Orbit and Ocular Adnexa

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Introduction

The orbital area contains a variety of anatomical structures including the eyelids, tarsal conjunctiva, caruncle, lacrimal gland, lacrimal drainage system, skin, skin adnexa, and soft tissues. It is surrounded by bone and cartilaginous structures and is highly vascularized and interspersed by the cranial nerves. This complex of neighboring, highly specialized tissues results in a large spectrum of inflammatory, benign, and malignant conditions. An extensive blood supply by the richly vascularized orbital area explains the occurrence of metastases from various organs, commonly from breast and lung neoplasms in adults and neuroblastoma in children. Fine-needle aspiration (FNA), by its simplicity and accuracy, can serve as an important diagnostic tool, solving some of the various clinical dilemmas in this complex anatomic area.

The role of FNA is to confirm the existence of primary, recurrent, or metastatic malignancies and to distinguish inflammatory from neoplastic lesions. FNA is particularly useful to assess nonresectable orbital lesions, such as hematolymphoid neoplasms and metastatic deposits, avoiding unnecessary surgery [1, 2]. In addition, FNA will provide crucial information in cases where surgery is being considered, e.g., before a major surgical or oncologic procedure is undertaken. Moreover, FNA may serve as the preferable technique to access and diagnose intraocular tumors and noncharacteristic clinical settings [3].

The most common malignant lesion in the orbit is orbital lymphoma. Valuable diagnostic modalities in such instances include aspiration cytology, in addition to ultrasound, computed tomography (CT) (see Fig. 18.1), and magnetic resonance imaging (MRI). Diagnosis based on routinely stained smears alone may be difficult. Combination of smears with ancillary techniques such as immunocytochemistry, flow cytometry, and molecular genetic techniques provide a reliable diagnosis and accurate typing in most cases [4–6].

Neoplasms of the lacrimal gland comprise a spectrum of lesions similar to primary major salivary gland neoplasms [7]. Roughly 50% of lacrimal gland tumors are of epithelial origin, 50% of epithelial tumors are benign pleomorphic adenoma, and 50% of malignant tumors are adenoid cystic carcinoma.

Primary or secondary sinonasal tract malignancies that first present as orbital lesions are rare, with a broad range of cytological findings in FNA smears. Specific features most often allow an accurate diagnosis in tumors such as in carcinoma similar to transitional and squamous cell carcinoma, carcinoma with specific differentiation, sarcoma, or melanoma [8].

There are a few case reports and review series [9–11] of orbital metastasis. The most frequently reported primaries are breast, lung, melanoma, and prostate cancer, but even metastasis from the liver, ovary, sacrococcygeal chordoma, thymic carcinoma, and skin has been reported. As indicated in a review of 80 patients with a mean age of 60 years [11], orbital metastases occurred usually in the late stages of a known malignancy. However, in some cases orbital metastasis may be the initial presentation of malignant disease. Char et al. [9] reported that metastasis was the first presentation of an unknown malignancy in 35% of the cases, whereas Valenzuela et al. [11] found that 15% of orbital metastasis had no known primary tumor.

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H. A. Domanski (ed.), *Atlas of Fine Needle Aspiration Cytology*, https://doi.org/10.1007/978-3-319-76980-6_18

Fig. 18.1 CT-guided FNA of a deep orbital tumor by a 23-gauge needle inserted through the larger 20-gauge needle in order to reach a small lesion and to avoid contamination from surrounding tissues. (**a**) Examination of the diagnostic CT by radiologist and ophthalmologist before FNA. (**b**) Insertion of the larger needle by the radiologist. The larger needle position (**c**) should be controlled (**d**) before aspiration

Sampling Technique

Orbital and intraocular FNA was initially accepted with enthusiasm [12], but some authors later underlined the possibility of complications and argued against this technique [13]. Significant series of orbital and periorbital lesions with cytological evaluation began to appear about 60 years ago [14–20]. In the Institut Curie in Paris, FNA examination of orbital tumors was introduced in 1970 [21].

The technique of cytological sampling is not more complicated than in other settings, but an experienced operator improves the results of the procedure. Palpable tumors in the orbit and palpebra may be assessed by palpation-guided FNA with 23–27-gauge needles (see Fig. 18.2). Gentle aspiration should be applied to obtain a representative material, but in many cases more vigorous aspiration is not recommended to avoid hemorrhagic smears. Many patients describe the procedure as "unpleasant," but they do not complain of pain, and anesthesia is not necessary in the case of most aspirations. In addition, injection of local anesthetic is not advocated because it usually leads to distortion of orbital and tumoral tissues. After the sampling is finished, a moderately forceful pressure with bandages is recommended to avoid hematoma. The rich vasculature of the orbit and the rigid bone structures around it tend to lead to hematomas.

FNA of nonpalpable tumors is performed under ultrasound guidance. In children and uncooperative patients, or in cases of intraocular tumor, general anesthesia is necessary. A 27-gauge butterfly needle is used and suction is applied (see Fig. 18.2). One drop of sample is smeared, and the remaining material is collected in ethylenediaminetetraacetic acid (EDTA) for molecular purposes. Cytological sampling of orbital lesions should be performed by either a cytopathologist or an ophthalmologist, occasionally by a radiologist, but the cooperation of both during the sampling procedure is preferred to secure representative samples. As in many other settings, on-site evaluation of aspirated material prevents a high percentage of nondiagnostic smears.

