A study of malignant serous effusions in a tertiary teaching hospital in western Uttar Pradesh

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Abstract

Background: The study of cells in effusional fluid was among the early domains in cytology to draw interest of clinicians and pathologists. Identification of effusional cells as benign reactive or malignant is a diagnostic primary purpose of evaluation. Clinical history when taken into account while evaluating effusions can avoid erroneous diagnosis.

Materials and Methods: It was a prospective type of study. A total of 540 cases of serous effusions were cytologically evaluated following detailed history taking and clinical examination. Out of 540 cases all cases of malignant effusions were segregated and categorized according to sex, site (peritoneal or pleural), and origin (primary or metastatic).

Results: A total of 50 cases were positive for malignancy.. Most common primary tumors associated with malignant effusions in males and females were of lung and ovary respectively. Most common cause of malignant pleural effusion in males was lung cancer and in females was breast cancer respectively. Most common cause of malignant peritoneal effusion in males was carcinoma GIT and in females was carcinoma ovary respectively.

Conclusion: Malignancy emerged as the third most common cause of serous effusions following inflammatory and reactive causes. Malignant effusions were more common in females. Malignant effusions were mainly due to metastatic cancers, mostly adenocarcinomas. The most common cause of malignant pleural effusion in males was carcinoma lung and in females is carcinoma breast, while the most common cause of malignant peritoneal effusion in males was carcinoma GIT and in females was carcinoma ovary respectively.

Keywords: Malignancy, Exudates, Effusion, Cytology

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Introduction

The studies of cells of effusional fluids were one of the first domains of cytology to draw the interest of clinicians seriously. The first microscopic studyof the cytology of effusions is now more than a century old. Among the pioneer works published on this matter, were those of Lucke and Klebs(1867), Quincke(1875), Ehrlich(1882), Chuquet(1875), Widal and Ravait(1900) and Dopfer and Touton. Lucke(1910) and Klebs(1867) were the first to describe malignant cells in ascitic fluid.

Diagnostic therapeutic approach to an effusion depends upon whether an effusion is transudate or exudate. The cytology of effusions is one of the most difficult to evaluate and as such must be approached with caution. Cytologicalevaluation of serous effusions is performed mainly to establish the presence or absence of malignancy.

The identification of cells as either malignant or benign reactive mesothelial cells in serous effusions is aday to day diagnostic problem. Because of its cytological nature and its exfoliation into a liquid, the cellular anarchy of mesothelial elements tendto overshadow the classic diagnostic criteria of cytological malignancy[1]. The conventional morphological criteria fail to allow a definite diagnosis in about 15% of cases although this has decreased tremendously by the use of other diagnostic modalities.

Clinical history is of paramount importance in evaluating fluid specimens and when taken into account can avoid erroneous diagnosis in most of the cases. Thus, the purpose of this study was to establish the usefulness of clinicopathological evaluation of serous body effusions as a diagnostic method in malignant effusions.

Material and Methods

The present study was carried out in the department of Pathology, Muzaffarnagar Medical College and Hospital after the approval of institutional ethical committee. This was a prospective type of study carried out from 1st July 2014 to 30 June 2015.The cases were collected from wards of medicine, surgery, TB & Chest. All the specimens of body fluids received in cytology unit of pathology department were included in the study.

Exclusion criteria:-

- Quantity less than 5ml.
- Synovial fluids.
- Frankly haemorrhagic fluids with no clinical suspicion of malignancy.

Detailed history and clinical examination of the patient was done. General haematological investigations and specific investigations if needed were done. Physical and chemical examination of effusion fluids was properly performed.

For microscopic examination conventional smears, cytospin preparations and cell blocks were made and stained with giemsa and PAP. Special stains such as mucicarmine, alcian blue and PAS were applied wherever needed. Cytological diagnosis was made and malignant cases from the total cases were segregated and were then categorized according to sex, site(peritoneal or pleural), origin(primary or metastatic).

Results

Out of the 540 cases of effusion studied 288 (53.3%) were male and 252 cases (46.7%) were females. Of these 163 cases in males and 131 cases in females were of peritoneal effusion, and pleural effusions in males and females were 125 and 121 respectively. 470 (87%) cases were exudates and 70 cases (13%) were transudates in nature.422 (78.2%) cases were inflammatory, 50 (9.2%) malignant, 60 (11.2%) were reactive. (Table 1)

The effusions were predominantly inflammatory in nature out of which 303 (56.1%) were chronic inflammatory and 50 (9.2%) were positive for malignancy. The cytology could not give a definitive diagnosis in 8 (1.4%) cases.

