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The Contribution of Cell Block Method to Histopathological and Immunohistochemical Diagnosis

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Abstract

As in all fields of medicine, the principle of giving the most accurate and detailed result to the patient with the least invasive method is on the agenda in pathology. In this way, invasive methods containing various complications will be applied to patients less frequently and the loss of time will be reduced. In this study, which includes 113 cases involving different organs, we performed in this context; The specificity of the technique we applied was determined to be 98%, the sensitivity was determined to be 95%, the positive prediction was determined to be 95%, the negative prediction was determined to be 98% accurate. We found that the contribution of the method we saw to be more remarkable, especially in the evaluation of joint fluids and abdominal aspiration fluids; we also found its contribution significant in the specification of lesions in soft tissue and thyroid fine needle aspiration. As a result, we think that the cell blocking method can be an important diagnostic support bridge between cytology and histology.

Keywords: Cytology; Cell block; Diagnosis; Histology

Introduction

Today, pathology is in an effort to give the most detailed diagnosis with the least invasive methods. As a result of these efforts, diagnosis can be made with increasingly small tissue samples. However; No matter how small the tissue sample is, its removal requires a variety of invasive methods. The quest for non-invasive diagnosis; resulted in a concentration on cytological investigations. But; cytological examination, especially fine needle aspiration cytology, may be insufficient for diagnosis. In such cases, the search for better use of these cytological samples instead of immediately turning to invasive biopsy methods; cytopreopreatory techniques have been introduced.

The most recent of these techniques is the one obtained by centrifuging cytological samples. Is the study of concentrated sediment with the 'Wet' film technique or cell block technique? Of these, cell block technique; It is becoming more and more popular every day because it can better reveal the cellular details in the organized structures formed by the cells (acinar structures, ductus structures, papillary structures, etc.), prepare a large number of sections and make a diagnostic contribution with special staining and immuno histochemical staining and reduce the need for biopsy.

Material and Method

Our cases; It includes the cases that took place in our thesis study between 1993-1995 and came to Gayrettepe Florance Nightingle Hospital between 2021-2022. Our cell block cases; 58 of them were prepared from fine needle aspiration cytology, 7 from washing and brushing fluid samples, 27 from pleuralic, peritonal, etc. effusion fluids and 1 from urine sample. When creating a cell block; Agar-gel method, plasma-thrombin method and modified cell block method were used at different stages.

Agar-Gel method application

a. Cytological example; It is transferred to a 10-milliliter centrifugal tube.

b. It is centrifuged at 2000 rpm for 15 minutes.

c. The liquid part of the centrifuge tube on the sediment is poured and the sediment is taken on a slide by means of a metal chuck.

d. A mixture is provided by dropping a drop of 3% bacterial agar kept in liquid form at 60 degrees Celsius on this slide.

e. Leave to freeze in a cool environment.

f. Solidified mass formed; It is scraped from the slide and taken to the tissue follow-up scrub.

g. The tissue follow-up cassette is placed in 10% formol and fixed for a few hours.

h. Then, together with other biopsy samples, they are followed up with a tissue tracking device.

i. Cast and cool, prepare 5 micron sections with microtome and paint with H&E and take the examination.

Application of plasma-thrombin method

a. The first 3 applications (a, b, c) are the same as the agar-gel method.

b. Created sediment; A clot is formed by dropping 4 drops of plasma and 4 drops of thrombin.

c. Clot formed; single or in pieces the tissue is taken to the follow-up cassette.

d. The next stage is as in the Agar-gel method (g, h, i).

Application of modified cell block method

a. The cytological sample is taken to a 10 millilitre centrifuge tube and centrifuged at 1000 rpm.

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b. The liquid on the sediment is poured and 70% alcohol is added to it.

c. It is centrifuged again at 1000 rpm for 10 min.

d. Instead of the liquid on the spilled sediment, this time 95% alcohol is added.

e. Centrifuged again at 1000 rpm for 10 min.

f. Liquid is poured over the sediment and the sediment is taken to the tissue follow-up cassette with the help of a thin spatula.

g. Then it is followed as in the Agar-gel method (g, h, i).

