it occurs in a reported 2.5% of thoracic lesions (35). Lymphangitic involvement, however, is described rarely with ovarian carcinoma. It is reported to be the principal thoracic lesion in only 1.8% of cases and frequently is associated with negative CXR findings (35).

In this study, we observed lung mass plus pleural effusion in 22% cases, pleural effusion in 19% cases & is second and third most common thoracic manifestation respectively due to ovarian malignancies. In a large review of malignant pleural effusions, ovarian carcinoma was the fourth most common etiology after lung, lymphoma, and breast cancer (41). Studies by Akahira et al (37) and Bonnefoi et al (42) observed that among thoracic metastases, pleural effusion is present in 77% and represents an estimated 31% to 40% of all extraperitoneal metastases. Kerr at al (35) mentioned that the presence of a pleural effusion does not, however, always represent a malignant etiology to the effusion. Kerr et al (35) observed that on the presence of pleural effusions in ovarian cancer did not differentiate cytology positive from cytology negative effusions. Curtin et al (43) observed that patients in whom pleural effusion was the only manifestation of metastasis may have a survival advantage over patients who have visceral involvement. Zang et al (44) in a retrospective review of patients who presented with peritoneal or liver involvement without evidence of primary ovarian carcinoma, such patients showed improved survival if they had a pleural effusion rather than other visceral involvement. Taken together, these observations imply a different tumor biology for ovarian carcinoma that is metastatic to the pleura only. In general, pleural disease rarely is the only site of metastatic disease (35).

In this study, we observed metastatic thoracic manifestation as endobronchial metastasis in 10 % cases due to ovarian malignancies. Metastatic disease that involves the tracheobronchial tree is extremely rare in patients who have ovarian cancer. Evidence of this process exists in the literature as a handful of case reports only (36, 45). Mateo et al (36) reported that the cell type that is involved in tracheobronchial metastasis is typically papillary or serous cystadenocarcinoma, although a granulosa cell tumor also was described. In some cases, by Merrill et al (46) & Asamura et al (47) the presentation of tracheobronchial metastases occurred several years after the original diagnosis. Patients who had endobronchial disease also tended to be younger with a more favorable course (36).

Thoracic Manifestations of Endometrial Malignancies in this Study

In study of 100 cases of endometrial cancer with thoracic manifestation, documented lung mass lesion as predominant involvement in 58% cases, endobronchial metastasis in 16% cases, and lung mass plus pleural effusion in 10% cases, pleural effusion in 10% cases & lymphangitic carcinomatosis in 6 % cases.

Greenlee et al (47) observed that uterine and cervical cancers when combined are more common than ovarian cancer, but are less likely to present as disseminated disease. Tellis et al (33) observed metastatic disease is clinically symptomatic

in 5% to 10% of cases, but is detected more frequently in autopsy studies. D'Orsi et al (50) observed that distant metastasis frequently is associated with intra-abdominal spread. Generally, multiple pulmonary nodules are more common than solitary nodules. Typically, patients present with metastases early in the course of their disease and outcomes are poor (50).

In this study, we observed lung mass lesion is the 58% cases & is most common thoracic manifestation in due to endometrial malignancies. Bouros et al (51) have reported that up to 34% of patients presented with pulmonary metastasis as the only site of recurrence. As seen in other malignancies, the autopsy- based rate of pulmonary metastasis is much higher documented by Turner et al (50). Because most patients present with early stage disease, pulmonary metastasis frequently is diagnosed as a recurrence during the course of initial treatment. Most pulmonary metastases occur within 30 months and frequently are associated with other sites of spread (50). Ballon et al (52) observed that patients who have metastases that are confined to the lungs had a higher response to chemotherapy. D'Orsi et al (50) in their study simultaneously reviewed metastatic cervical and endometrial carcinoma, the incidence of pulmonary metastasis was 5.1% and 3.6%, respectively. Few studies have focused solely on the patterns of thoracic involvement in metastatic uterine cancer. Bouros et al (51) in their study reviewed 1550 patients who were admitted with a diagnosis of uterine cancer over a 27-year experience. The study identified 90 (5.8%) patients who had pulmonary involvement, with varying histopathology. Multiple pulmonary nodules of various sizes were the most common radiographic abnormality and were present in 72% of the 90 patients. Older series (52) similarly reported multiple bilateral nodules as the primary pattern of thoracic metastasis. Solitary pulmonary nodules are not as common, and represent between 12% and 18% of all thoracic metastases (51, 52).

In this study, we observed lung mass plus pleural effusion in 10% cases, pleural effusion in 10% cases & is third most common thoracic manifestation respectively due to endometrial malignancies. In a study by Bouros et al (51), only 6 of the 90 patients who had pulmonary metastasis manifested a pleural effusion. Of those patients, 50% had concurrent parenchymal disease. In an older review by Ballon et al (52) mentioned that of 33 patients who had pulmonary metastasis, only 2 had evidence of pleural involvement. D'Orsi et al (50) also reported that pleural disease was rare among patients who had pulmonary metastasis. They found that only 5 of 42 patients had a pleural effusion, all of whom had concurrent parenchymal disease.

In this study, we observed endobronchial metastasis in 16% cases & lymphangitic carcinomatosis in 06 % cases as metastatic thoracic manifestation due to endometrial malignancies. D'Orsi et al (50) Bouros et al (51) & Ballon et al (52) observed the incidence of lymphangitic carcinomatosis, endobronchial disease, and cavitating nodular disease has been reported rarely in clinical series of metastatic uterine malignancy.

Thoracic Manifestations of Benign Ovarian Tumors in this Study

In this study, 6 cases of total 30 cases with benign ovarian tumors were having thoracic manifestation in form of pleural effusion. Meig's syndrome describes a benign ovarian fibroma with associated ascites and pleural effusion. It is important to distinguish Meig's syndrome from malignant ovarian cancer because of obvious prognostic differences. [53] Pseudo-Meig's syndrome refers to non-ovarian tumors that also present with ascites and pleural effusion and typically are benign (54).

Other Important Observations in this Study

Lung metastasis and endobronchial involvement documented predominantly in ovarian and endometrial malignancies while pleural effusion and lymphangitic carcinomatosis documented predominantly in cervical malignancies. ($p<0.00001$)

Involvement of airway (endobronchial metastasis) and lung parenchymal mass lesion predominantly documented in endometrial malignancies; lung parenchymal (mass lesion) with lymphangitic carcinomatosis in ovarian malignancies and predominantly pleural involvement with lymphangitic carcinomatosis documented in cervical malignancies. ($p<0.003$)

CONCLUSION

Thoracic metastatic manifestations of gynecological tumors are underdiagnosed & less reported in clinical practice because of lack of suspicion & use of modern radiological techniques to diagnose these lesions.

Airway and lung parenchymal lesions are common in endometrial and ovarian malignancies while pleural and interstitial involvement is predominant in cervical malignancies.

Cases with gynecological tumors with respiratory symptoms should be evaluated with all possible conventional & advanced diagnostic methods to document metastatic manifestations of these tumors.

High index of suspicion is must in all the cases irrespective of respiratory symptoms and needs cautious evaluation to have successful treatment outcome and longevity in survival.

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