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Diagnostic Utility of Fine Needle Aspiration Cytology of the Orbit: A 26 Year Retrospective Study of a Single Institution's Experience

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Abstract

Objectives: Diagnosing orbital tumors is challenging due to the intricate anatomy of the orbit and associated risks of surgical biopsy. Fine needle aspiration (FNA) of the orbit provides a less invasive alternative to surgical biopsy.

Study Design: The surgical pathology database was retrospectively searched and analyzed for orbital specimens obtained by fine needle aspiration at Wake Forest Baptist Medical Center between the years 1990 and 2016.

Results: Of the 62 specimens from 61 patients, 38 cases (38/62, 61.3%) were malignant neoplasms, 9 cases (9/62, 14.5%) were benign lesions, and 15 cases (15/62, 24.2%) were unsatisfactory/non-diagnostic. The most common neoplastic diagnosis was hemato/lympho-proliferative processes (33/38, 86.8% of the malignant neoplastic lesions), predominantly non-Hodgkin's lymphoma (NHL) (29/38, 76.3% of the malignant neoplastic lesions). 19 NHL cases (65.5% of NHL cases) had been confirmed by subsequent flow cytometric analysis. FNA results from 12 cases had been compared with surgical biopsy diagnosis. The diagnostic accuracy was 11/12 or 91.7%.

Conclusions: FNA of the orbit is a relatively non-invasive and cost-effective method in diagnosing orbital tumors; it is especially valuable in identifying hematolymphoid malignancies in the orbit, mainly non-Hodgkin's lymphoma.

Keywords: Orbit; Fine needle aspiration; Non-Hodgkin's lymphoma; Malignancies

Introduction

Orbital tumors are rare and often referred to tertiary care specialized medical centers for management. The anatomy of the orbit is complex and invasive surgical biopsy raises the risk of globe rupture/injury. These factors can make diagnosing orbital lesions challenging. As a result, there is limited familiarity with orbital specimens and the diagnostic differential they pose.

Fine needle aspiration (FNA) of the orbit with or without the use of imaging guidance (radiologic assistance) is a relatively non-invasive, well-accepted and reliable procedure that can aid in the initial stages of diagnosis. Herein, we review a single institution's experience with FNA of the orbit. Our study shows that FNA provides a cost-effective diagnostic approach to orbital tumor diagnosis, especially for non-Hodgkin's lymphomas.

Materials and Methods

The surgical pathology database was retrospectively searched for orbital specimens obtained by fine needle aspiration at Wake Forest Baptist Medical Center between the years 1990 and 2016. Ultrasound or computed tomography (CT)-guided FNA were performed by a radiologist with a cytopathologist or a cytotechnologist physically present at the time of the procedure to assess sample adequacy, provide on site evaluation and triaging the obtained material. The aspirate smears were stained by modified Romanowski stain (Diff-Quik) and Papanicolaou stain. Syringes were rinsed with saline solution to prepare a cell block, or rinsed into flow media for flow cytometry analysis. A total of 62 specimens were identified and classified into three categories: neoplastic, non-neoplastic, and unsatisfactory/non-diagnostic.

Results

Of the 61 patients, 34 were female and 27 were male, with an age range of 3 months to 94 years (mean 63 years). There was only one pediatric patient. Evaluation of the fine needle aspiration cytology yielded the following diagnoses: 38 cases (38/62, 61.3%) were malignant neoplasms, 9 cases (9/62, 14.5%) were benign lesions, and 15 cases (15/62, 24.2%) were unsatisfactory/non-diagnostic.

The most common neoplastic diagnosis was hemato/lympho-proliferative processes (33/38 neoplastic cases, 86.8%), predominantly non-Hodgkin's lymphoma (NHL) (29/38, 76.3%). 3 cases were plasmacytoma (3/38, 7.8%); and 1 hemato/lympho-proliferative case was diagnosed as atypical leukocytes favor benign (1/38, 2.6%) (Figure 1).

Of the 29 cases diagnosed as NHL, 7 cases were small lymphocytic lymphoma (SLL) (7/29), 5 cases were suspicious for lymphoma (5/29),

4 cases were follicular lymphoma (4/29), 4 cases were mantle cell lymphoma (4/29), one case was marginal zone lymphoma (1/29), and the other 8 cases were unclassified NHL (8/29) (Figure 2).