Throughout our study; All 3 methods were used, and the 'Modified Cell Block Method' was found to be more successful and practical and the study was continued with this method. In our study; to the sections we prepare from the cell block; Special histochemical dyes such as PAS, Muscin, Silver, acid-fast and gram, as well as immuno histochemical markers such as cytokeratin, CEA, S-100 etc. were also applied.

Results

Our 93 cell block cases presented in Table 1; it was composed of appropriate aspiration fluids, lavage fluids and cytological samples obtained by different techniques. Cases; It consisted of 32 female and 61 male patients. The age distribution is 19-80 and the average age is 46. Cytological diagnosis of 83 of 93 cases with cell block study and histological diagnosis of 13 of 21 cases diagnosed with MRP is available Table 2.

In the cytological study, 19 of the total 64 cases defined as MYN and MYP could be given a specific diagnosis (approximately 30%), while 26 out of 79 cases could be given a specific diagnosis with cell block. (Approx. 33%).

Table 1: Distribution of Cytological Samples Working in Cell Block by Organs.

Sample	Sayı	%
Thyroid aspiration fluid	15	16
Pleural fluid	13	14
Abdominal aspiration fluid	12	13
Soft tissue lesions aspiration fluids	11	12
Breast aspiration plasters	10	11
Bronchial lavage	7	8
Joint fluids	7	8
Aspiration fluid of the lymph node and peritonsillar region	4	4
Pericardial fluid	2	2
Pancreas	2	2
Lung needle aspiration fluid	2	2
Liver needle aspiration fluid	2	2
Aspiration fluid in lesions of the oral region	2	2
Saliva gland aspiration fluid	2	2
Urine	1	1
Brain aspiration fluid	1	1
Total	93	100

Table 2: Diagnostic comparison of cell block and cytology is presented.

	Cytology	Cell block
Negative for malignancy	54%65	58%62
Suspected of malignancy	4%4	2%2
Positive for malignancy	10%12	21%23
İnsufficient	16%19	12%13
TOTAL	83%100	93%100

It is a known fact that the diagnostic contribution of the cell block varies significantly from organ to organ. In our non-study, this contribution difference is sometimes partially and sometimes significantly encountered in every organ.

In cell block preparations prepared from thyroid aspiration fluids; the incompetence rate seems to be quite low. Compared to cytology preparations, the contribution of cell block to cytology is around 7%. In one of our cases diagnosed with MYP; the diagnosis of 'medullary thyroid carcinoma', which can be given by cell block, was confirmed by the detection of amorphous eosinophilic material on polarized light microscopy with 'Congo' stain (Figure 1, 2).

In our studies in P leura fluids; 3 of the 13 cases evaluated with cytology were diagnosed positively in terms of malignancy with the contribution of cell block, 2 of these cases were diagnosed as squamous cell carcinoma and 1 as pancreatic adenocarcinoma metastasis (Figure 3-6).

In our study; abdominal aspiration fluids (paracentesis); the contribution to cytological diagnosis seems to be quite high. Of the 12 cases, 2 of which we could call positive in terms of malignancy with cytological smear samples, 4 of them could be diagnosed as positive in terms of malignancy with cell block. These cases are; colon and stomach adenocarcinoma, breast invasive ductal carcinoma and ovarian serous cyst have been diagnosed as adenopapillary carcinoma metastases (Figure 7-10).

