Original Article

Comparison of the Results of Fine Needle Aspiration Biopsy Specimens and Permanent Histopathologic Preparation in Orbital Mass Lesions

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ABSTRACT

Background and Objectives: We aimed at evaluating the efficacy of fine needle aspiration biopsy (FNA) in comparison with histopathology and demonstrating whether cytological study could be a proper diagnostic tool in orbital mass lesions.
Materials and Methods: In a cross sectional study during 36 months, patients referred to our ophthalmologic center affiliated to Tehran University of Medical Sciences, for evaluation of orbital masses, were selected for FNA. After the surgery, the results of FNA were compared against histopathologic diagnoses as our gold standard method. Finally, the frequencies of specimen adequacy, the accuracy of FNA in distinguishing benign and malignant lesions and in the exact definitive diagnosis of the disorders were reported.
Results: In 27.4% of the total 62 cases, the specimens were inadequate for cytologic evaluations. The rate of specimen adequacy in malignant and benign lesions was 82.6 % and 66.66%, respectively. From the morphologic point of view, the rate of the exact definitive diagnosis of malignant and benign disorders in the total 62 cases was 78.2% and 38.46% and; in the adequate specimens, it was 94.73% and 57.69%, respectively. There was no false positive FNA result for malignant cells and only in one malignant case, the FNA report was falsely negative. All data wee analyzed by SPSS software and p value <0.05 was considered as significant.
Conclusion: FNA was considered more beneficial in the diagnosis of malignant lesions. FNA is a relatively noninvasive, rapid, specific, and accurate method for the preoperative primary diagnosis of orbital mass lesions and especially in malignant lesions and in some conditions, specific diagnoses can be achieved.

Keywords: Fine Needle Aspiration, Orbits, Tumor, Histopathology

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Introduction

For several years, exfoliation and aspiration cytology were the acceptable methods of evaluation and preliminary or definitive diagnoses of orbital and periorbital lesions. In recent years, Fine Needle Aspiration (FNA) has become a substantial preferred method and there is an increase in the number of ophthalmologic lesions evaluated by FNA, especially in large medical centers. Results of several studies have shown that FNAB provides a rapid, reliable, and relatively safe method of obtaining materials for cytological evaluations (1-7). The most frequent complication that may occasionally be seen is retro bulbar hemorrhage that should not cause permanent disability if promptly treated (8).

Therefore, FNA can be used as a good screening method in orbital and periorbital mass lesions. Specimen adequacy and effectiveness may be guaranteed, especially by CT scan or ultrasonographic guided techniques (9).

On the other hand, surgical open biopsies provide a definitive diagnosis but it is a difficult and laborious technique. In addition, in some instances, surgery is not the appropriate treatment and the use of other therapeutic modalities is adequate. Therefore, in proper situations, FNA can reduce the turn around time and increase the cost effectiveness in the diagnosis of orbital and periorbital lesions.

Sometimes FNA cytologic diagnoses help the ophthalmologist to know about the behavior of the neoplastic lesion (i.e. benignancy or malignancy) and to make the best decision for managing the patient. By the use of FNA, it is possible to identify the metastatic origin of an orbital mass in a known case of malignancy (10, 11).

In Iran, like many other countries, there are limited cytologic studies in the territory of orbital and periorbital tumors and this experiment requires further expansion. Therefore, we decided to perform FNA in orbital and periorbital masses in Farabi Hospital, an ophthalmologic center affiliated to Tehran University of Medical Sciences. After the surgical excision of the tumor, FNA results were compared to their permanent histopathological diagnosis.

In this study, we aimed at demonstrating whether cytologic studies can be a proper substantial or primary diagnostic tool at least for some of the solid tumors in those regions and also if it can estimate the efficiency of FNA in these lesions.