Papanicolaou stain and Diff-Quik stain were used for cytomorphologic analysis on aspirate smear slides. As shown in Figure 3, cases diagnosed with NHL demonstrated dis-cohesive, monotonous lymphocytic population which was characteristics of lymphoma. Flow cytometric analysis was utilized to confirm the diagnosis in the majority of NHL cases (19/29). 3 NHL cases were confirmed by immunohistochemical staining on surgically resected specimens (3/29). One NHL case was confirmed by immunohistochemical staining on FNA cell block material (1/29).

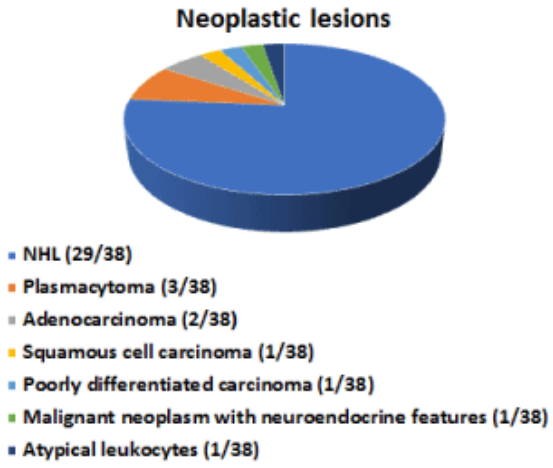

Figure 1: Distribution of thirty eight cases diagnosed as neoplastic lesions.

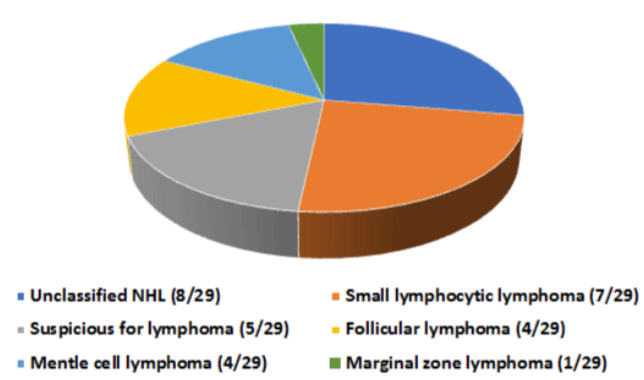

Figure 2: Distribution of twenty nine cases diagnosed as non-Hodgkin lymphoma.

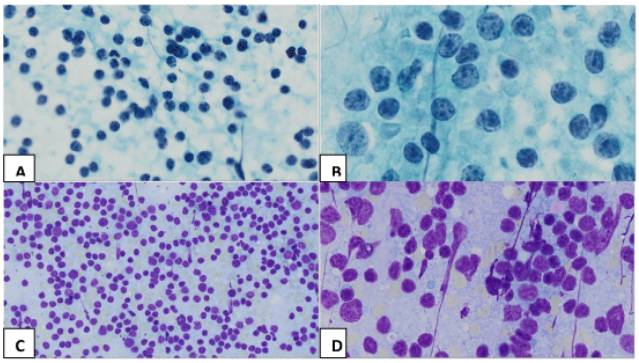

Figure 3: (A and B) Papanicolaou stain of small lymphocytic lymphoma (CLL/SLL) demonstrates a dis-cohesive, monotonous small lymphocytic population (Papanicolaou stain, original magnification A: 20x, B: 40x). (C and D) Modified Romanowski (Diff-Quik) stain of non-Hodgkin's lymphoma, NOS demonstrates a dis-cohesive, medium-sized lymphocytic population with lymphoglandular bodies in the background (Diff-Quick stain, original magnification C: 20x, D: 40x).