The diagnostic contribution of fine needle aspiration materials made from soft tissue lesions also seems to be significant. Cytological sampling of 11 soft tissue lesions was examined by cytological examination, while

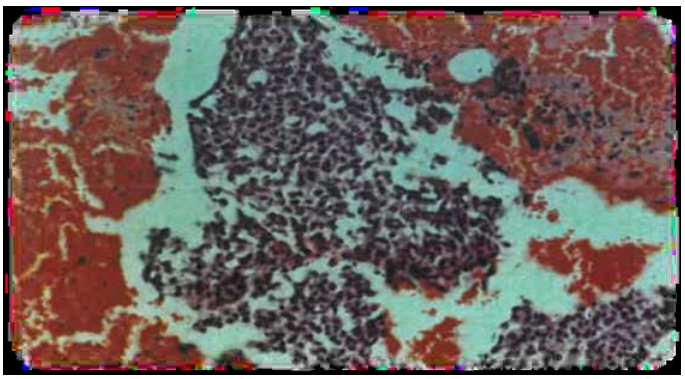

Figure 1: Thyroid fine needle aspiration fluid; medullary carcinoma. Neoplastic cells in clusters, round-polygonal shape (cell block, HE x 200).

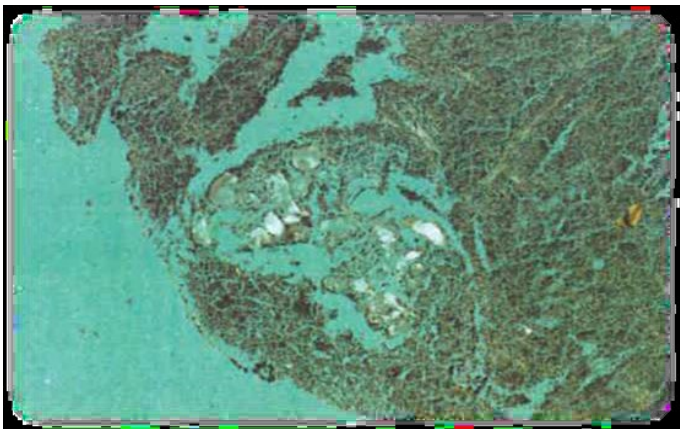

Figure 2: Thyroid fine needle aspiration fluid; medullary carcinoma. Areas of accumulation of amorphous eosinophilic material (cell block, Congo x 200).

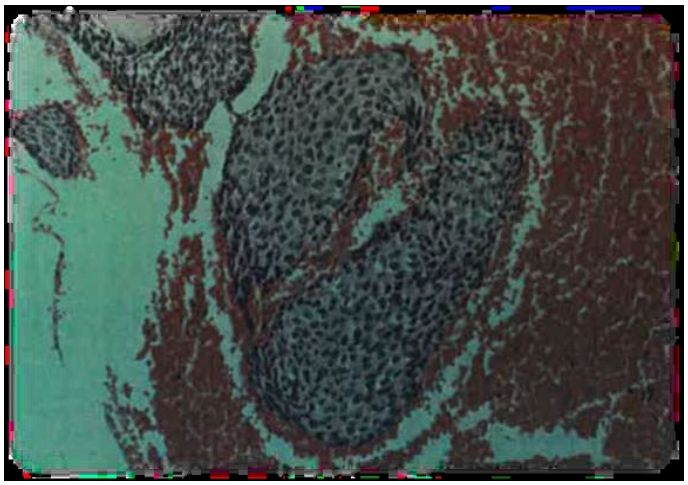

Figure 3: Pleura fluid: metastasis of squamous cell carcinoma. Atypical epithelial cells in irregular clusters. Cell block, HEx200.

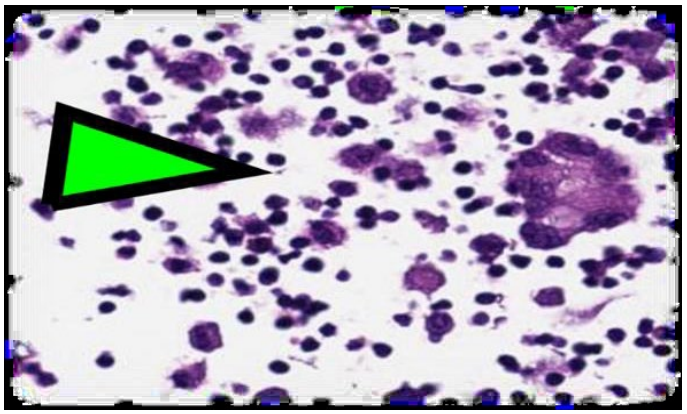

Figure 4: Pleura fluid: pancreatic adenocarcinoma metastasis. Atypical epithelial cells organized to form individual and irregular acinar structures (Digital pathology, cell block HE x400).