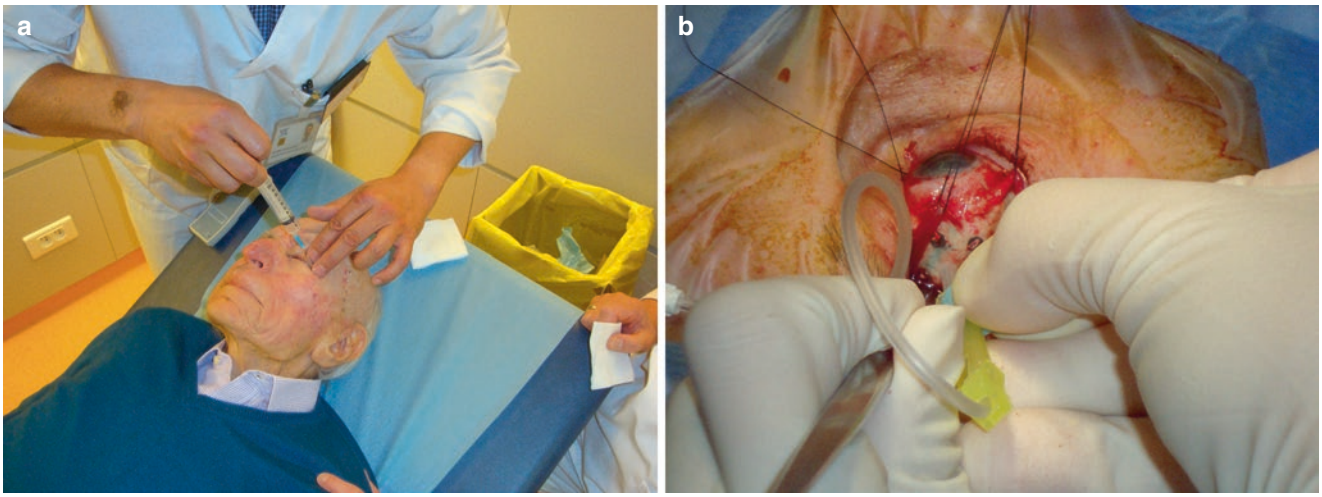

Fig. 18.2 (**a**) Palpation-guided aspiration of the lacrimal gland. (**b**) FNA of an intraocular tumor

Diagnostic Accuracy and Complications

In a series of 286 aspirates of palpable orbital and eyelid tumors reported from the Curie Institute, FNA was a highly accurate diagnostic procedure with a concordant diagnosis of malignancy and tumor type achieved in 87% of cases. False-positive diagnoses were made in 1.6% and false-negative diagnoses in 1.8% cases [20]. Sensitivity of orbital FNA ranging from 75% to 99% in other larger series has been reported [14, 17, 22–24].

Complications of FNA of intraorbital lesions are minor and usually consist of hematoma in surrounding tissues. More severe potential complications may be puncture of the eyeball, vitreous or subretinal hemorrhage, and retinal detachment, but such complications have never occurred in this author's institution where more than 40 years of experience with FNA of orbital, paraorbital, and viral lesions has been accumulated. To minimize this hazard, Liu [25] recommended that the needle should be inserted in the quadrants of the orbit only and not directly above or below the globe. Other reported complications constitute vitreous hemorrhage, transient visual loss, and ocular motility disturbance.

Tumor Classification A classification according to the anatomical structures of the orbital region may be useful from a practical point of view. We systematize the tumors as palpebral, intraorbital, or intraocular.

Palpebral Tumors

Palpebral tumors correspond to skin tumors described in Chap. 14. The most common malignant tumor of the eyelid is basal cell carcinoma, and it is a relatively frequent target for FNA [26, 27]. The diagnosis is obvious if smears from a superficial eyelid tumor display cytological features such as well-formed and often cohesive sheets and nests of relatively uniform basaloid cells in palisades (see Fig. 18.3). Larger, dyscohesive cells, differentiation toward squamous epithelia, and keratinization favor primary squamous cell carcinoma, the second most common malignancy of the eyelid (see Fig. 18.4). Palpebral eccrine spiradenoma (see Fig. 18.5), pilomatrixoma (see Fig. 18.6), and other skin appendix tumors comprise important differentials to basal cell carcinoma and squamous cell carcinoma. Classical and diagnostic features of pilomatrixoma are its three components: basaloid cells, ghost cells with an admixture of amorphous keratin deposits, and multinucleated giant cells. Sebaceous carcinoma is the third most common eyelid malignancy and most commonly arises from the Meibomian glands.

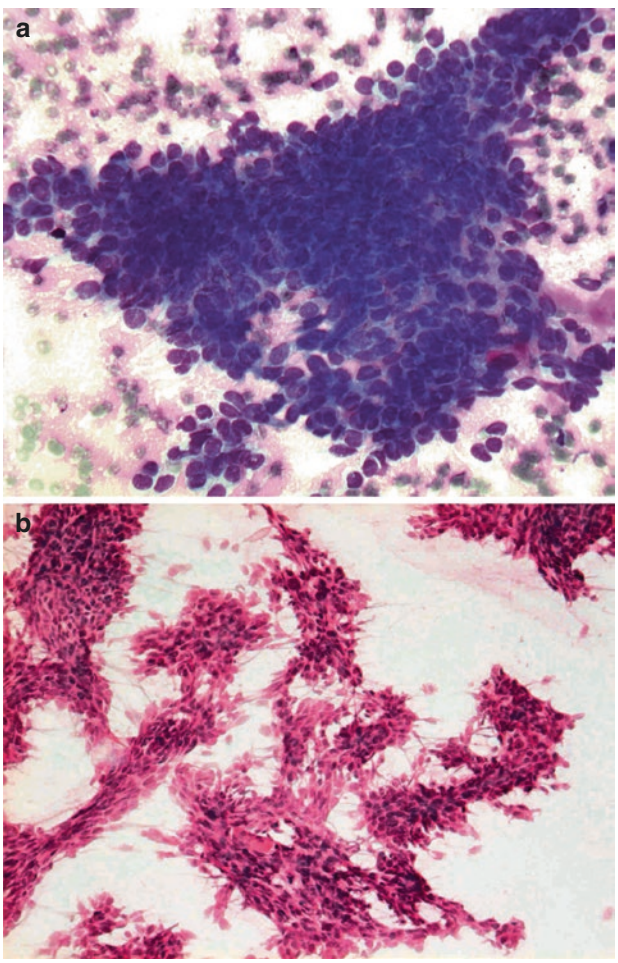

Fig. 18.3 Cutaneous basal cell carcinoma in palpebra. (**a**, **b**) Cohesive sheets of uniform or slightly pleomorphic basaloid cells with occasional nuclear palisading in the periphery of the tumor sheets (MGG; H&E)