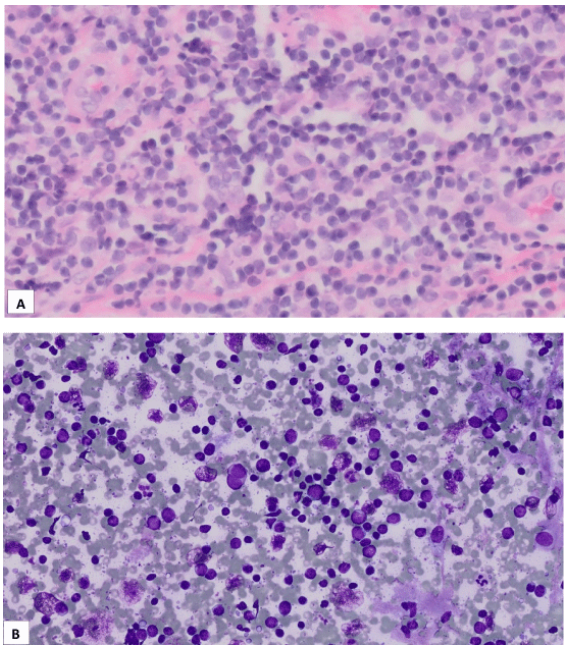

Figure 4: A typical lymphoid proliferation, favor benign. A, Histology shows a diffuse lymphocytic infiltrate composed of small- to medium-sized lymphocytes and scattered histiocytes. (Hematoxylin-eosin, original magnification 40x) B, FNA cytology shows a heterogenous population of small- to medium-sized lymphocytes (Diff-Quick stain, original magnification 20x).

There were 9 other neoplastic cases including plasmacytoma (3/38), adenocarcinoma (2/38), squamous cell carcinoma (1/38), poorly differentiated carcinoma (1/38), neoplasm with neuroendocrine features (1/38), and atypical leukocytes favor reactive (1/38) (Figure 1).

Most of the benign lesions were diagnosed as lymphoid infiltrate/proliferation (4/9 benign cases). 4 benign cases underwent surgical resection and were all confirmed benign (4/4, 100%).

There were 15 unsatisfactory cases due to scant cellularity, crushing and drying artifacts, 11 of which were further diagnosed by surgical resection, including inflammatory infiltration (5/11), meningioma (1/11), infantile myofibromatosis (1/11), amyloidosis (1/11), atypical fibroxanthoma (1/11), SFT (1/11), and B cell lymphoma (1/11).

In total, 23 cases including 11 cases with unsatisfactory FNA diagnosis underwent subsequent surgical excision/incision. Among the 12 cases with original satisfactory FNA diagnosis, 11 cases had a surgical excision/incision diagnosis concordant with the prior FNA results (11/12, 91.7%) (Table 1).

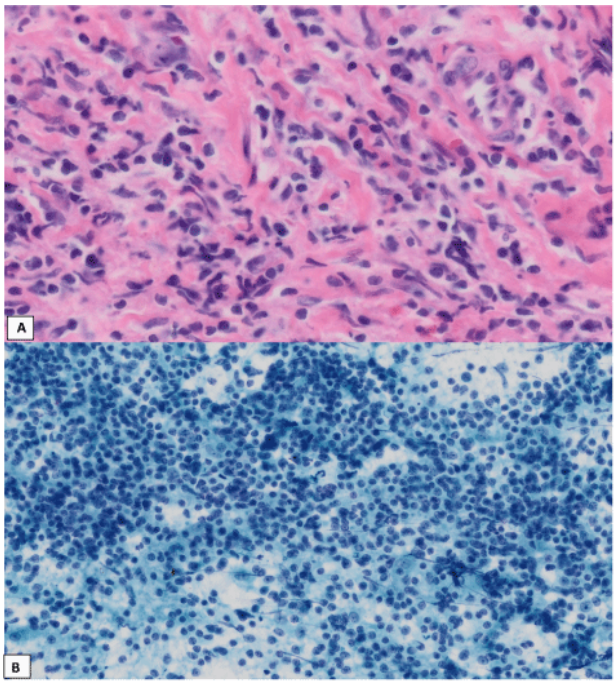

Figure 5: Large B-cell lymphoma. A, Histology shows an infiltrate of predominantly large lymphocytes (Hematoxylin-eosin, original magnification 40x) B, FNA cytology shows a hypercellular aspirate with a monomorphic population of large lymphocytes (Papanicolaou stain, original magnification 20x).

