The following images are representative of a vitreous fine needle aspiration. The patient is a 57-year-old male who presented with a 6 month history of decreased vision.

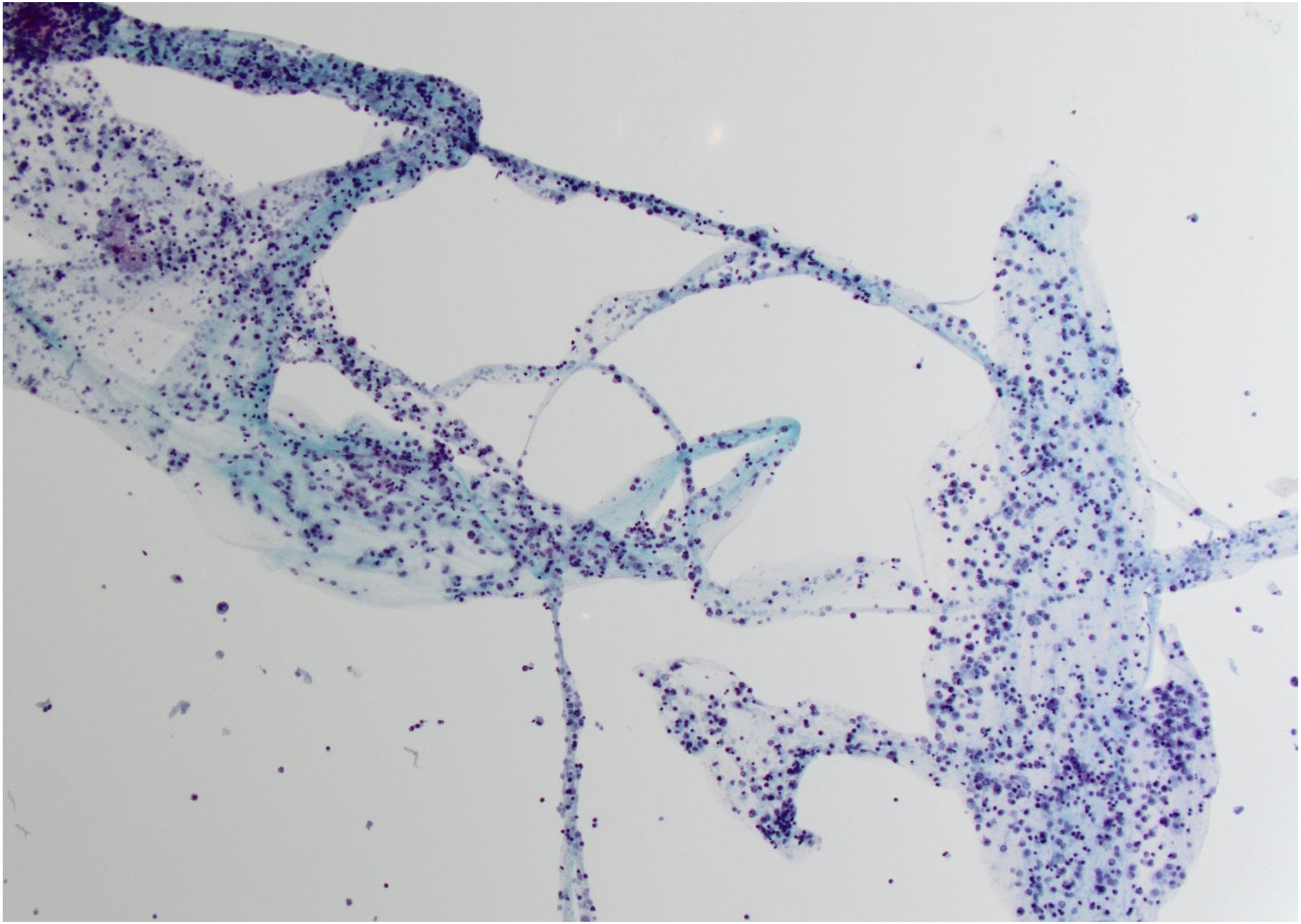

Image 1. ThinPrep – Pap stained x10

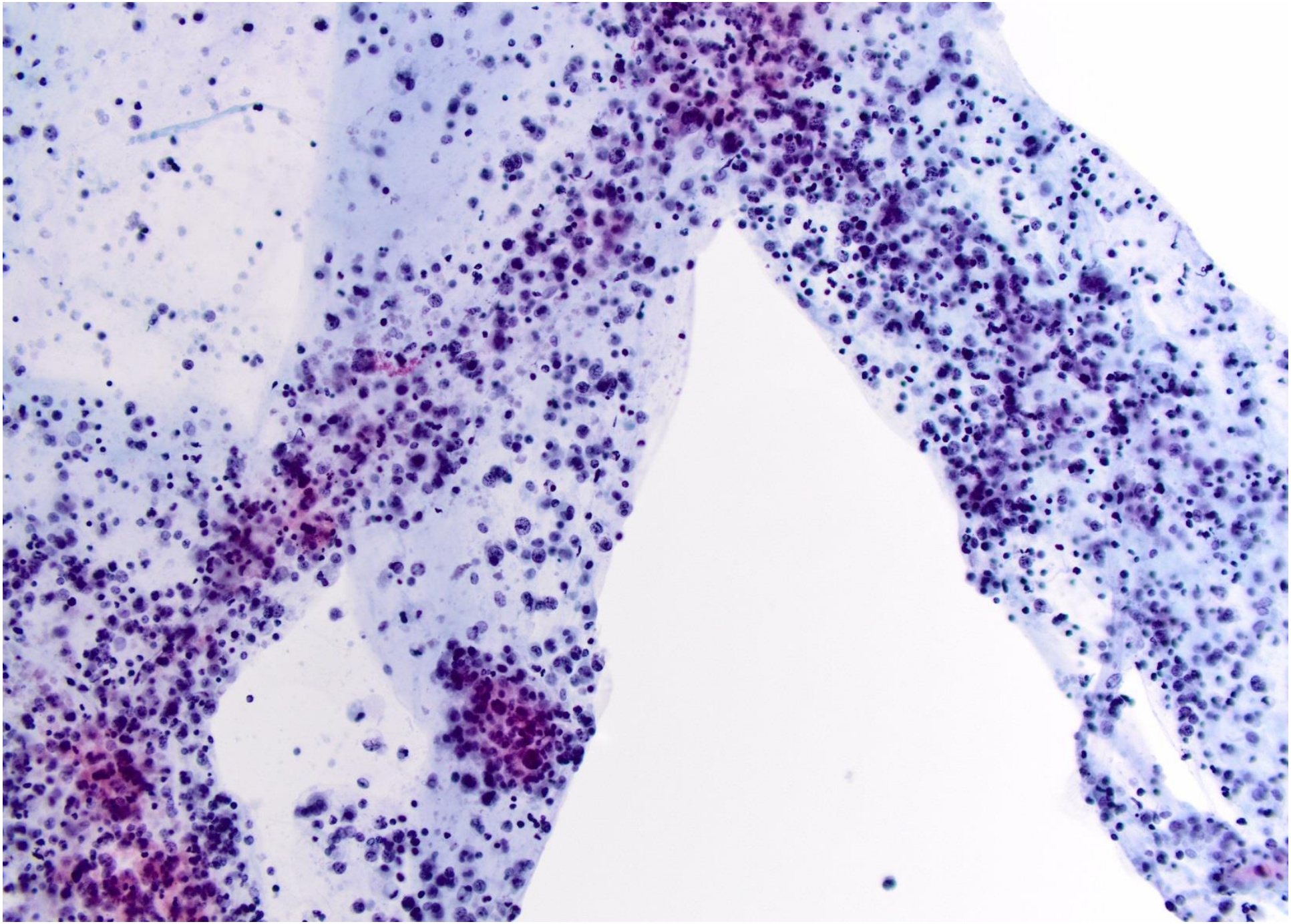

Image 2. ThinPrep – Pap stained x20

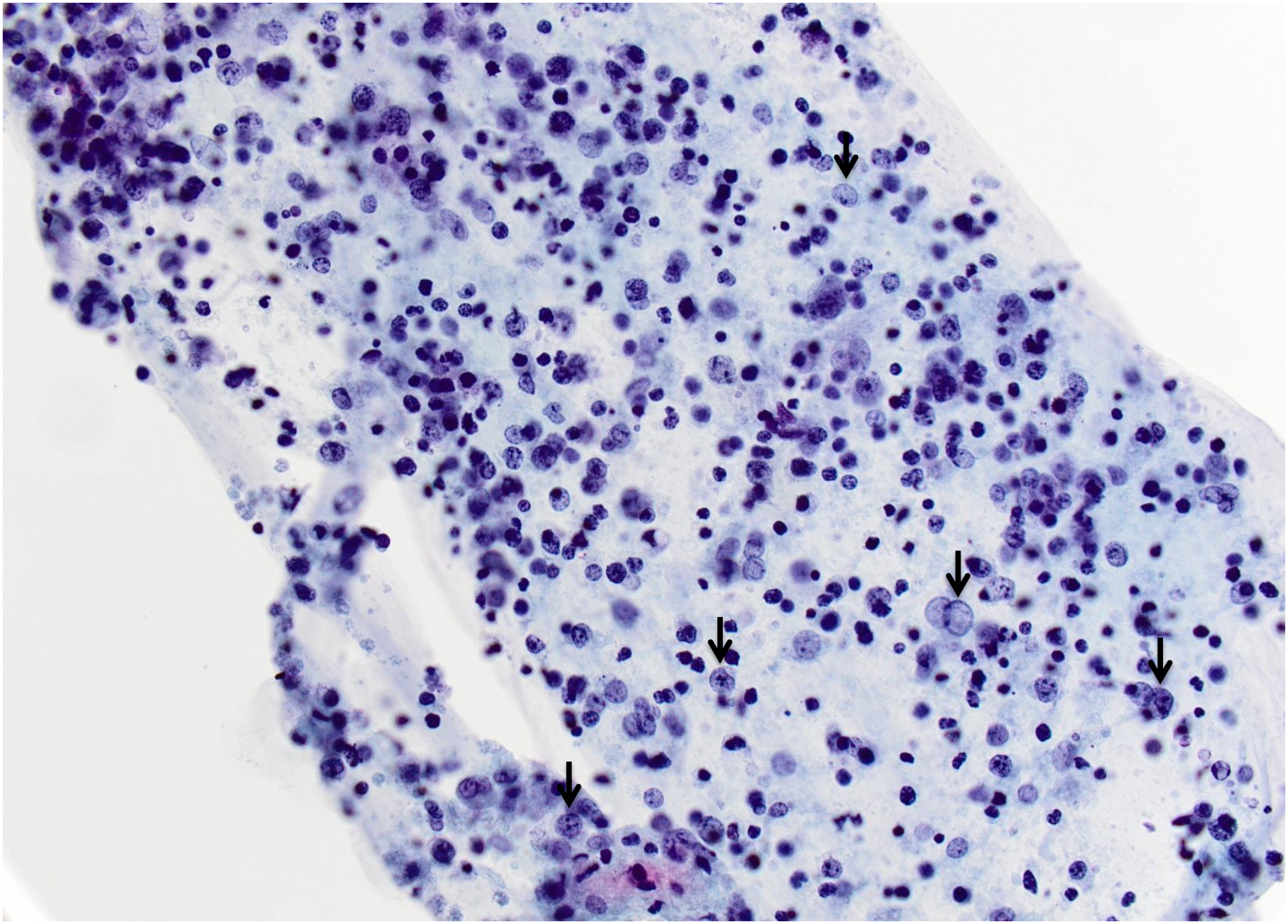

Image 3. ThinPrep – Pap stained x40

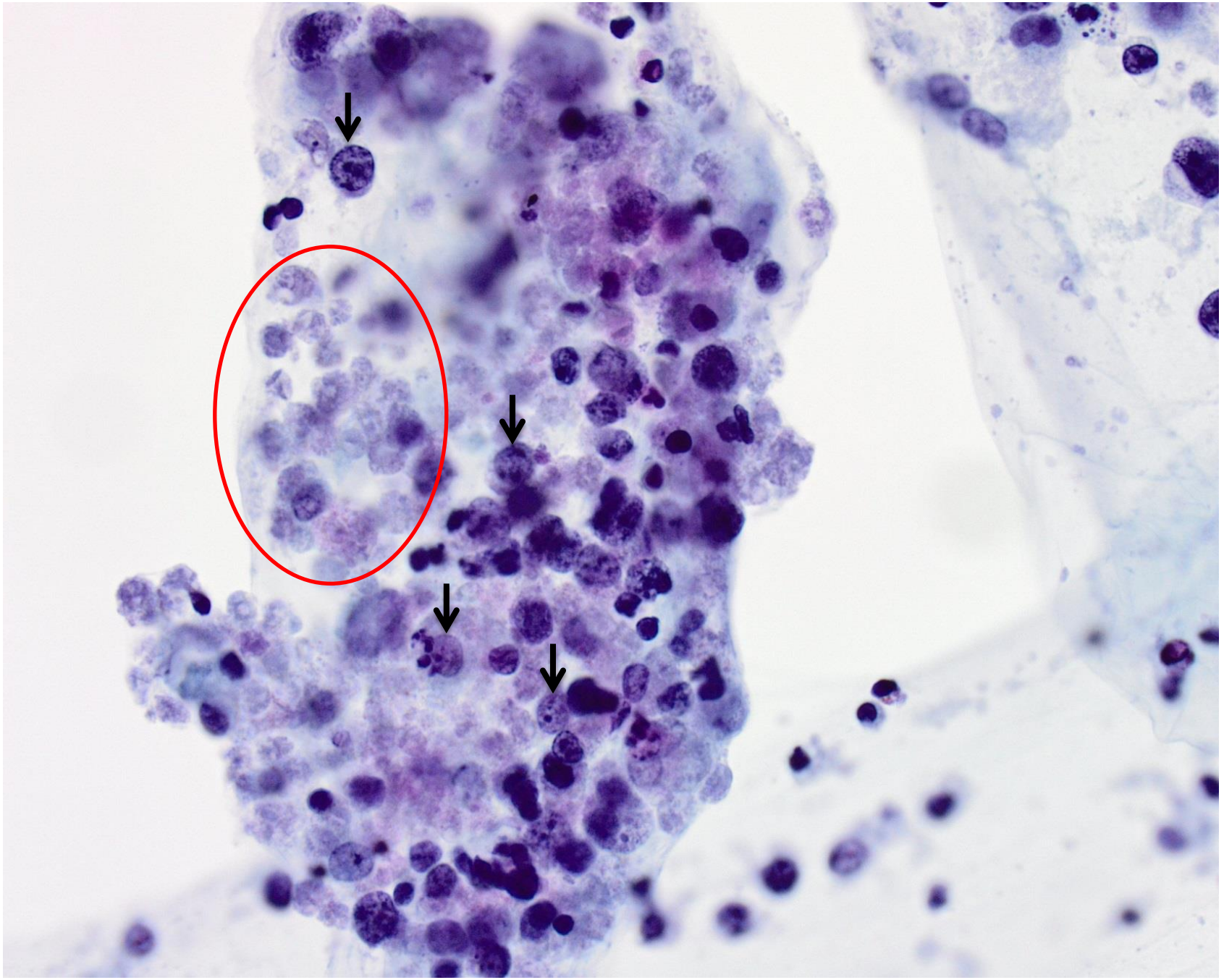

Image 4. ThinPrep – Pap stained x60

Question 1:

The MOST LIEKLY diagnosis is:

1) Uveal melanoma
2) Vitreoretinal lymphoma
