

# Malignant effusion with unknown primary cytodiagnosed using cell block technique – A case report

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## Abstract

Poorly differentiated carcinoma of lung is a very aggressive tumor. It lacks typical morphological and architectural features posing great diagnostic difficulties. Diagnosing cells as being 'reactive mesothelial cells', benign or malignant in effusions is a common diagnostic difficulty on conventional smear (CS) examination. Cell blocks (CB) are valuable when the cytological features on CS examination are inconclusive. The main advantage of CB technique is obtaining multiple sections for special stains and immunohistochemistry (IHC). CB technique also offers many other advantages like better preservation of architectural features, cytoplasmic and nuclear details. Coupling CB with IHC not only helps to detect the tumor-type but it also pin points the unknown primary site in cases especially unfit for surgery/biopsy. We report a case of 70yr non-smoker female known case of Ischemic Heart Disease (IHD). She presented with breathlessness, chest pain and recurrent pleural effusions since last 2 months.

**Keywords:** Cell block, Conventional smear, Immunohistochemistry, Malignant effusion.

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## INTRODUCTION

Cytological examination of body fluids has increasingly gained acceptance in clinical medicine to such extent that once positive diagnosis is made it is often considered definitive.<sup>1</sup> CS examination has got a lower sensitivity due to the overcrowding of the cells, cell loss and also due to the different laboratory processing methods.<sup>2</sup> CB technique not only increases the positive results but can also be of great help in approaching the correct diagnosis and the primary site.<sup>3</sup> This case highlighting the advantage of coupling CB with IHC in cases unfit for surgery/biopsy to accurately diagnose the tumor-type and unknown primary site has prompted us to report this case.

## CASE REPORT

A 70yr non-smoker female known case of IHD presented to the medicine outpatient department with breathlessness, chest pain and fourth episode of pleural effusion. Initial pleural effusions were non haemorrhagic and lymphocyte rich. She was started with Anti-Kochs Therapy (AKT) as chest X-ray showed left apical lobe lesion. Despite on regular AKT medication she developed recurrent fourth episode of pleural effusion which was grossly haemorrhagic. High Resolution CT-Thorax was performed which revealed left sided severe hydropneumothorax with underlying collapse and consolidation of lung parenchyma. In view of her elderly age, increasing severity of breathlessness, frequency of pleural effusion and effusion fluid turning into grossly haemorrhagic, repeat Contrast enhanced CT-Thorax was performed after Intra Costal Drainage insertion. It showed a heterogeneous enhancing mass (Figure 3) of size 3 x 2cm at junction of left apical lobe and pleura forming an obtuse angle with pleura suggestive of malignant mesothelioma. CS examination (Figure 1a) of effusion showed small groups of highly pleomorphic cells having high nucleo-cytoplasmic ratio in midst of predominantly lymphocytic infiltrate suggestive of malignant effusion. Patient was medically unfit for surgery/biopsy.

So, CB was prepared from effusion fluid using Nathan alcohol formalin substitute (NAFS) consisting of 9 parts of 100% ethanol and 1 part of 40% formaldehyde.<sup>4</sup> Microscopic examination of sections prepared from CB (Figure 1b) revealed cells arranged in small groups and dispersed singly in midst of inflammatory infiltrate and necrosis. Tumor cells showed overlapping pleomorphic nuclei with increased nucleocytoplasmic ratio, exhibiting coarse chromatin and prominent nucleoli. Occasional multinucleated cell forms were seen. CB was reported suggestive of poorly differentiated malignancy. To find out definitive tumor-

type and unknown primary site CB was coupled with IHC.

Immunohistochemistry findings (CB): IHC was performed on CB with the following panel of antibodies utilized for the differential diagnosis of Malignant Mesothelioma, Lung/Metastatic adenocarcinoma and Squamous Cell Carcinoma of lung. The tumor cells showed strong CK7-cytoplasmic positivity (Figure 2a), nuclear TTF-1 positivity (Figure 2b), focal Napsin-A positivity (Figure 2c) and bushy plus membranous HMBE-1 positivity (Figure 2d). They were Immunonegative for Calretinin, CK20 and CK 5/6.