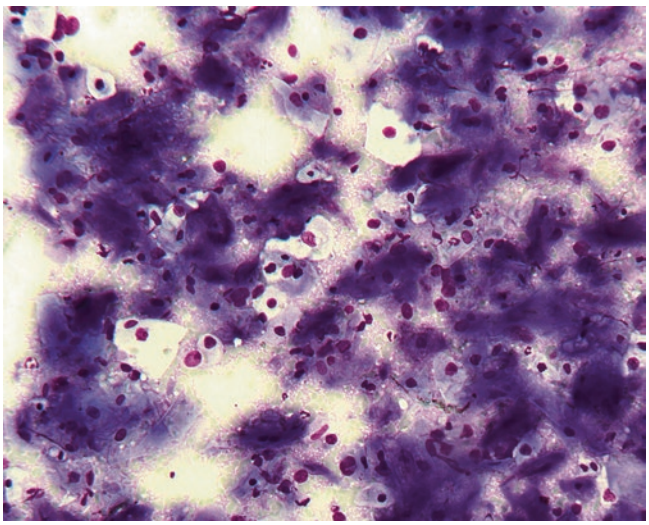

Fig. 18.4 Palpebral squamous cell carcinoma. Dispersed slightly atypical tumor cells with apparent squamous differentiation and some cells with enlarged and hyperchromatic nuclei (MGG)

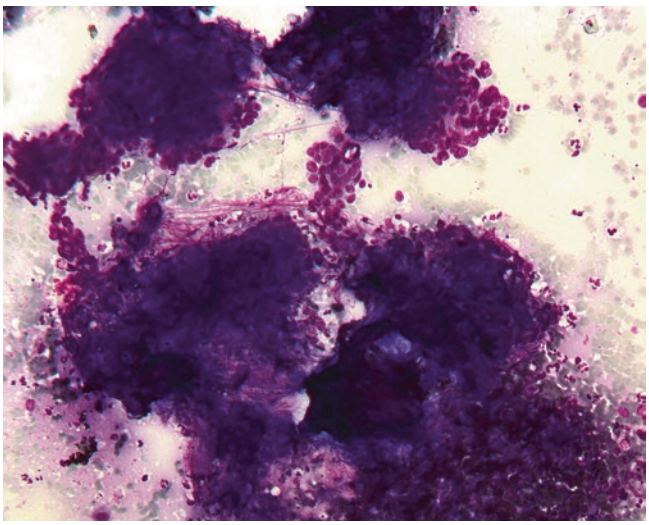

Fig. 18.6 Pilomatrixoma. Squamous, partially calcified deposits and small clusters of the basaloid cells in the background of the smears (MGG)

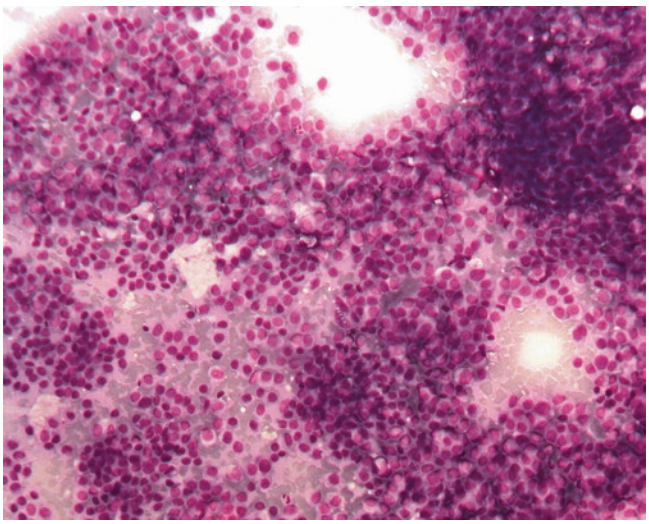

Fig. 18.5 Eccrine spiradenoma. Smears contain dispersed roundish and oval cells with eccentrically placed nuclei (MGG)

Orbital Tumors

Reactive and Inflammatory Conditions

Granulomatous lesions, including Wegener's granulomatosis, sarcoidosis, chalazion, xanthogranuloma, and aspergillosis [28], may be encountered in the orbit and the orbital adnexa. Wegener's granulomatosis may be identified as a necrotizing granulomatous inflammation, whereas sarcoidosis and chalazions are identified as non-necrotizing granulomatous inflammations. Other inflammatory lesions include pseudotumors [29], histiocytosis X (see Fig. 18.7), and rare in this location Rosai-Dorfman disease [30, 31]. Benign cystic lesions in the orbit mainly include epidermal inclusion cysts, mucoceles, and dermoid cysts. Anucleate and occasional nucleate squames represent microscopic findings in smears from epidermal inclusion cysts and admixture of debris in dermoid cysts.

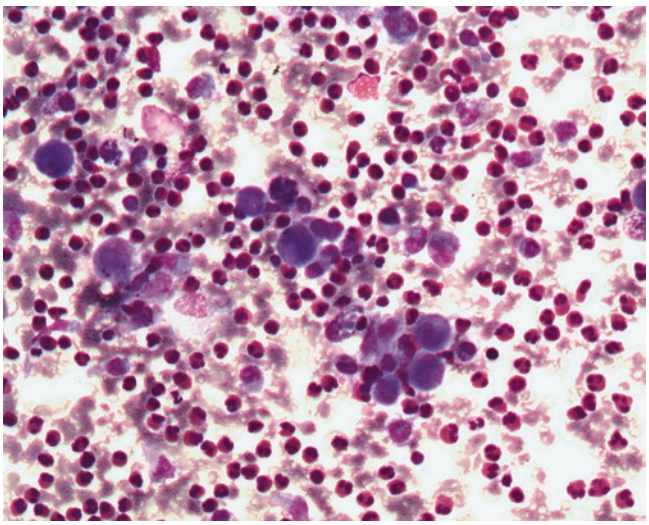

Fig. 18.7 (**a**) Histiocytosis X (Langerhans cell histiocytosis). Langerhans histiocytes with admixture of numerous eosinophilic leukocytes (MGG)

Benign Neoplasm

Meningioma

Meningothelial neoplasms in smears can be readily identified due to the presence of cohesive clusters with a whorling pattern of relatively uniform cells with bland, ovoid nuclei and moderate to abundant cytoplasm. Intranuclear pseudoinclusions and psammoma bodies are often visible in smears (see Fig. 18.8) [32–34].