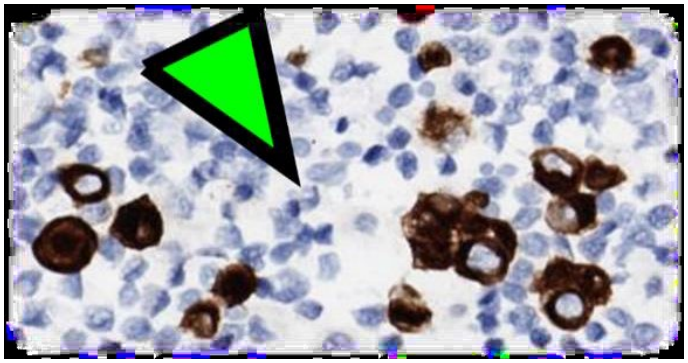

Figure 5: Pleura fluid: pancreatic adenocarcinoma metastasis. Atypical epithelial cells in individual and three-dimensional clusters. (Digital pathology, cell block. CK7 x400).

this number increased to 4 with cell block compared to only 2 positive diagnoses in terms of malignancy. 3 of our cases who were diagnosed positively in terms of malignancy; taken from different extremities and diagnosed as Ewing's sarcoma, malignant mesanchymal tumor, possibly osteosarm, malignant mesanchymal tumor, possibly chondrosarcoma. One of our cases was diagnosed as 'germ cell tumor metastasis' with the contribution of cell block and clinical correlation to fine needle aspiration from retroperitoneal mass (Figure 11, 12).

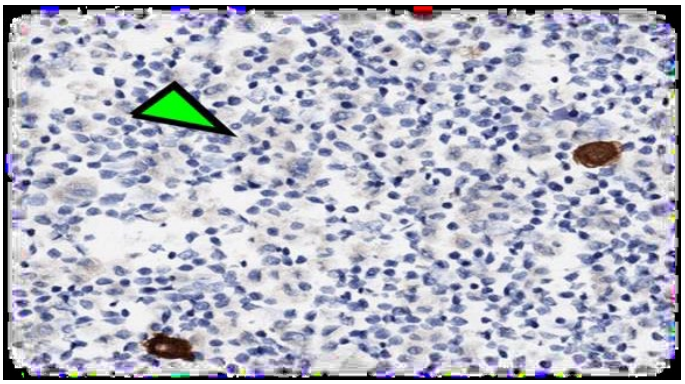

Figure 6: Pleura fluid: pancreatic adenocarcinoma metastasis. Atypical epithelial cells distributed individually. (Digital pathology, cell block. Mapsin x 200).

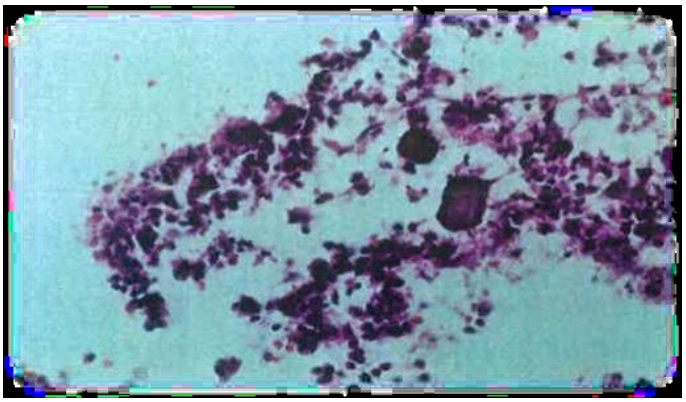

Figure 7: Abdominal aspiration fluid: metastasis of ovarian serous papillary cystadenocarcinoma. Atypical epithelial cells and 'psammoma bodies' that form irregular papillary structures. Cell block, HE x 200.