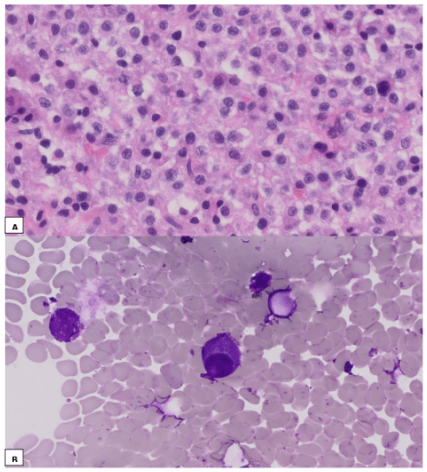

Figure 6: Plasmacytoma. A, Histology shows sheets of plasma cells with eosinophilic cytoplasm and round, eccentric nuclei (Hematoxylin-eosin, original magnification 40x) B, FNA cytology shows plasma cells with round, eccentric nuclei and perinuclear clearing (Diff-Quick stain, original magnification 60x).

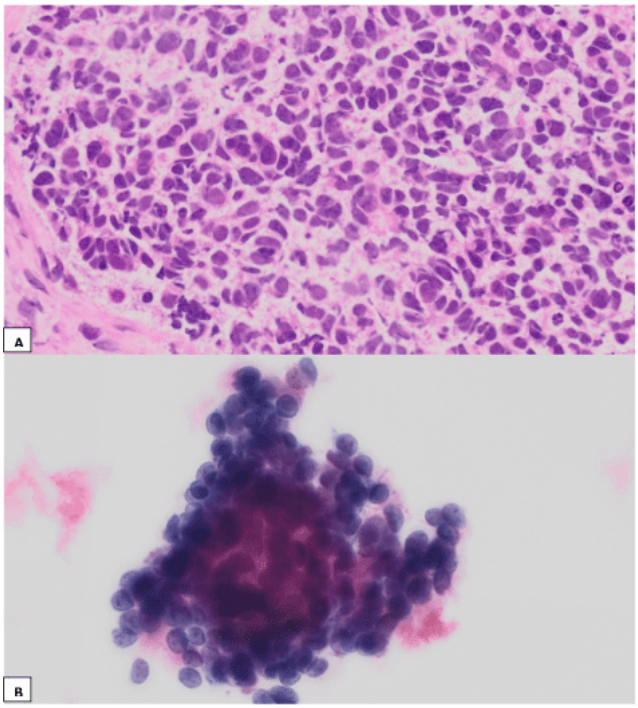

Figure 7: Poorly differentiated carcinoma. A, Histology shows nests of tumor cells with angulated, hyperchromatic nuclei and occasional prominent nucleoli. (Hematoxylin-eosin, original magnification 40x) B, FNA cytology shows cohesive clusters of tumor cells with scant cytoplasm, dark nuclei, and prominent nucleoli (Papanicolaou stain, original magnification 60x).

No.	Age	sex	Race	Site	FNA Diagnosis	Histology Diagnosis
1	66	F	W	orbit	Unsatisfactory for diagnosis	Chronic inflammation
2	55	F	W	orbit	Unsatisfactory for diagnosis	Inflammation (Inflammatory Pseudotumor)
3	40	F	W	orbit	Unsatisfactory for diagnosis	Meningioma
4	83	F	W	orbit	Atypical cells worrisome for malignancy	Invasive Squamous Cell Carcinoma
5	25	M	W	orbit	Benign-Appearing Glandular Cells	Eosinophilic granuloma
6	3m	M	W	orbit	Unsatisfactory for diagnosis	Infantile myofibromatosis
7	55	F	B	orbit	Unsatisfactory for diagnosis	Amyloidosis
8	40	F	W	orbit	Atypical cells worrisome for neoplasm	Poorly differentiated adenocarcinoma.
9	76	M	W	orbit	Unsatisfactory for diagnosis	Atypical Fibroxanthoma
10	74	F	W	orbit	Atypical lymphoid proliferation suspicious for lymphoma.	Malignant lymphoma, low grade B-cell, follicular type.
11	42	F	W	orbit	Suspicious for neoplasm	Poorly differentiated carcinoma.
12	94	M	W	orbit	Atypical lymphoid proliferation suspicious for B-cell lymphoma.	Malignant non-Hodgkin's lymphoma, large cell type, B-cell variant
13	46	M	W	orbit	Atypical lymphoid proliferation suspicious for lymphoma.	Sclerosing orbital pseudotumor (Benign)
14	41	M	W	orbit	Negative for malignancy	Cavernous hemangioma.
15	55	M	W	orbit	Unsatisfactory for diagnosis	Reactive lymphoid infiltrate
16	71	M	W	orbit	Unsatisfactory for diagnosis	Solitary fibrous tumor
17	87	F	W	orbit	Unsatisfactory for diagnosis	Intravascular B cell Lymphoma
18	53	M	W	orbit	Scattered plasmacytoid cells	Plasmacytoma
19	59	F	W	orbit	Unsatisfactory for diagnosis	Inflammation Mixed inflammatory infiltration
20	34	F	B	orbit	Unsatisfactory for diagnosis	Chronic inflammation
21	90	M	W	orbit	Atypical cellular proliferation suspicious for lymphoma.	Diffuse large B-cell lymphoma
22	65	M	B	orbit	Lymphoma, not otherwise specified	Large B-cell lymphoma
23	32	F	B	orbit	Atypical lymphoid proliferation, favor benign	Reactive lymphocytic proliferation with germinal center formation