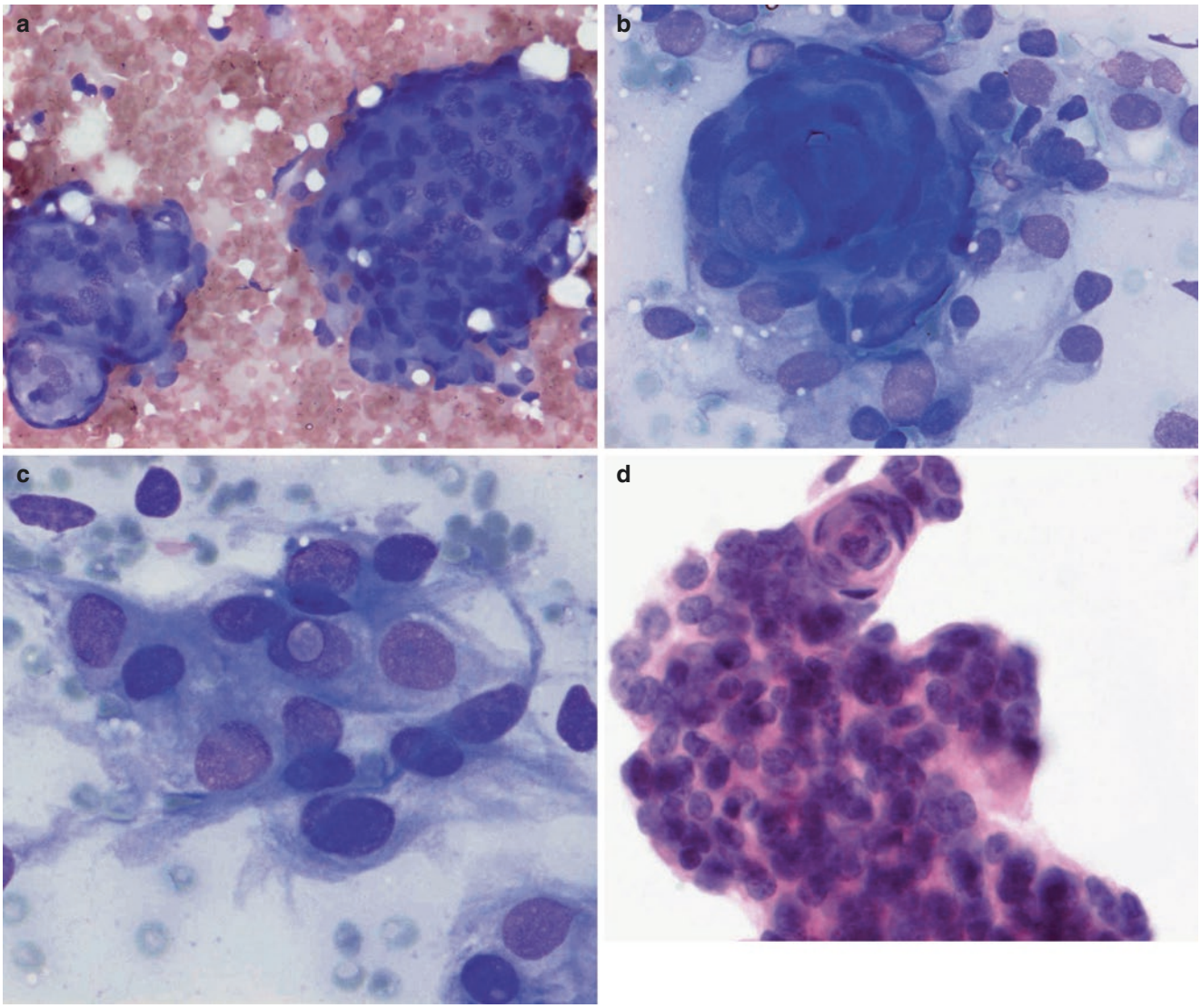

Fig. 18.8 Meningioma. (**a** and **b**) Aspirated cells arranged in syncytial sheets and clusters with a typical whorling pattern. (**c**) Note intranuclear pseudoinclusions (MGG). (**d**) In liquid-based specimens, the whirling pattern in cell clusters is appreciated (ThinPrep; H&E)

Pleomorphic Adenoma

The most common tumor of the lacrimal gland is pleomorphic adenoma [35]. These adenomas are generally well circumscribed on imaging studies. They may indent the sclera or cause bony remodeling but are not invasive in bone. These lesions should be diagnosed by FNA, as more invasive incisions may violate the pseudocapsule and lead to contamination and implantation of tumor cells in adjacent tissues. Pleomorphic adenoma typically harbor both epithelial and mesenchymal components in smears. The epithelial cells may be arranged individually, in sheets, or in clusters. The mesenchymal component consists of a chondromyxoid matrix and associated spindled (myoepithelial) cells [36] (see Fig. 18.9).