The common sites of primary malignancy giving rise to malignant effusions were from GIT, lung, ovary & breast.(Table 2)

Malignant effusions were more common in females than males.(Table 3) The most common primary tumour site associated with malignant effusions in males was carcinoma lung and in females carcinoma ovary.(Table 4)

Out of 32 cases of malignant peritoneal effusions 22 cases were females (68.7%) and 10 were males (31.3%). Out of 18 cases of malignant pleural effusions, 10 were males (55.5%) and 8 were females (44.5%) (Image 1).

Most common cause of malignant pleural effusion in males was lung cancer (80%) and in females was breast cancer (75%) (Image 2) Most common cause of malignant peritoneal effusion in males was carcinoma GIT (60%) (Image 3) and in females was carcinoma ovary (45.5%).

There were two cases of lymphoma. Both were male patients and of small cell type (Image 4).

Table 1: Distribution on the basis of cytology

Nature	No. of Cases	Percentage
Inflammatory	422	78.2
• Acute	119	22.1
• Chronic	303	56.1
Malignant	50	9.2
Reactive	60	11.2
Suspicious	8	1.4
Total	540	100

Table 2: Distribution of malignant effusions according to the primary tumor site

Site	No. of Cases	Percentage
GIT	12	24
Lung	10	20
Ovary	10	20
Breast	10	20
Female genital tract	2	4
Lymphoma	2	4
Occult	4	8
Total	50	100

Table 3: Sex wise distribution of malignant effusion

	Male	Female
Intestine	6	6
Lung	8	2
Ovary	0	10
Breast	0	10
Endometrium	0	2
Lymphoma	2	0
Ouccult	4	0
Total	20	30

Table 4: Distribution of primary tumor site according to location

Ascites	Male	Female	Total	Pleural	Male	Female	Total
Ovary	0	10	10	Breast	0	6	6
Breast	0	4	4	Ovary	0	0	0
GIT	6	6	12	GIT	0	0	0
Lymphoma	2	0	2	Lung	8	2	10
Female genital tract other than ovary	0	2	2	Lymphoma	0	0	0
Occult	2	0	2	Occult	2	0	2
Total	10	22	32	Total	10	8	18

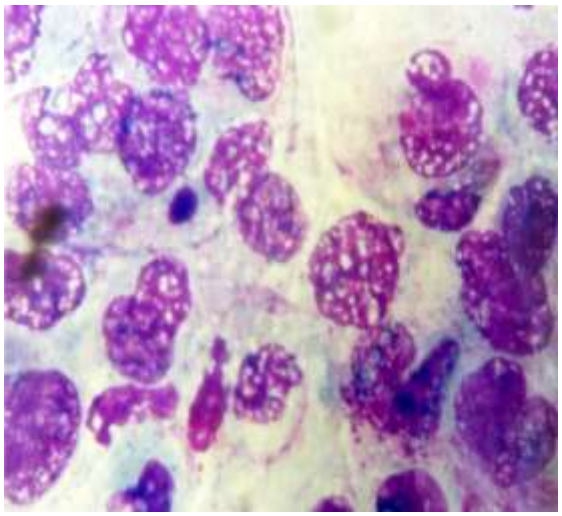

Image 1: Malignant effusion due to lung cancer showing malignant cells with marked nuclear abnormalities and multiple nucleoli (poorly differentiated carcinoma)