3) Intraocular retinoblastoma
4) Granulomatous vitreitis

Question 2:

Which of the following ancillary studies is MOST LIKELY to be positive in this specimen

1) Immunoglobulin heavy chain gene rearrangement
2) Retinoblastoma 1 (RB1) gene deletion
3) Gamma chain gene rearrangement
4) PCR study for V600E mutation

Question 3:

Which of the following statements is CORRECT regarding intraocular fine needle aspiration?

1) It plays a major role in the diagnosis of retinoblastoma
2) Is required for the diagnosis of all uveal masses
3) It requires minimal coordination between the surgeon and laboratory
4) It may be associated with subretinal or vitreous hemorrhage

Description:

Image 1: Cellular specimen consistent of discohesive population of large atypical cells admixed with small mature lymphocytes
Image 2: Higher power view highlighting the discohesive and lymphoid nature of the atypical cells. The background shows small mature lymphocytes and scant necrosis.
Image 3: Large atypical lymphoid cells with irregular nuclear membrane, stippled chromatin and prominent nucleoli (black arrows). Background of small lymphocytes and necrotic debris.
Image 4: Large pleomorphic atypical lymphoid cells with prominent nucleoli (black arrows). Apoptosis and necrotic debris are present in the background (red oval).

Discussion:

Intraocular lymphoma encompasses a heterogeneous group of lymphoid neoplasms, the majority of which are of B-cell linage. They are generally classified based upon site of involvement and whether the lymphoma is primary or secondary. Intraocular lymphoma is therefore subdivided into: primary vitreoretinal lymphoma (PVRL), primary uveal lymphoma, and secondary intraocular lymphoma (in the setting of systemic lymphoma) [1].