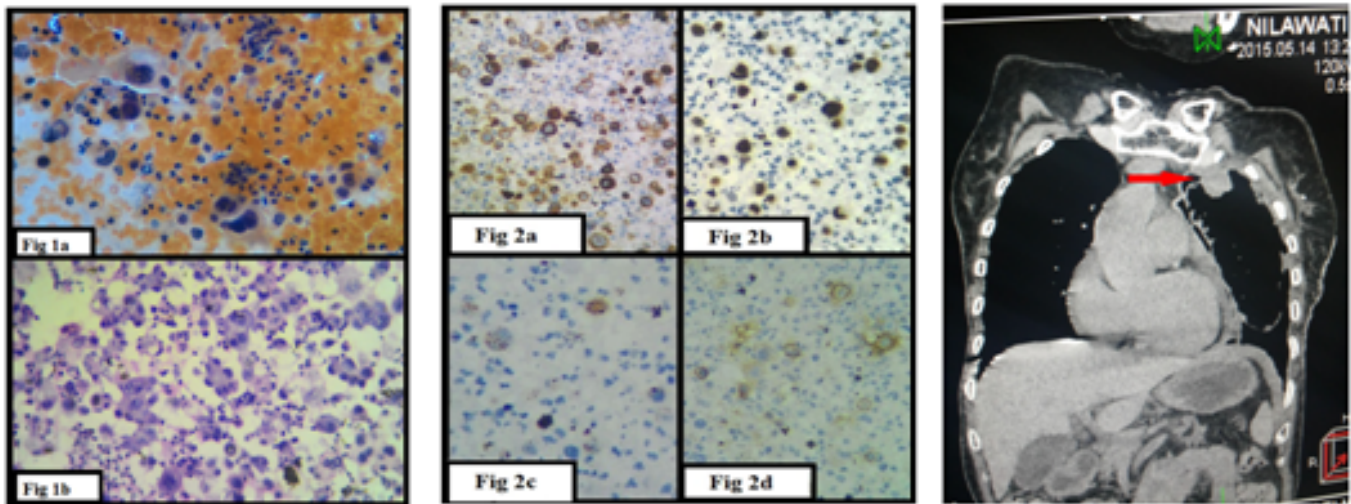


Figure 1

Figure 2

Figure 3

**Legend**

**Figure 1a (original):** CONVENTIONAL SMEAR 400 X (PAP STAIN) - Highly pleomorphic cells with hyperchromatic nuclei in midst of inflammatory infiltrate. Suggestive of malignant effusion.

**Figure 1b (original):** CELL BLOCK 400X (H&E) - Poorly formed acini, highly pleomorphic cells, overlapping nuclei with prominent nucleoli.

**Figure 2a (original):** CK7(400X)- Strong cytoplasmic positivity.

**Figure 2b (original):** TTF 1(400X)- Strong nuclear positivity.

**Figure 2c (original):** Napsin A(400X)- Focally positive.

**Figure 2d (original):** HMBE 1(400X)- Bushy plus membranous positivity.

**Figure 3 (original):** CECT- Heterogeneous enhancing mass (arrow) of size 3 x 2cm at junction of left apical lobe and pleura forming an obtuse angle with pleura suggestive of malignant mesothelioma.

**DISCUSSION**

Accumulation of fluid in a serous cavity in excess of the normal amount is referred to as an effusion.<sup>3</sup> The development of malignant pleural effusion is a common complication of cancers like pulmonary and gastric carcinomas.<sup>5</sup> The cytological examination of serous effusions has increasingly gained acceptance in clinical medicine, to such an extent that a positive diagnosis is often considered the definitive test and obviates explorative surgery.<sup>5</sup> It is important not only in the diagnosis of malignant lesions, but also helps in staging and prognosis.<sup>5</sup> The accurate identification of cells as either malignant or reactive mesothelial cells is a

diagnostic problem on CS examination.<sup>5</sup> The difficulty is either secondary to marked atypia of mesothelial cells caused by the microbiological, chemical, physical, immunological, or metabolic insults to the serous membranes or to the subtle cytomorphological features of some malignant neoplasms.<sup>5</sup> Although a positive diagnosis is highly reliable, a negative result does not rule out a malignant cause.<sup>3</sup> Although the preparation of CS is a much simpler procedure than that of paraffin sections, it has limitations, that is, lack of tissue architecture.<sup>5</sup> In some cases, appreciation of tissue architecture makes diagnosis easier.<sup>5</sup> The CB method is the oldest method of processing cytological material, described by Mandlebaum in 1900

for studying exudates.<sup>6</sup>The CB study provides additional information for a definitive diagnosis, as it allows the recovery of even minute cellular materials and it is valuable for the histochemical and the immunohistochemical methods.<sup>2</sup>The main advantages of the CB technique are preservation of tissue architecture and obtaining multiple sections for special stains and immunohistochemistry.<sup>5</sup>The other advantage of CB is concentration of cellular material in one small area that can be evaluated at a glance with all cells lying in the same focal plane of the microscope.<sup>5</sup> It bridges the gap between cytology and histology.<sup>5</sup>Our patient presented with massive recurrent left sided pleural effusion which was found to be malignant on CS examination. Biopsy was not possible as the patient was medically unfit. So, Cell block preparation was coupled with IHC.IHC panel revealed strong cytoplasmic CK7 positivity, nuclear TTF-1 positivity and Napsin-A positivity along with negative Calretinin, CK20 and CK5&6 indicating that the primary site was lung.<sup>7</sup>Also conflicting HMBE-1 positivity, along with architectural pattern and tumor cell morphology on cell block indicated poorly differentiated adenocarcinoma of lung as the tumor type.<sup>8</sup> According to various studies, an additional diagnostic yield for malignancy and its type was noted if the CS was supplemented by the CB.<sup>9</sup>

## CONCLUSION

In suspicious cases of poorly differentiated malignancy with unknown primary presenting with serous effusion, Cell block technique plays a vital role in arriving at accurate diagnosis and hence avoiding unnecessary biopsies.

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