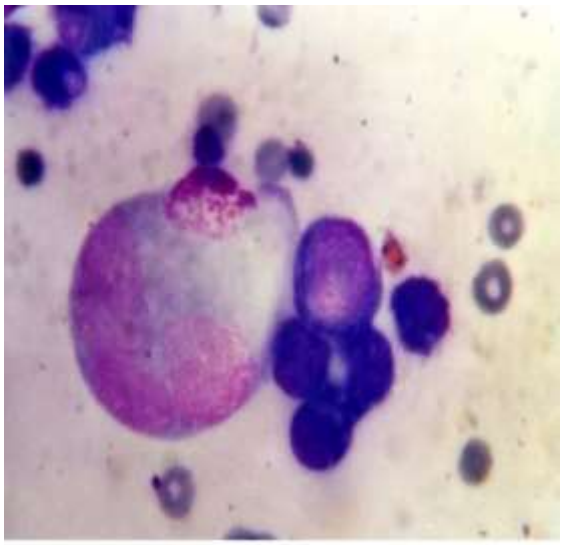

Image 2: Malignant pleuraleffusion in carcinoma breast showing tumor giant cell

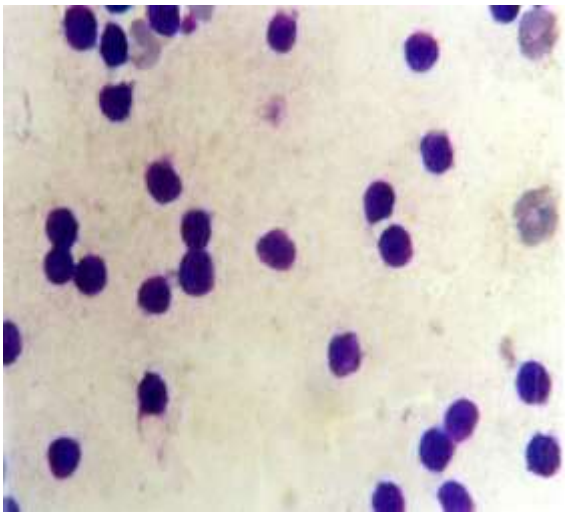

Image 3: Malignant effusion showing malignant cells with vacuolated cytoplasm arranged in a glandular pattern in an intestinal adenocarcinoma

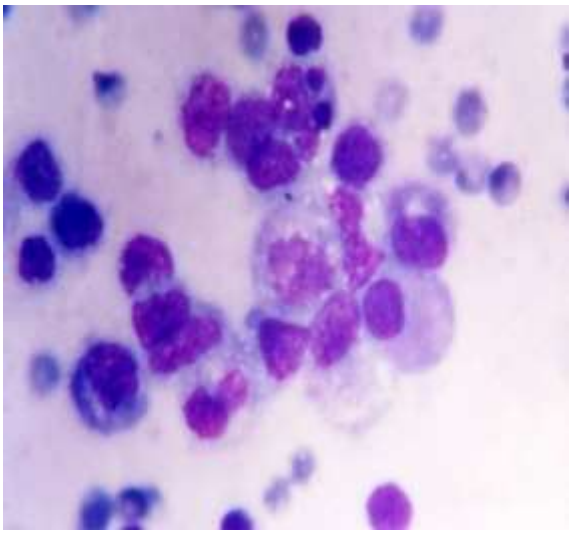

Image 4: Malignant effusion due to lymphoma showing monomorphic cells slightly larger than small lymphocytes spread out singly with little cytoplasm, round nucleus, coarsely clumped chromatin and irregular nuclear membrane (Small cell lymphoma)

Discussion

Fluid cytology is mainly performed in order to see the type of inflammation and establish the presence or absence of malignancy. Out of the total 540 cases of effusions which were studied, 50 cases (9.2%) were malignant. This finding goes hand in hand with the findings of Cakir[2] who reviewed 4684 sample of pleural effusions and found 364 samples (7.8%) to be positive for cancer cells.

All the malignant effusions were associated with metastatic cancer and no primary tumor of the body cavity was detected. Of these adenocarcinomas, (44/50,

88%) were most common. These findings were supported by various authors like Ramzy[3], Koss[4], and Cibas and Ducatman[5]. Monte et al[6]reported that most common type of neoplasm in the malignant effusions was adenocarcinoma (80% of peritoneal and 78% of pleural). Irani et al[7] and Hsu[8] reported that adenocarinoma was the most common type of lung carcinoma in effusion which supports the observation made in the present study also(6/10,60%) . Kondo et al[9] also observed that adenocarcinoma was the commonest malignancy to be detected in pleural effusions. Beside adenocarcinoma, two cases were of large cell undifferentiated carcinoma, two of lymphoma and two of poorly differentiated carcinoma.

The common primary tumors found to be associated with malignant effusions in the present study were GIT cancers(12;24%), lung(10;20%), ovary(10;20%) and breast(10;20%). Naib[10] has reported that the tumors of the adult patients that frequently metastasize into the serous cavity are the adenocarcinomas of the ovary, GIT, breast, lungs, testes and kidney.

The common primary tumors in males were lung (8/20;40%) and GIT (6;30%) and in females were gynaecologic site(12/30;40%) and breast (10/30; 33.3%). These findings were supported by Di Bonito et al[11] who found carcinoma GIT as most common primary associated with malignant effusions in males and carcinoma of gynaecologic site in females.