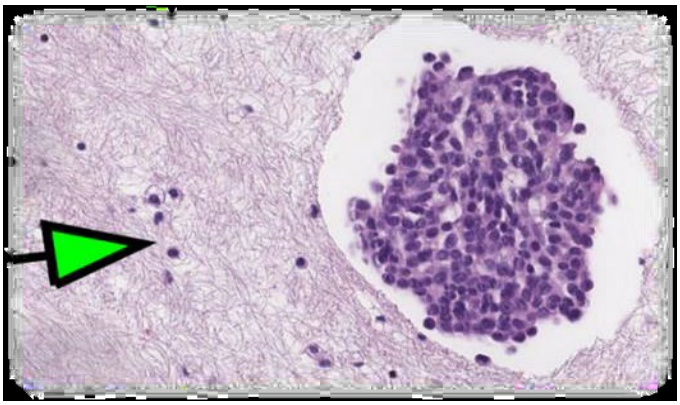

Figure 8: Abdominal aspiration fluid: metastasis of breast ductal carcinoma. Atypical ductal epithelial cells located in cohesive clusters. (Digital pathology, cell block, HEx400).

Discussion and Conclusion

In recent years; both in the diagnosis and treatment phase, there is an intense tendency to procedures that are less harmful to patients. In almost all areas of medicine; the main principle of these studies is based on the principle of 'less invasive method better results'.

In this context; there have also been significant developments in pathology, from wedge biopsies to needle biopsies, from needle biopsies to fine needle biopsies and cytological examinations.

In addition; cytological examination, especially in areas where

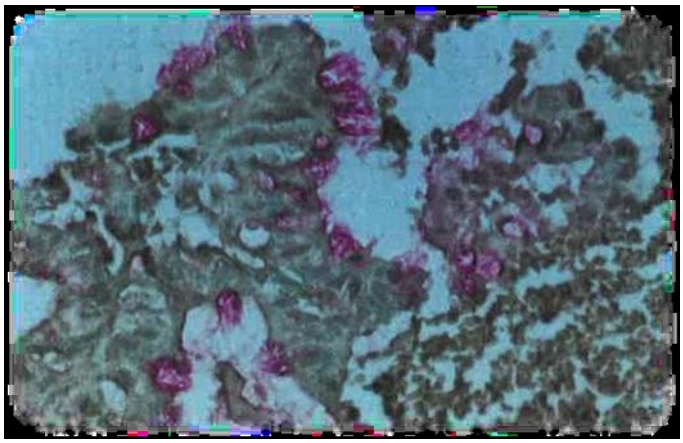

Figure 9: Abdominal aspiration fluid: gastric adenocarcinoma metastasis. Atypical epithelial cells with prominent intrastoplasmic mucin. Cell block, Mucins x 200.

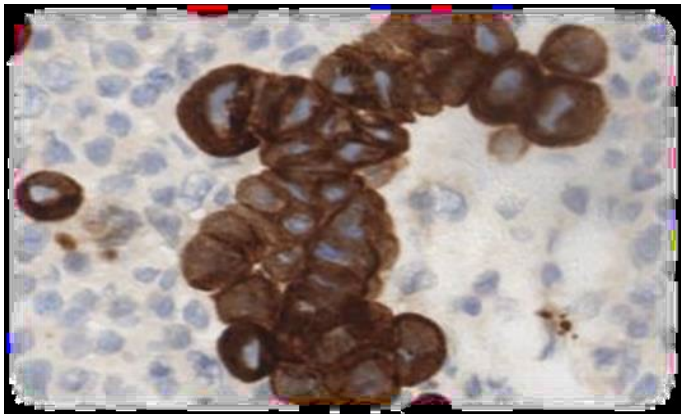

Figure 10: Abdominal aspiration fluid: gastric adenocarcinoma metastasis. Organized atypical epithelial cells in irregular clusters. (Digital pathology, cell block, CK7 x1000).