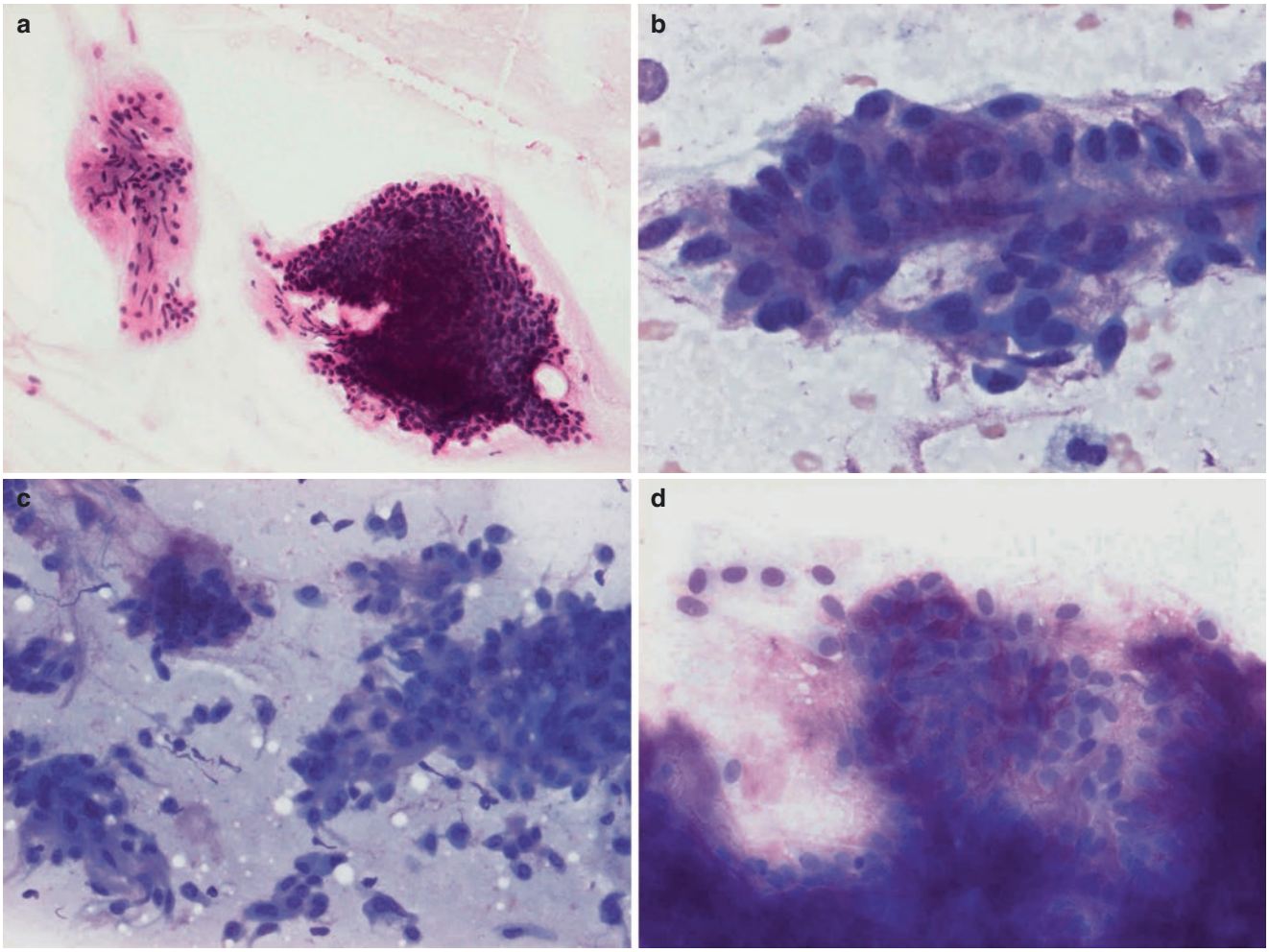

Fig. 18.9 Pleomorphic adenoma. (**a**–**d**) Fragments of mesenchymal stroma and clusters or small dyscohesive fragments of plasmacytoid myoepithelial cells embedded in myxoid-chondromatous, metachromatic matrix (H&E; MGG)

Hemangioma and Other Benign Mesenchymal Neoplasms

Hemangioma is more of a clinical and radiological rather than a cytological diagnosis. Mesenchymal neoplasm (e.g., schwannoma, lipoma, pleomorphic lipoma) may also involve the orbit as the primary setting [37]. Cytomorphology is similar to those described at other anatomical locations.

Malignant Tumors of Lacrimal Structures

Patients with lacrimal gland malignancy frequently present with swelling of the eyelid, diplopia, and pain. CT shows a soft tissue lesion centered on the lateral orbital margin. Morphologically, malignant tumors arising in the lacrimal gland are similar to those of their salivary gland counterparts. The most common malignancies are adenoid cystic carcinoma, carcinoma ex pleomorphic adenoma, and salivary duct carcinoma.

Adenoid Cystic Carcinoma

FNA smears show numerous basaloid cells with sparse cytoplasm. The cells usually form characteristic "rosettes" by growing around extracellular globules of homogenous basement membrane material (see Fig. 18.10). The stroma is characteristic and shows fingerlike and tubular structures, which are pathognomonic [38].

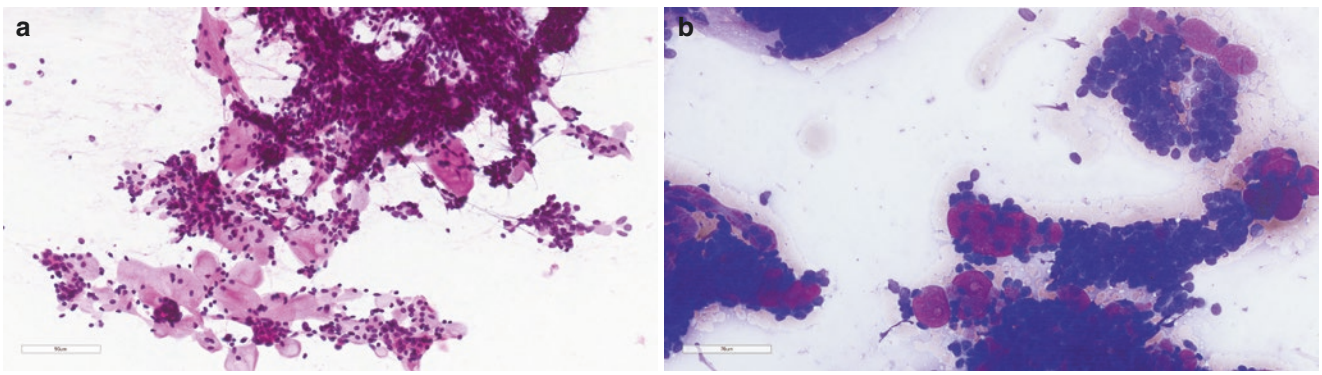

Fig. 18.10 (**a, b**) Adenoid cystic carcinoma. Smears with small basaloid cells surrounding globules of homogenous basement membrane material (H&E and MGG)

Other Salivary-Type Carcinomas

Carcinoma ex pleomorphic adenoma, salivary duct carcinoma, and adenocarcinoma not otherwise specified (NOS) may arise in the lacrimal glands [39]. Carcinoma ex pleomorphic adenoma (salivary duct type, mucoepidermoid carcinoma) and primary salivary duct carcinoma show cytological characteristics previously reported (see Fig. 18.11) [40]. Carcinoma NOS may be morphologically nonspecific. Primary mucinous adenocarcinoma may also arise in the lacrimal gland (see Fig. 18.12).