The most common tumors associated with malignant pleural effusion were carcinoma lung(10/18;55%) and carcinoma breast(6/18;33.3%) and the most common tumor associated with malignant pleural effusions were carcinoma GIT (12/32;37.5%) and carcinoma ovary(10/32;31.2%). These observations were supported by the observation of Monte et al[6] who found ovary to be the most common site in malignant peritoneal effusions and lung cancer in malignant pleural effusion. Lopez et al[12] also reported lung and breast cancers to be the commonest malignancy detected in pleural effusions.

Sears and Hajdu[13] observed, most common primary neoplasms causing malignant pleural effusion were carcinoma breast, lung and lymphoreticular system and most common primary tumors causing malignant peritoneal effusions were carcinomas of ovary, breast and lymphoreticular system. In the present study 4 malignant ascites were found to be due to carcinoma breast. Thus, the observation in the present study is in accordance with most of the studies done so far.

Vargas et al[14] found carcinomas of lung, breast and lymphomas to be responsible for approximately 75% of all malignant pleural effusions. In this study they accounted for 89% cases. Parsons et al[15] reviewed 164 patients with malignant ascites and found that ovarian ascites accounts for 28% of the total. In the present study it accounted for 31.2%.

In the present study the most common primary site associated with malignant pleural effusion in males was carcinoma lung and in females was carcinoma breast and the most common primary associated with malignant peritoneal effusion in males was carcinoma GIT and in females carcinoma ovaries. The observation is supported by Ringenberg et al[16] who reviewed cases of malignancy peritoneal effusion and found common primary site in females to be carcinoma ovary and in men to be colon, rectum and stomach(GIT).

Sears et al[13] Johnston[17], Zaleska et al[18] and Ong et al[19] also reported that lung cancer is the most common cause of malignant pleural effusion in men, as is breast cancer in women and Sears et al[13] also observed that pancreatic carcinomas were the most common cause of malignant peritoneal effusion in men, whereas in women the most common primary site was ovary. All the observations match with the observation in the present study except the one regarding pancreatic carcinoma. But Naib[10] has stated that the carcinomas of the pancreas, gall bladder, liver, prostate and urinary bladder rarely metastasize to the serous cavities. This observation in the present study is also supported by Ramzy[3] and Koss.[4]

In 4 out of 50(8%) cases of malignant effusion the primary tumor was occult. Cibas and Ducatman[5] have stated that most patients with malignant effusions have a previously documented primary neoplasm. In some cases, however, a malignant effusion is the first manifestation of an occult malignancy. The most common occult primary in both women and men who present with a malignant pleural effusion is lung cancer. It is extremly uncommon for breast cancer to manifest itself initially as a malignant effusion. [6,13,17] The most common occult sources of a malignant peritoneal effusion were intestinal and pancreatic cancer in men and ovarian cancer in women.[13,16] In some patients the primary site was never discovered.[13,17] Sears et al[13] reported an incidence of 15% of occult primary sites. Ong et al [19] reported an incidence of 9.7% of occult primaries.

A correlation between the clinical diagnosis and cytological diagnosis was made on which the sensitivity of the effusion cytology was found to be 82.14%, specificity to be 98.6%, positive predictive value to be 92% and negative predictive was 96.7%. False positive percentage was 17.86% and a false negative percentage was 1.4%. Oyafuso[20] reported effusion cytology to be 44.5% sensitive, 95.7% specific, 98.7% positive predictive value and 90% negative predictive value. We found it to be more sensitive and almost equally specific.

Shikha[21] also found exfoliative cytology for malignant cells is highly specific though less sensitive.

Conclusions

On cytology, 422(78.2%) cases were inflammatory, 50(9.2%) were malignant, 60(11.2%)

reactive and (1.4%) were suspicious. The most common cause of effusion is inflammation followed by reactive changes followed by malignancy and cytology cannot give a definite diagnosis in few cases. The primary tumor sites in malignant effusions were GIT (12), Lung (10), ovary (10), breast (10), endometrium (2), lymphoma (2) and occult (4).

Eighty eight percent of cancers were adenocarcinomas, 4% were lymphoma, 4% poorly differentiated carcinoma and 4% large cell undifferentiated carcinoma. Malignant effusions were mostly due to metastatic cancers and most of them are adenocarcinomas. The most common cause of malignant pleural effusion in males was carcinoma lung and in females is carcinoma breast. The most common cause of malignant peritoneal effusion in males was carcinoma GIT and in females was carcinoma ovary.

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