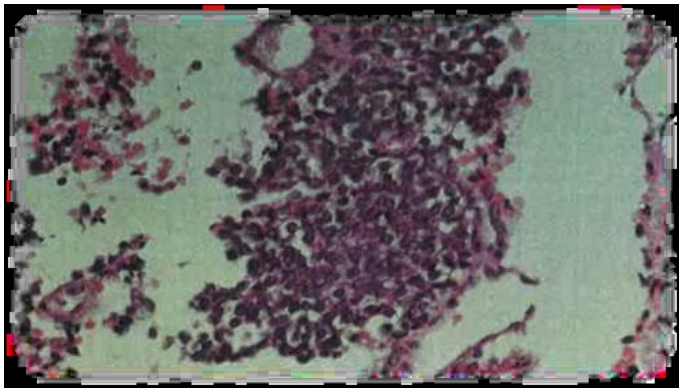

Figure 11: Soft tissue aspiration fluid: Ewing's sarcoma. In clusters, tumor cells with small rounded shape eosinophilic cytoplasma. Cell block, HEx200.

biopsy is difficult to take (thorax, retro peritoneum, retro orbital region, etc.) may be without options. In pathology; although cytological study techniques are quite old, sometimes causes such as cellular insufficiency, overlap of cells, ground problems have initiated studies to increase the diagnostic contribution of cytological example.

This quest is; in 1896, Bahrenburg and his colleagues initiated the first cell block study by following the Para synthetic fluids by passing them through the 'celloid's film' [1].

However; when it was understood that significant cell loss was revealed in this study; Bussalati; By centrifuging the fluids rather than passing them through the membrane, he proposed the follow-up of the obtained sediment such as biopsy using substances (agar) that would hold the sediment together and laid the foundation of today's applications [2].

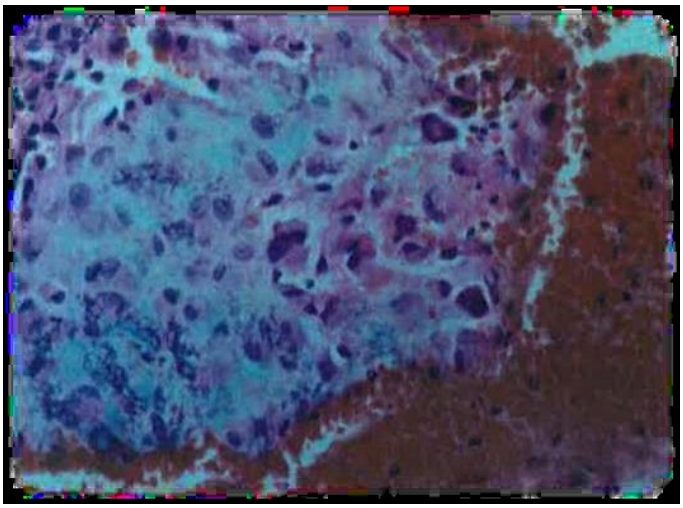

Figure 12: Soft tissue needle aspiration fluid: Malignant mesanchymal tumor, possibly osteosarcoma. Atypical mesanchymal cells with pronounced pleomorphism and mitotic activity. Cell block, HE x400.

In the first period of our work; we used the agar-gel method, then applied the plasma-thrombin method that Bibbo insisted on [3], this method; although it significantly reduces cell loss according to the agar-gel method, it has been observed to impair cell morphology in some cases.

While our work continues; we directed our studies in this direction with the successful reports [4] obtained by Zito and his colleagues in cell block studies using different detection solutions.

In our study, we performed 93 cytological sampling in classical cytology and cell blocking applications; In terms of the cases we call 'positive in terms of malignancy', cytologically approximately 12% (10 cases) and 23% (23 cases) in cell block were contributed.

Our Results; it agrees with previous large-scale studies on this subject [1, 3 and 4].

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Our Results; it agrees with previous large-scale studies on this subject [1, 3 and 4].

In our study; in cases evaluated as 'negative in terms of malignancy', the rate of diagnosibility; similar rates were found as 65% for cytological samples and 63% for cell block. However; in these cases, it is understood that the cell block is slightly superior to cytology in order to distinguish the diagnosis (granuloma, etc.). (29% vs. 34%) As a result of this study; it is consistent with the cell block study conducted by Dekker from cytology samples taken from body cavities [5].