Table 1: 23 cases including 11 cases with unsatisfactory FNA diagnosis underwent subsequent surgical excision/incision.

Discussion and Conclusion

Orbital tumor diagnosis has long been a challenging task for ophthalmologists. A surgical excisional or incisional biopsy carries significant risks and complications. FNA has been a reliable approach in the diagnosis of lesions from multiple organs including lung, thyroid gland, lymph nodes, pancreas, and salivary gland since the 1960s. In 1975, Dr. Schyberg first introduced FNA to orbital tumor diagnosis [1]. Although the discrepancy about the application of FNA to orbital tumors still exists [2-4], a growing number of institutions are showing interest in applying this technique as an alternative to surgical biopsy [5-10].

Our current retrospective study analyzed data collected from 61 patients (62 cases) who underwent FNA in our institution between the years 1990 and 2016. Of the 62 cases, 15 cases were unsatisfactory/non-diagnostic, so the positive identification rate was (47/62, 75.8%). More than half of the cases were malignant neoplasms, the majority of which were non-Hodgkin's Lymphomas. Flow cytometry has been proven to be a rapid and virtually diagnostic method for non-Hodgkin's lymphoma [11]. Our study shows FNA provides adequate materials for flow cytometry to make a definitive diagnosis in (19/29, 65.5%) NHL cases.

We compared the FNA results with surgical biopsy diagnosis in 12 cases with adequate materials. The diagnostic accuracy was 11/12, or 91.7%, which was comparable with other reports [6-10]. On the benign end of the spectrum, a reactive lymphoid proliferation specimen showed a heterogenous population of small to medium-sized

lymphocytes on both cytology and histology, with germinal center formation seen on histology and a background of lympho-glandular bodies on cytology (Figure 4). Both cytology and surgical specimens for a case of large B-cell lymphoma showed an infiltrate of large, atypical lymphocytes, with prominent nucleoli and irregular nuclear contours (Figure 5). An FNA of an orbital mass in a patient with a prior history of plasma cell neoplasm showed scattered plasma cells; surgical biopsy confirmed the diagnosis of plasmacytoma, showing sheets of plasma cells which were lambda light chain restricted by in situ hybridization (Figure 6). Concordance was also seen in the diagnosis of non-hematopoietic neoplasms. A poorly differentiated carcinoma showed nests of tumor cells on histology and tight clusters of tumor cells on cytology; in both specimens the malignant cells had a basaloid appearance, with high nuclear: cytoplasmic ratio and dense, hyperchromatic nuclear chromatin (Figure 7).

Although surgical biopsy is considered the "gold standard" in diagnosing orbit tumors, it also carries significant risks and complications, as well as time and labor cost. Thus, FNA provides ophthalmologists and pathologists an ideal diagnostic approach for unresectable or high-risk orbital tumors.

Overall, this study demonstrates FNA of the orbit is a relatively non-invasive and cost-effective method in diagnosing orbital tumors; it is especially valuable in identifying hematolymphoid malignancy in the orbit, such as non-Hodgkin's lymphoma.

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