Materials and Methods

In a cross sectional study conducted during 36 months (2006-2008), patients referred to our center (Farabi Hospital, an ophthalmologic center affiliated to Tehran University of Medical Sciences) for the evaluation of an orbital mass lesion, were examined. Those patients who were clinically candidate for open surgery and excision biopsy and had no contraindication for aspiration (such as suspicion for vascular lesions or hypercoagulatory states) were selected for fine needle aspiration prior to surgery. After obtaining an informed consent from participants, two expert ophthalmologists were aspirated the lesion by the use of a fine needle (21 – 23 gauges) that was passed through the upper or the lower lid and entered the lateral or medial aspect of the mass. All FNAs were performed under local anesthesia. The position of the mass was determined by palpation and/or CT scan. After the aspiration, three slides were prepared for each tumor and all were immediately fixed by alcohol 95%. Two slides were stained by Hematoxylin & Eosin (H&E) and Papanicolaou (PAP) methods; the other one was stored for cytochemistry and other special staining, if required. Two experienced pathologists (one cytopathologist and one ophthalmopathologist) reported the aspiration results, separately.

After reporting the FNA results, open surgery and excisional biopsy of the aspirated masses were performed. The same two pathologists evaluated the histopathologic ex-

amination of the tumors in a blind fashion and without knowledge of previous FNA diagnosis.

The results of FNA were compared against histopathologic diagnoses as our "gold standard" diagnostic method. Finally the frequency of specimen adequacy of FNA, accuracy of FNA in distinguishing benign and malignant lesions and the accuracy of FNA in exact definitive diagnosis of the disorders compared to the histopathologic diagnoses as well as the kappa agreement index (between FNA and histopathologic reports) were evaluated and reported. The kappa agreement index above 0.8 was considered as the desirable value. All data wee analyzed by SPSS software and *P* value <0.05 was considered as significant.

Results

Totally, 62 patients were eligible for FNA during 36 months of our study; among the patients, 58% were male and 42% were female (M/F=1.38). The age range was between 1 and 84 year(s) (40 ± 22.5 years old). In 51% of the patients, the lesion was located in the right orbit, in 47%, it was placed on the left side, and 1.8% had a bilateral tumor. There was a statistically significant relationship between clinical impressions of the tumor behavior (i.e. suspicion for benign or malignant lesions) before surgery and post-surgery permanent histopathological diagnoses (*P*<0.001).

In 17 cases (27.4%) of fine needle aspiration, the received specimen was inadequate for cytologic evaluations; in other words, the frequency of the specimen adequacy was 72.6%.

Table 1 and 2 show the details of all 62 cases, including gender and mean age of the patients in each group, different histopathological diagnosis and FNA results of each disorder. FNA results were evaluated in three sections including specimen adequacy, exact definitive diagnosis, and indefinite diagnosis. In the cases with indefinite diagnoses, the type of tumor could not be exactly determined; however, its benign or malignant behavior was specified. Immunohistochemical staining of aspiration slides was used for diagnosis of low grade B cell lymphoma and rhabdomyosarcoma.

In two cases (the last row of table No 1), the biopsied samples were not appropriate for marking the diagnosis while the FNAs were completely diagnostic; one of these two cases was a patient with metastatic carcinoid tumor to the orbit. In the other case, the FNA findings were highly suggestive for a metastatic carcinoma.

Table 3 reveals the comparison of FNA results according to presence or absence of malignant cells with final histopathological diagnosis of benign and malignant lesions, on an overall basis.

Excluding the two mentioned cases in which the histopathologic results were not convincing, the kappa agreement index between FNA and biopsy materials was 0.95 (*P* value<0.001) for the diagnosis of benign and malignant lesions.

Table No 4 shows the frequency of exact definite diagnosis of FNA results in total cases and adequate specimens, according to the final histopathological diagnosis of benign and malignant lesions.

The frequency of the exact definitive diagnosis of FNA for each group of disorders is mentioned in Table 1. In our patients, there was no major traumatic complication for FNA in orbital lesions and all patients tolerated the procedure well.

Figure 1(A-F) shows some illustrations of FNA and histopathological diagnoses of our cases.

