International Journal of Research in Medical Sciences
Gamit B et al. Int J Res Med Sci. 2019 Sep;7(9):3556-3558
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20193946

Case Report

Diagnosis of malignant effusion using cell block and immunohistochemistry

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Received: 17 June 2019
Revised: 18 July 2019
Accepted: 30 July 2019

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ABSTRACT

The distinction between reactive mesothelial and adenocarcinoma cells specially signet ring type in serous effusions may be very difficult based only on morphological features particularly in early stage. Reactive mesothelial cells show varying degree of cytological atypia hence posing difficulty in differentiating it from adenocarcinoma cells. We report a case of 45 year old female patient presented with abdominal distension. Patient was an operated case of adenocarcinoma of stomach. Smears prepared from ascitic fluid and cell block shows large number of reactive mesothelial cells and few atypical cells. Atypical cells were immunoreactive for cytokeratin, epithelial membrane antigen and carcinoembryonic antigen. These confirmed the presence of malignant epithelial cells so we reported it as a malignant effusion.

Keywords: Cell block, Immunohistochemistry, Serous effusion

INTRODUCTION

The distinction between reactive mesothelial and adenocarcinoma cells specially signet ring type in serous effusions may be very difficult based only on morphological features particularly in early stage.

Cytological features used to identify malignancy includes nuclear pleomorphism, prominent nucleoli, large cellular aggregates and cell in cell engulfment are helpful features but have limited use in effusions because they may also be present in florid reactive mesothelial hyperplasia.

Reactive mesothelial cells show varying degree of cytological atypia hence posing difficulty in differentiating it from adenocarcinoma cells specially when malignant cells are few in number and unrecognized in the presence of large number of reactive mesothelial cells.[1]

CASE REPORT

Authors report a case of 45 year old female patient presented with abdominal distension. Ultrasonography suggestive of moderate ascites. Ultrasonography guided ascitic fluid tapping done. Patient was an operated case of adenocarcinoma of stomach. Total gastrectomy and esophagojejunostomy done for it 2 month back. Smears prepared from ascitic fluid and cell block show large number of reactive mesothelial cells having central to eccentric nucleus, binucleation, multinucleation, prominent nucleoli, dense perinuclear cytoplasm, fuzzy cytoplasmic border, cytoplasmic vacuolation and mesothelial window. Few atypical cells having hyperchromatic eccentric nuclei, irregular nuclear membrane and scattered singly were also present raising the suspicion of malignant epithelial cell. So we performed immunohistochemistry for the confirmation of malignant epithelial cells. Immunohistochemistry was

performed on cell block prepared from ascitic fluid. Atypical cells were immunoreactive for cytokeratin, epithelial membrane antigen and carcinoembryonic antigen. These confirmed the presence of malignant epithelial cells so we reported it as a malignant effusion.

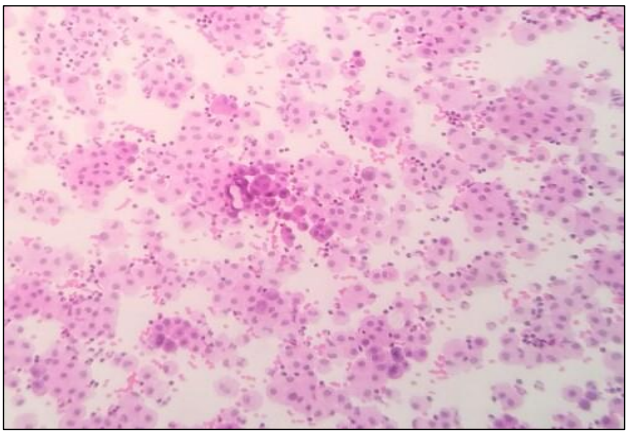

Figure 1: 40x magnification view Hematoxylin& eosin stained smear showing large number of reactive mesothelial cells and few atypical cells.

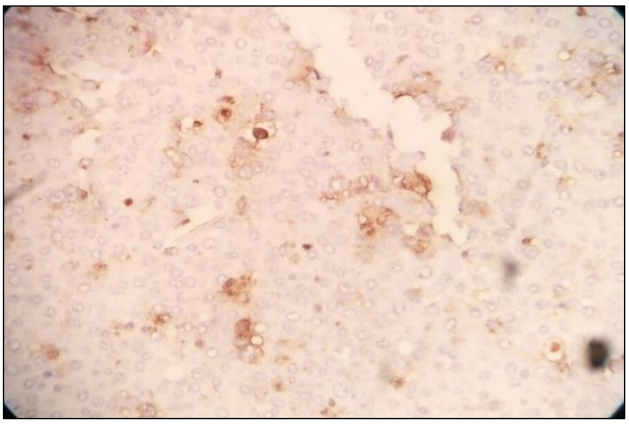

Figure 2: 40x magnification view showing CEA positive malignant cells.

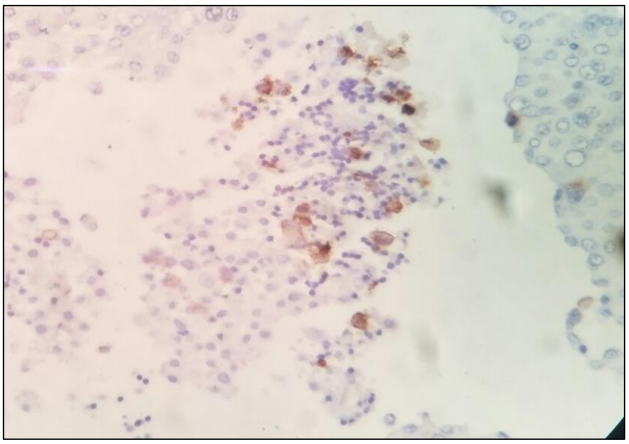

Figure 3: 40x magnification view showing EMA positive malignant cells.