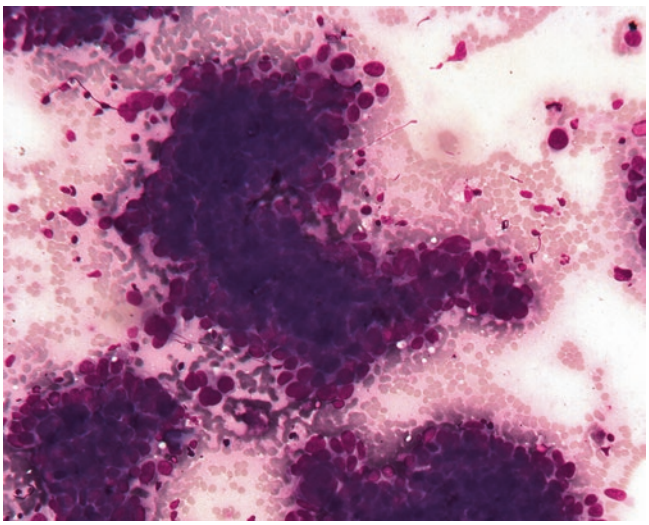

Fig. 18.11 Carcinoma ex pleomorphic adenoma. Salivary duct carcinoma arising in the lacrimal gland pleomorphic adenoma. Tumor cells with enlarged hyperchromatic, pleomorphic nuclei indicate malignancy (MGG)

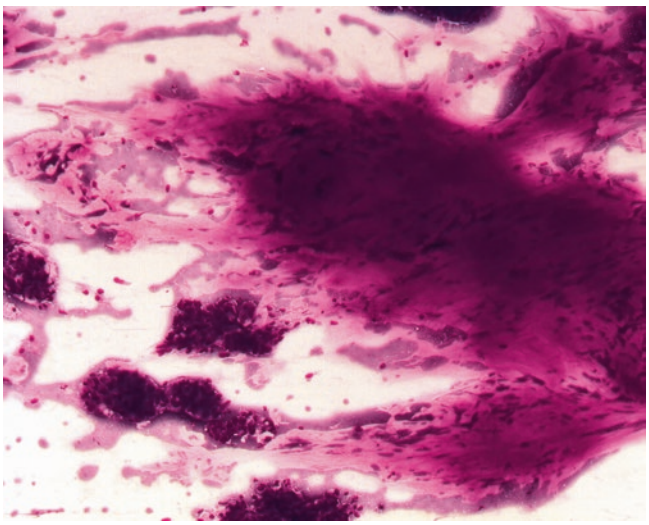

Fig. 18.12 Primary mucinous carcinoma of the lacrimal gland. Loosely cohesive clusters of moderately pleomorphic tumor cell with abundant vacuolated cytoplasm and abundant mucinous material in the background (MGG)

Primary Malignant Neoplasms of the Lacrimal Sac

Primary lacrimal sac tumors are uncommon, among them squamous cell carcinoma is the most common. FNA presents findings similar to those of smears from squamous cell carcinoma in other locations. Smears most often contain cohesive groups and clusters or dispersed moderately pleomorphic tumor cells with irregular nuclei. Necrotic cell fragments, cell debris, and keratin masses may be identified in the background.

Orbital Malignant Tumors Outside Lacrimal Structures

A large spectrum of tumors including olfactory neuroblastoma (see Fig. 18.13), different types of sarcomas, and metastases occur in this location [2, 41]. FNA of many of them yields diagnostic material and in some entities, such as rhabdomyosarcoma (see Fig. 18.14) and other small cell malignancies, makes cellular material accessible for immunocytochemistry and molecular diagnostics. Sinonasal tract malignancies may occasionally present as orbital tumors (see Fig. 18.15).

Orbital metastases usually reflect advanced malignant disease (see Figs. 18.15, 18.16, and 18.17) [42–45]. Breast, lung, and prostatic adenocarcinomas are the most common primary sites.

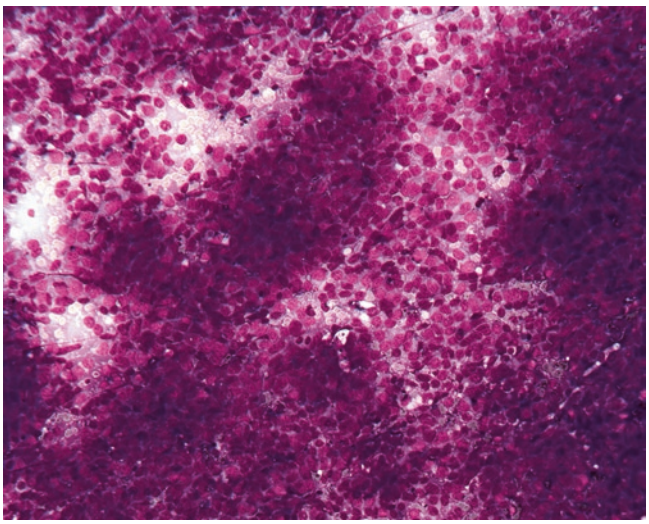

Fig. 18.13 Esthesioneuroblastoma in the orbit. Dispersed, moderately pleomorphic blastema-like cells (MGG)

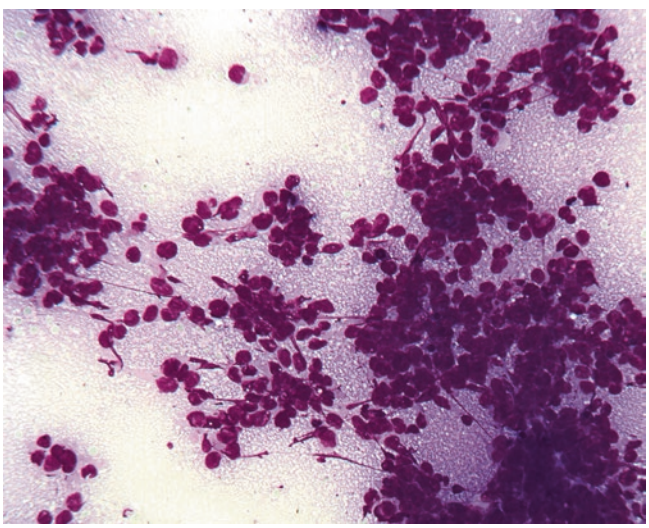

Fig. 18.14 Rhabdomyosarcoma. Loosely cohesive clusters and dispersed single cells of poorly differentiated embryonal rhabdomyosarcoma showing moderately pleomorphic cells with hyperchromatic nuclei and poorly preserved cytoplasm (MGG)