Table 1- Demographic information of the patients according to different histopathological diagnosis

Histopathology	Mean Age (yr)	Sex	
		F	M
Meningioma (Meningotheliomatous type)	49.67	3	0
Malignant Small Round Cell Tumor	2	1	0
Langerhans Cell Histiocytosis	2	0	2
Angiomatous Lesion	31.67	2	4
Inflammatory Pseudo tumor			
Acute or Subacute	33.2	3	2
Chronic without significant fibrosis	32.83	4	2
Chronic with fibrosis	40.71	5	2
Lymphoid Infiltration			
Reactive	23	1	
Atypical	50.5		2
Low Grade B-Cell Lymphoma	61.71	2	5
Leukemic Infiltration	5	0	1
Carcinoma			
Metastatic	61.5	1	1
Nonmetastatic	71.33	1	5
Embryonal Rhabdomyosarcoma	6	0	4
Benign Nerve sheath tumors	43.5	0	2
Mucocele	44.5	2	0
Complex choriostoma	13	0	1
Ruptured dermoid Cyst	36	1	0
Fungal Infection	66	0	1
Inadequate Biopsy	51	1	1
Total	36.25	27	35

Table 2- Comparison of FNA results and different histopathological disorders with respect to adequacy and definite or indefinite diagnosis

Histopathology		FNA		
		Exact Definite Dx	Indefinite Dx (Neg For Malignancy)	Inadequate
Meningioma (Meningothelio-matous type)	3	1		2
Malignant Small Round Cell Tumor	1	1		
Langerhans Cell Histiocytosis	2	2		
Angiomatous Lesion	6		6*	
Inflammatory Pseudo tumor				
a. Acute or Subacute	5	5		
b. Chronic without sig-nificant fibrosis	6	6		
c. Chronic with fibrosis	7	1		6
Lymphoid Infiltration				
a. Reactive	1		1	
b. Atypical	2		1	1
c. Low Grade B-Cell Lymphoma	7	5	1	1
Leukemic Infiltration	1			1
Carcinoma				
a. Metastatic	2	1		1
b. Nonmetastatic	6	5		1
Embryonal Rhabdomyosar-coma	4	4		
Benign Nerve sheath tumors	2			2
Mucocele	2		2	
Complex choriostoma	1			1
Ruptured dermoid Cyst	1			1
Fungal Infection	1		1	
Inadequate Biopsy**	2	2		
Total	62	33	12	17

Dx: Diagnosis

*Many Red Blood Cells are seen

**In two cases the received samples for histopathologic diagnosis were inadequate for diagnosis but FNA results were conclusive

Table 3- Comparison of FNA results according to presence or absence of malignant cells with final histopathological diagnosis of benign and malignant lesions

Final Diagnosis	FNA Results			
	Negative For Malignant Cell No.(%)	Positive For Malignant Cell No. (%)	Inadequate Specimen No. (%)	Total No.
Benign Diseases	26(66.66)	0(0)	13(33.33)	39
Malignant Diseases	1(4.34)	18(78.26)	4(17.39)	23
Total	27(43.54)	18(29.03)	17(27.41)	62

Table 4- Frequency of exact definite diagnosis of FNA results in total cases and adequate specimens, according to the final histopathological diagnosis of benign and malignant lesions

Final Diagnosis	FNA Results		
	Exact Definitive Diagnosis/No of total cases (%)	Exact Definitive Diagnosis/ No of adequate specimens (%)	Specimen Adequacy No (%)
Benign Diseases	15/39 (38.46)	15/26 (57.69)	26 (66.66)
Malignant Diseases	18/23 (78.26)	18/19 (94.73)	19 (82.60)
Total	33/62 (53.22)	33/45 (73.33)	45 (72.58)