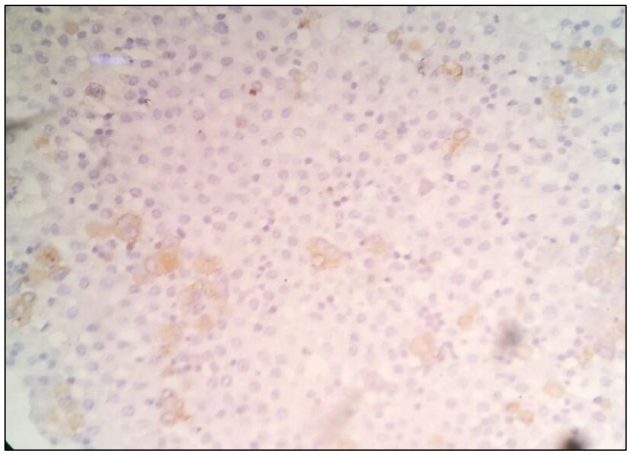

Figure 4: 40x magnification view showing CK positive malignant cells.

DISCUSSION

Excess fluid accumulation within the serous cavity is referred as effusion.[2] Effusion may be transudate or exudate. The common causes of transudate include congestive cardiac failure, cirrhosis of liver and renal failure. Causes of exudates include infection, collagen vascular diseases and malignancy.[3] Among malignancies, diffuse malignant mesothelioma is the most common primary cancer of the serosal membrane, but it is relatively an uncommon cancer. Metastatic carcinomas include lung carcinoma, breast carcinoma, gastrointestinal and genitourinary carcinoma. In abdomen, gastrointestinal and genitourinary malignancies are the most common cause of malignant effusion.[2]

Effusion secondary to malignancy are usually recurrent and hemorrhagic. Non traumatic massive haemorrhagic effusions are almost always due to cancer. With the exception of central nervous system tumours, malignant neoplasm from almost any site can metastasize to serous cavity and present as an effusion. Although any type of cancer including carcinoma, melanoma, hematopoietic neoplasms, sarcomas and mesotheliomas could spread to serous cavity, adenocarcinomas are the most common neoplasm to do so.

Reactive mesothelial cells are a universal component of effusion fluids. They may show wide morphological spectrum such as presenting as cohesive cluster, high nuclear cytoplasmic ratio, hyperchromatic nuclei, prominent nucleoli with scant/ pale vacuolated cytoplasm as they imbibe water from the effusion fluid which may overlap significantly with that of malignant cells in effusion fluids.[4] Classic cytological features of malignant cells in malignant effusion includes enlarged cells with high N:C ratio, coarse chromatin, enlarged and multiple nucleoli, irregular or indented nuclear contours and mitoses.[2]

In some situations, the diagnosis of malignancy may be equivocal due to paucity of neoplastic cells. In such case correlation with the clinical setting or repeat examination

of serous fluid is helpful. As malignant effusion re-accumulates rapidly in comparison to reactive effusions. It is recommended to repeat the specimen if the initial specimen is suspicious but not conclusive for malignancy as it is easy to obtain a repeat sample when it re-accumulates. This can lead to a definitive diagnosis without the danger of false positive interpretation.[4]

Radiotherapy may cause various cytological changes including cytomegaly, degenerative hyperchromasia, vacuolation of cytoplasm. This may lead to false positive interpretation, suggesting recurrence of the initial disease.[4]

Because of these diagnostic pitfalls, use of ancillary techniques like cell block preparation and immunohistochemistry is required. Cell block sections may demonstrate certain histological features helpful for final interpretation of a particular neoplasm such as papillary, acinar/duct like formations and psammoma bodies. This is particularly helpful while evaluating peritoneal fluids.[4] IHC can be performed on smears and cytospins, but protein in the fluid may coat cells and create false staining, while cell blocks more closely resemble paraffin embedded tissue sections. So cell blocks are preferred for immunohistochemistry over the cytospin smear.[2]

No singal marker on its own is capable of predicting the presence or absence of malignant cells with 100% accuracy and consistency, although EMA proved to be highly efficient. Epithelial membrane antigen proved to be best single marker for the adenocarcinoma with 100% sensitivity and 97% specificity. It has been suggested that minimum of two markers should be selected. Of the two marker combinations, EMA positive and CEA positive proved to be 100% specific for adenocarcinoma. So it becomes imperative that the final interpretation should be based on the combined efficacy of the markers to maximize the predictive potential.[5]

In our case, patient was an operated case of adenocarcinoma of stomach. Cell block prepared from ascitic fluid showed large number of reactive mesothelial cells along with few atypical cells raising the suspicion of malignant epithelial cells. So authors performed immunohistochemistry for confirmation of malignant nature of atypical cells. Atypical cells highlights epithelial membrane antigen(strong), cytokeratin and carcinoembryonic antigen. So in support with clinical details, cytological features and immunohistochemical findings, authors reported it as a malignant effusion.

CONCLUSION

In view of difficulty in distinguishing reactive mesothelial cells from adenocarcinoma cells, ancillary techniques like cell block and immunohistochemistry are useful in the diagnosis of malignant effusion.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not Required

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Cite this article as Gamit B, Dave D, Shahu N. Diagnosis of malignant effusion using cell block and immunohistochemistry. Int J Res Med Sci 2019;7:3556-8.