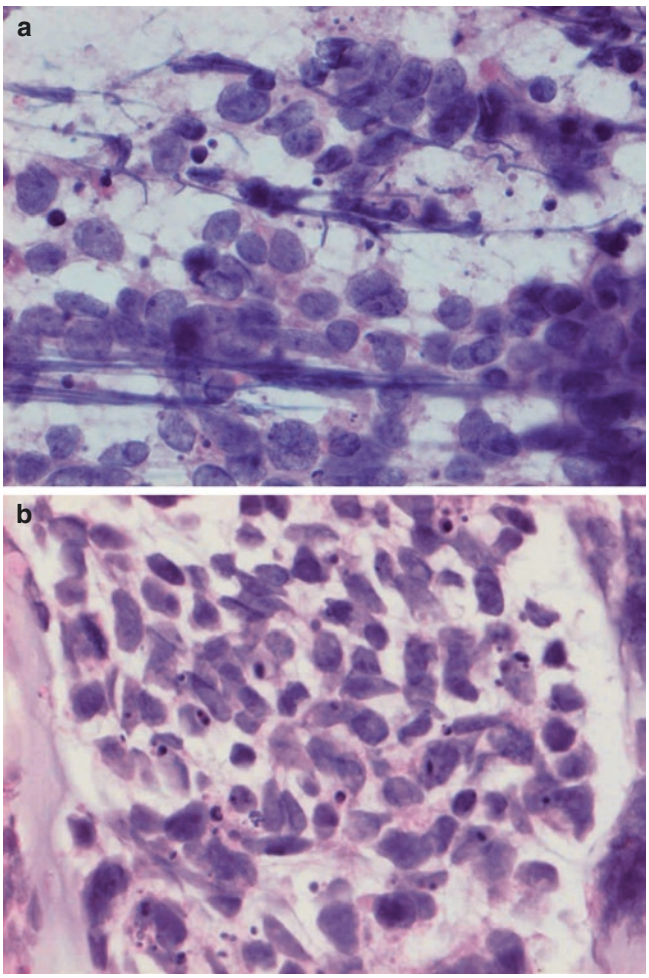

Fig. 18.15 Small cell neuroendocrine carcinoma of the maxillary sinus. (**a**) Small groups of dyscohesive cells and dispersed cells with scant cytoplasm, irregular nuclei with occasional molding, and crush artifacts. (**b**) Cell block section showing morphology similar to FNA smears (H&E)

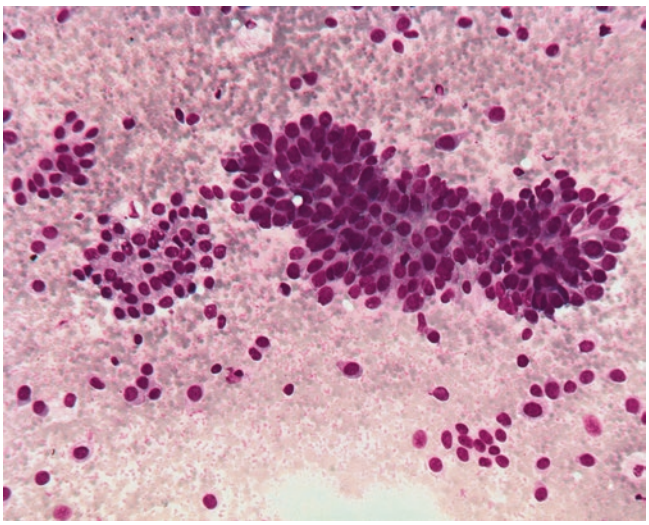

Fig. 18.17 Orbital metastasis from transitional cell carcinoma of the bladder. Dyscohesive clusters and some dispersed tumor cells without any specific signs of differentiation. Without clinical history of previous urinary tract carcinoma, it could be difficult to diagnose the primary (MGG)

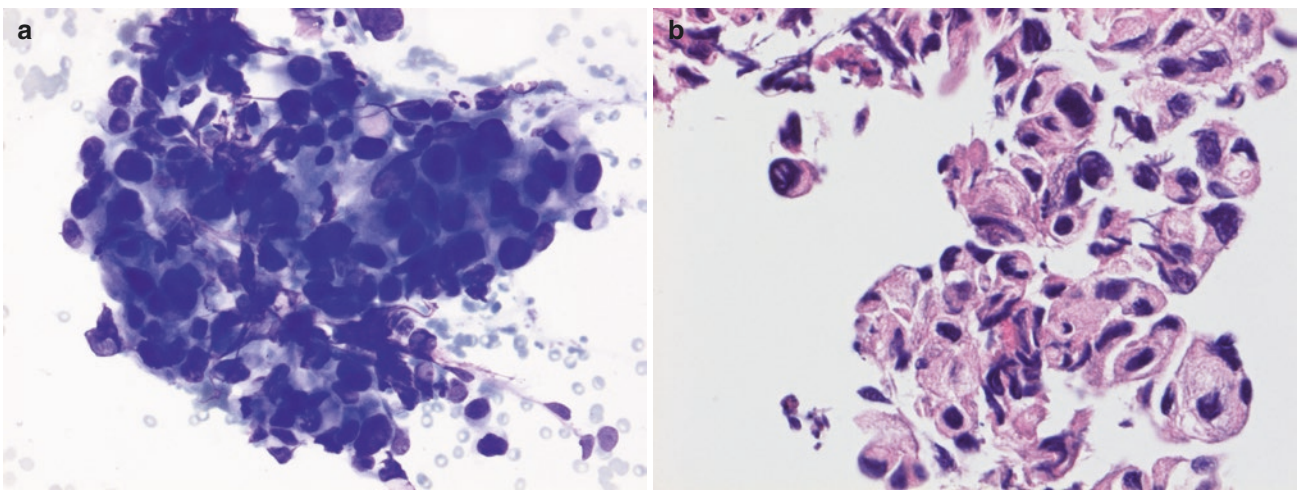

Fig. 18.16 Orbital metastasis from poorly differentiated carcinoma of the lung. Dyscohesive clusters of pleomorphic tumor cells without any specific signs of differentiation in the FNA smears (**a**) and the cell block section (**b**). Without clinical history of previous lung carcinoma and ancillary techniques, it could be difficult to diagnose the primary (MGG; H&E)

Hematolymphoid Lesions

Non-Hodgkin Lymphoma

These may occur in the orbit and can also be related to the lacrimal gland. Lymphomas are primary or metastatic [46–48]. FNA has proven to be a very efficient modality to provide diagnostic yield (see Fig. 18.18) and, in the majority of cases in combination with other diagnostic modalities, lead to a diagnosis reliable enough to allow initiation of treatment without further invasive diagnostic procedures [48, 49].