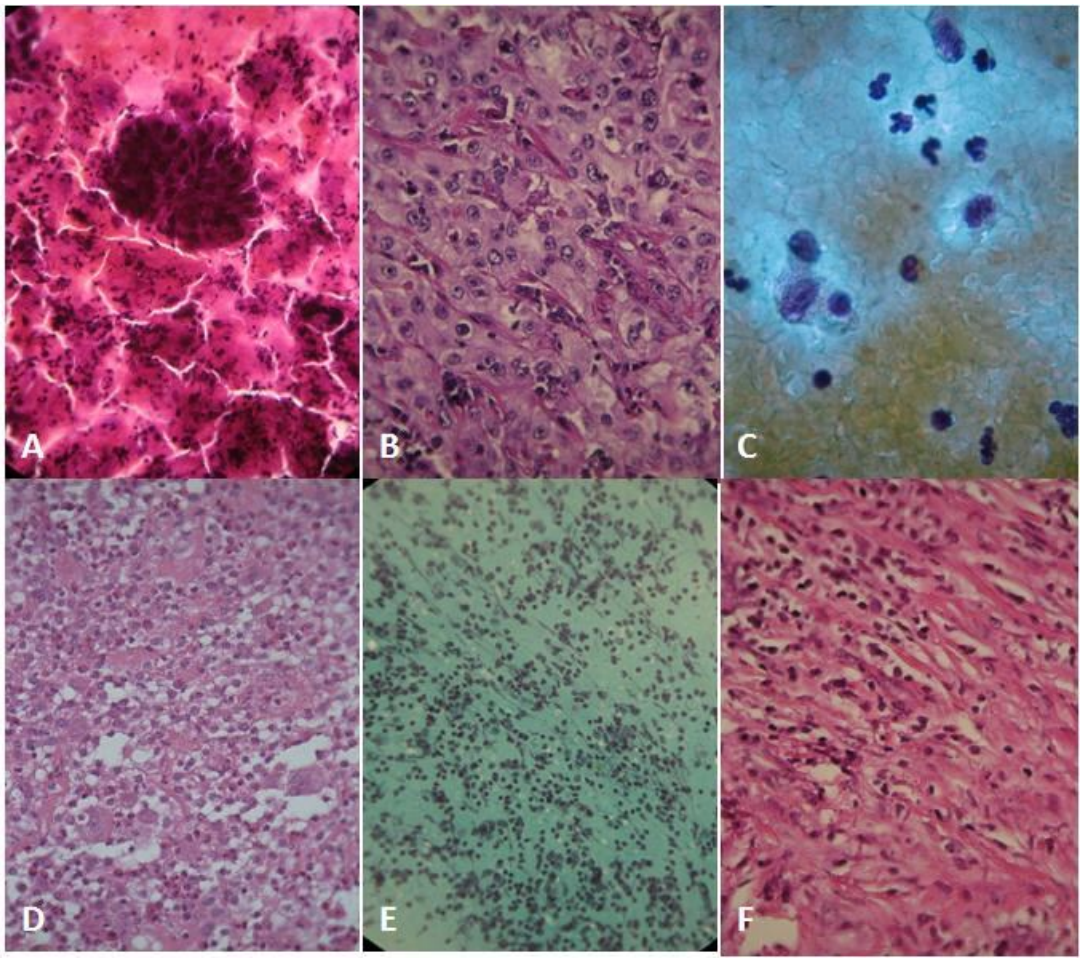

Fig. 1- FNA (A) and histological (B) findings of a case with metastatic carcinoma to the orbit. Clusters and nests of highly atypical cells are seen in FNA and histology, respectively. FNA (C) and histological (D) findings of a 2 years old child with langerhans cell histiocytosis of the orbit. FNA reveals scattered isolated histiocytes and histology shows many histiocytes admixed with eosinophils. FNA (E) and histological (F) findings in a patient with inflammatory pseudotumor of the orbit. Infiltration of lymphoplasma cells in a fibrotic background are noted. (Hematoxylin & Eosin staining ×400)

Discussion

Orbit is a virtual space and the eye glob occupies only 1/5 of its volume and the remainder is composed of connective and adipose tissues, muscles, nerves, lacrimal sacs, etc.; because of the variety of its content, many primary tumors (benign or malignant) including lipoma, hemangioma, lymphangioma, nerve sheet tumors, rhabdomyosarcoma, lymphoma, langerhans cell histiocytosis and many others can involve this space. On the other hand, malignant tumors of adjacent organs may involve the orbit by local invasion. Orbit may also be a metastatic site for invasive tumors of distant organs.

FNA is a relatively noninvasive, safe, and reliable method with the minimal probability of tumor seeding that can be used in place of open biopsy, the usual method for the preoperative diagnosis of orbital tumors (1). The accuracy rate varies from 50-94%, depending on the skill of the operator, size of the lesion and the expertise of the cytopathologist in interpreting the smears (8).