Primary uveal lymphoma is generally a unilateral, low-grade B-cell lymphoma with an indolent, benign course. Extranodal marginal zone lymphoma [mucosa-associated lymphoid tissue (MALT) type] is the most common subtype [2]. The lymphoid nature of vitreous specimens involved by uveal lymphoma is readily apparent; however, differentiating uveal lymphoma from reactive processes may present a significant challenge to the cytopathologist. This can be resolved with ancillary studies such as flowcytometry and molecular testing [3].

PVRL is usually a bilateral, high-grade lymphoma with an aggressive, rapid course. Over 95% are diffuse large B cell lymphomas (DLBCL) and fewer than 5% are T cell lymphomas. The malignant nature of specimens involved by PVRL is usually clear; however, ancillary studies maybe required to confirm the cytomorphologic diagnosis and exclude other malignancies. These studies may include: immunohistochemistry to confirm lymphoid linage and evaluate clonality in B-cell neoplasms (CD20, kappa and lambda light chain expression), flow cytometry and molecular testing (PCR performed on fresh or fixed tissue).

Uveal Melanoma is the most common intraocular malignancy in the developed world. Similar to cutaneous melanoma, individuals with light skin/light eye color and increased sun exposure are at an increased risk. Specimens involved by uveal melanoma are usually cellular with individual cells demonstrating a spindled or epithelioid morphology [4]. The epithelioid variant tend to demonstrate classic features of malignancy: nuclear pleomorphism, nuclear enlargement and irregularity and prominent nucleoli. In comparison, the spindled variant (identified at least focally in majority of cases) demonstrate bland fusiform nuclei with fine chromatin and inconspicuous nucleoli. This may be misleading for the novice practitioner. Cytoplasmic melanin is frequently identified.

Intraocular retinoblastoma is the most common intraocular malignancy in childhood and most frequent intraocular malignancy worldwide. The diagnosis is usually based on clinical examination and imaging studies with a limited role for fine needle aspiration cytology. If sampled, retinoblastoma characteristically consists of uniform, small, round tumor cells arranged singly and in clusters with nuclear molding. Individual neoplastic cells demonstrate a uniformly distributed nuclear chromatin and inconspicuous nucleoli [5].

Granulomatous vitreitis may occur secondary to fungal infections (Candidiasis, histoplasmosis or Cryptococcal Chorioretinitis) and sarcoidosis. They are characterized by tight clusters of epithelioid histiocytes in a background of chronic inflammatory cells.

Intraocular fine needle aspiration is generally indicated when clinical examination and ancillary testing fails to establish an accurate diagnosis. In fact, it is considered contraindicated in uveal masses with well-established diagnosis. Although rare, complications associated with this procedure include hemorrhage (subretinal and vitreous), retinal detachment, endophthalmitis and needle track seeding (in malignant conditions). The risk of complications generally decreases with small diameter of the aspiration needle [4]. Due to the invasive nature of the procedure and limited amount of tissue obtained, it is preferable for the surgeon to coordinate with the laboratory prior to obtaining the specimen to allow timely transportation of the specimen (preferably fresh specimen delivered in hand, immediately following the procedure) and adequate specimen triage for ancillary studies (flow cytometry and gene rearrangement studies in cases of suspected lymphoma and immunohistochemistry is cases of suspected melanoma or suspected metastatic malignancy of unknown primary).

[1] Aronow M.E. (2018) Intraocular Lymphoma. In: Chhablani J., Majumder P., Arevalo J. (eds) Retinal and Choroidal Imaging in Systemic Diseases. Springer, Singapore.
[2] Sagoo et al. Primary intraocular lymphoma. *Surv Ophthalmol*. 2014 Sep-Oct;59(5):503-16.
[3] Biscotti Charles (2015). Eye In: Comprehensive Cytopathology, 17, 353-362. Elsevier, Philadelphia.
[4] Biscotti CV, Singh AD (eds): FNA Cytology of Ophthalmic Tumors. Monogr Clin Cytol. Basel, Karger 2012, vol 21, pp 44–54
[5] Chawla et al. Intraocular fine needle aspiration cytology as a diagnostic modality for retinoblastoma. *Int J Ophthalmol*. 2016 Aug 18;9(8):1233-5

* Case and discussion Contributed by:
Omar Al-Nourhji, MD, FRCPC
Assistant Professor
Department of laboratory Medicine and pathology
University of Saskatchewan