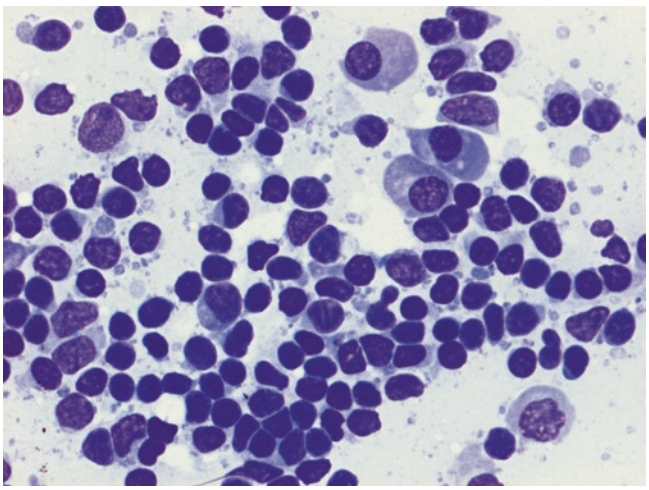

Fig. 18.18 Orbital non-Hodgkin lymphoma. Dispersed atypical lymphoid cells with plasmacytoid morphology. The correct diagnosis is difficult to render from aspiration smears alone, necessitating ancillary techniques (MGG)

Myeloma

Orbital myeloma is composed of numerous dissociated tumor cells with abundant basophilic cytoplasm, eccentrically placed round nuclei with a prominent wheel-spoke-shaped chromatin pattern and a small nucleolus.

Intraocular Tumors

Transocular FNA is a safe and reliable diagnostic method for suspected intraocular tumors and inflammatory conditions in which noninvasive diagnostic modalities have failed to establish the diagnosis and in which cytological verification of the diagnosis is necessary to institute appropriate treatment [50].

Malignant Melanoma

Transscleral FNA is justified in adult patients when tumor presentation is not characteristic (differential diagnosis between primary and metastatic tumors) or in cases when prognosis is examined [50–52]. Similar to other locations, melanomas may show melanin or not (see Fig. 18.19). Cells are spindled, roundish, or epithelioid. Binucleation is common.

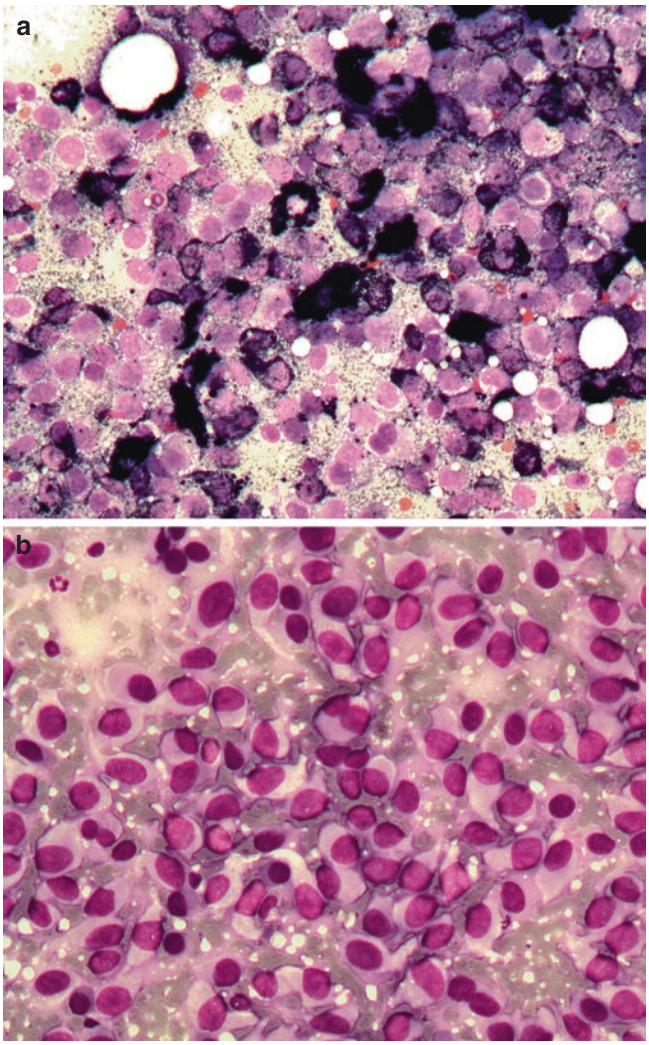

Fig. 18.19 Intraocular malignant melanoma. (**a**) Dispersed single tumor cells and abundant melanin pigment (MGG). (**b**) Amelanotic melanoma with dispersed single cells showing plasmacytoid morphology. Note binuclear tumor cells (MGG)

Retinoblastoma

Unilateral or bilateral retinoblastomas are intraocular tumors in children. The diagnosis is clinical in combination with a typical ultrasound appearance. Intraocular FNA should be avoided. Usually FNA is used in metastases or orbital recurrences [53–55]. Cells are roundish or poorly differentiated with or without rosette formation. Mitotic figures are numerous (see Fig. 18.20). Focal background necrosis is common.

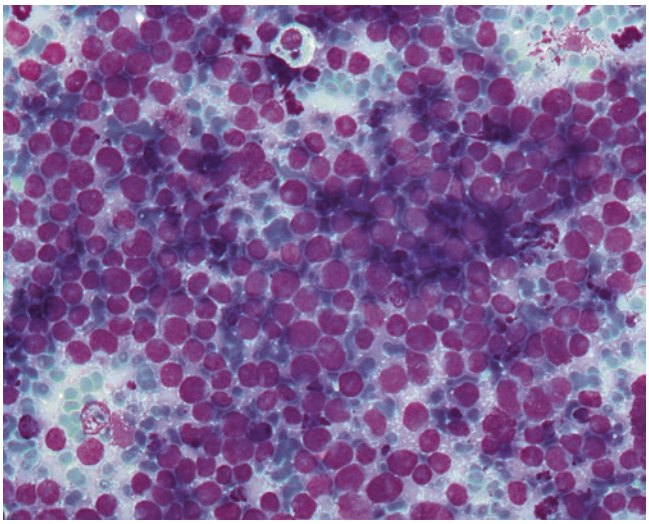

Fig. 18.20 Orbital recurrence of retinoblastoma. Smears show dispersed single cells of poorly differentiated small cell malignancy with dark nuclei and scant cytoplasm (MGG)

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