In this study, 27.4% of the aspirated specimens were insufficient for cytological evaluations. In a review of our cases, we found out that there might be several reasons for this relative high rate of inadequacy. Specific kinds of tumor account for most inadequate FNA specimens. For example, 2 out of 3 meningiomas were *enplaque* form and unsatisfactory specimen sampling is reasonable. In another situation, 6 out of 7 cases of chronic inflammatory psuedotumors had unsuccessful FNA samplings because of extensive fibrosis. The other group of disorders with inadequate FNA specimens was benign nerve sheet tumors (i.e. schwanomma and neurofibroma). Again, in these cases, the characteristics of the tumor should be the major cause. Crushing artifacts and poor preservation during slide preparation, the presence of necrotic materials in some kind of malignant tumoral tissues and the expertise of the ophthalmologist who performed the aspiration were some other influencing factors on FNA results in our study.

To improve the specimen adequacy of FNA specimens, we can propose aspiration under ultrasonographic or CT scan guides and liquid-based preparation methods instead of direct smearing. When aspiration biopsy is performed by the guidance of ophthalmologic examinations and conventional radiologic techniques, the rate of inadequacy may be high. In a study in which an ultrasonographic guide was used for performing FNA of orbital mass lesions, the rate of insufficient specimen was 22% (9). This rate was different among other studies, for example, 2 out of 18 cases (12) or 4 out of 30 cases (13). Direct smearing is the routine and popular method for FNA study in our country. It is obvious that by using liquid-based preparation methods the quality of smears will be improved, though this method is more expensive.

According to our study, FNA was considered more beneficial in the diagnosis of malignant lesions, because compared to the benign lesions, the rate of the specimen adequacy was higher in malignant lesions (82.6 % vs. 66.66%); in addition, from the morphologic point of view, malignant lesions can be diagnosed more exactly and accurately than benign disorders not only in the total 62 cases (78.2% vs. 38.46%) but also in the adequate specimens (94.73% vs. 57.69%). Tijl JW *et al*. performed FNA in 46 patients having an orbital mass with histopathological control; the accuracy was 81% in their study. They also accepted that FNA is a valuable method in establishing a diagnosis of malignancy in orbital tumors (14). In Cangiarella study, 75% of FNA results (18 of 24 cases), were specific diagnoses (15) and these results were specific in 82% of the cases (14 out of 17 patients) in Rastogi *et al* study(16) . Tani *et al* studied a series of 82 fine needle aspiration from orbital masses, which in malignant ones IHC staining were performed. They mentioned the usefulness of FNA in diagnosing orbital mass lesions and emphasized the value of IHC in tumor characterization (17).

In this study, there was no false positive FNA result for malignant cells and only in one malignant case, the FNA report was falsely negative. It means that if the specimen suffices for evaluation, FNA sensitivity and specificity is more than 90% for finding malignant disorders. Besides as it is mentioned above, we emphasized that in two cases, the biopsied materials were inconclusive and the clinician decided on the clinical and FNA findings. Glasgow *et al*. also found no false positive results in their study (12).

To conclude, FNAB is a relatively noninvasive, rapid, specific and nearly accurate method for the preoperative primary diagnosis of some types of orbital mass lesions and especially in malignant lesions, specific diagnoses can be achieved in a substantial number of cases. We also concluded that in some conditions, orbital FNA has the best (near to 100%) correlation with histological findings such as langerhans cell histiocytosis, acute, subacute or chronic inflammatory pseudo tumor without significant fibrosis and rhabdomyosarcoma. In some other situations, this correlation is rather high (More than 70%), like as carcinomas and lymphomas. In other disorders, especially

benign masses, including angiomatous lesions, meningioma, or chronic inflammatory pseudotumor with extensive fibrosis the correlation is very poor and diagnostic utility of FNA is questionable.

Conclusion

Radiologic guided mass aspiration and liquid-bases preparation method were not available and we had some limitation in this regards. It might be proposed that in the hands of an experienced ophthalmologist, the specimen adequacy of FNA can be improved. In addition, we propose that by the use of specific techniques such as ultrasonography or CT scan guided aspiration and the performance of immunohistochemistry on FNA slides, more specific and accurate results may be gained.

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