In our study; 61% (13 cases) of the cases diagnosed as 'positive for malignancy' from cell block were confirmed histopathologically. In this ratio; seems to be in line with the studies on this subject [1 and 4].

The results of our thyroid fine needle aspiration study are also as follows; it is consistent with the work of Pietribiasi [6] and the work of Kung and Yuen [7].

In our study from paracentesis fluid samples that are stated to be the most meaningful diagnostic contribution of cell block; when combined with cytology, we observed an extra diagnostic contribution of 33% for 'malignancy-positive' cases. In these results; it seems to be in line with the work of Zito and Dekker [4, 5].

In our studies on soft tissue fine aspiration cytology; In addition to contributing to the 'positive in terms of malignancy' diagnosis, and perhaps more than that, the contribution to the specification of the diagnosis has attracted attention. (Ewing's sarcoma, osteosarcoma, chondrosarcoma etc.) Schwartz and Zollars in their study; in the case of soft tissue malignant melanoma (clear cell sarcoma) diagnosed with two cell blocks; they performed electron microscopic studies and showed premelanosome structures in tumor cell stoplasms [8].

In the cell block cases we studied from joint fluids; the number of cases we defined as 'negative in terms of malignancy'; it was significantly higher than in cytology. (43% vs. 86%) However; since we did not have a 'positive case in terms of malignancy', a healthy evaluation could not be made.

Cell block, in our study on the specification of the presence of infective inflammation for 'malignancy-negative' cases (in cases with abscesses, gram-positive bacteria and fungi), we could not reach significant conclusions.

The results were generally negative. Pinto and his friends; They published a case in which they diagnosed 'actinomyces' by seeing 'Sulfur granules' and silver methenamine stain and filaments in the cell block studied from breast aspiration cytology performed on a case with suspected inflammatory carcinoma.

The number of cell blocks we prepare from the transthoracic lung fine needle aspiration fluid is limited to 2 [9]. However; while both cases could be cytologically diagnosed as 'negative in terms of malignancy' and insufficient, both cases were not only evaluated as 'positive in terms of malignancy' but also were specific as 'primary adenocarcinoma' and 'renal cell carcinoma' with cell block. Pilotti and his friends; 271 transthoracic needle aspiration in their work by adding cell blocks to their cytology; they reported that 'malignancy-positive' cases were often diagnosed without immuno histochemical or electron microscopic studies [10].

In our study; when all cell block cases were considered, the sensitivity was 95%, the specificity was 98%, the positive prediction was 95%, and the negative prediction was 98%. These results are; it is in complete agreement with the results of Zito [4].

After all; although it does not seem to be an adequate and alternative examination on its own, it provides very important diagnostic support to cytological diagnosis and serves as a bridge with histological diagnosis.

Another striking result of our study; is that the contribution of the cell block to the diagnosis and specification of the diagnosis shows significant differences from organ to organ. For example; while the diagnostic complementary contribution (positive/negative in terms of malignancy) is much more prominent in paracentesis and joint fluids, this contribution is more prominent in soft tissue fine needle aspirations and pleural fluids in the specification of the lesion.

In the cell block cases in which we conducted Immunohistochemical studies; CK7, CEA, S-100, ER and Mapsin Immunohistochemical markers were applied to 15 tumor patients diagnosed as 'positive for malignancy' and in 5 of them CK 7 and 1 had positive staining with mapin. These results are; it is consistent with the Immunohistochemical study of Kung on 43 cell blocks [11]. The positivity and staining quality in the Immunohistochemical studies were also found to be so good as to look for biopsy sections. This is in line with the assessment of Kung [11].

As a final word for the cell block; especially in selected cases, we can say that it is an important diagnostic method because of its indisputable contribution to cytological diagnosis, reducing the biopsy applications to be performed and exposing the patient to less invasive application and being economical in today's conditions.

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Contributions: There are no contributors other than me.

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