Image-Guided Fine-Needle Aspiration Cytology

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Several factors may make image guidance necessary in fine-needle aspiration cytology (FNAC): A lesion may be diffuse and difficult to palpate; the cytopathologist may require image guidance for all deep-seated nonpalpable lesions; there may be sampling issues in a nonhomogeneous lesion with areas of different tissue characteristics (e.g., necrosis versus viable tumor or purely fatty areas versus contrast-enhancing areas in liposarcomas); or the lesion may be inaccessible behind bony structures [1, 2] or located inside bone [3–5]. In many cases, the cytologist may simply prefer to use image guidance for a more exact needle placement. In all cases, however, the first step should be a thorough and careful review of all pertinent imaging studies to select the appropriate guiding modality, to evaluate all possible access routes, and to select appropriate needles and devices to reach the lesion. At this stage, the patient should also be considered: Is there coagulopathy or is the patient on an anticoagulant, antiplatelet, or thrombolytic medication? Are there any other absolute or relative contraindications to the procedure or to any imaging modality (e.g., magnetic resonance imaging [MRI])? If needed, the coagulant status should be corrected to acceptable levels.

Imaging Modalities

Several imaging modalities are available to assist in the best approach to the target lesion. The choice of imaging modality is dictated by several factors (see Table 2.1) such as personal preference, availability on site and available time slots, ease of performing the biopsy, procedural cost, and radiation dose to the examiner and patient. The use of fluoroscopy has waned in recent years due to the ease of performing ultrasound-guided biopsies and the introduction of multidetector computed tomography (CT) scanners. Today, fluoroscopy-guided FNAC is usually reserved for destructive bony lesions in easily accessible areas of the peripheral skeleton, for spinal biopsies using mostly biplane imaging, and for biopsy of high-contrast pulmonary lesions in the lower lung fields where breathing motion may render other modalities virtually useless. Instead, CT has come to replace fluoroscopy for almost all skeletal biopsies, for most lung biopsies, and for many deep-seated extra-abdominal biopsies. Ultrasound is frequently used for breast biopsies and for most intra-abdominal biopsies, due to both the excellent soft-tissue contrast and the ability to direct the biopsy needle from any direction. MRI-guided biopsies are still rare because the strong magnetic field requires special equipment. In breast biopsies, stereotactic biopsies are frequently used in addition to ultrasound guidance.

Table 2.1 Available imaging methods for biopsy guidance: their use and limitations

Modality	Objective	Disadvantages
Fluoroscopy	Bony lesions in extremities, spinal biopsies, lung biopsies	Radiation
CT	Bony and soft-tissue lesions in musculoskeletal system and chest	Radiation
Ultrasound	Abdominal biopsies, subcutaneous musculoskeletal soft-tissue biopsies	Operator dependent. Not for bony lesions
MRI	–	Magnetic field
Stereotactic biopsy	Breast lesions. Gives direction and depth	

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Anatomical Regions

Breast

Image-guided breast core biopsies have been accepted as an alternative to open surgical biopsies in nonpalpable lesions, detected at mammography [6]. Biopsies may be performed using ultrasound or MRI for image guidance or by stereotactic-guided biopsies [6]. Of almost 150,000 breast biopsies performed in the USA in 2004, 86% were performed with image guidance [7]. Long-term follow-up has shown that stereotactic-guided biopsies have the same accuracy as open surgical biopsies [8, 9]. Recently published meta-analyses report that FNAC is an accurate biopsy when using stringent criteria, but that further invasive procedures are necessary if the sampling is unsatisfactory [10]. Compared with core biopsy, both are reported to have good clinical performance, sometimes with a slightly higher sensitivity for core biopsy, and both can be considered as the first choice for evaluation of a suspicious breast lesion [11]. The advantage of ultrasound guidance is that it not only allows for cytological evaluation by FNA and histologic tissue sampling by core biopsy but also for image characterization of breast lesions and locoregional lymph nodes [12], where the ultrasound examination may be at least as important as the image-guided biopsy for some patients [13]. In a report from a European discussion forum in 2007, it was reported that most participating countries used a triple assessment approach (i.e., a clinical, imaging, and pathological evaluation) to ensure a definitive pretreatment diagnosis [14]. FNAC was used as the first-line pathological investigation, particularly in symptomatic patients and in some screening populations. Core biopsy was used as a first biopsy modality in some screening populations in, for example, the UK. Another review reported FNAC as the most common method for evaluation of breast lesions in developing countries mainly for reasons of cost, whereas core needle biopsy is the initial method of choice in developed and Western countries [15]. Breast MRI has evolved in the past decades into an imaging modality well suited for breast imaging. Imaging is usually performed in the prone position, with the breasts falling dependently from the patient, and using special coils. Most lesions will enhance after intravenous contrast administration, making image-guided biopsy possible. The limitations are mainly that biopsy is only possible from the lateral side in most systems, that the time duration for biopsy is short due to washout of contrast from the tissues, and that the biopsied sample cannot be imaged by MRI, as living tissue is needed for MRI [16]. The cost of breast MRI and breast MRI-guided biopsy is high.

Thyroid

Thyroid gland FNAC may be improved by image guidance [17–19]. In one study, 215 patients with palpable thyroid nodules between 10 and 25 mm diameter were biopsied using both palpation-guided FNAC and ultrasound-guided FNAC by the same examiner, and the samples were evaluated by the same cytologist [17]. There were significantly more cases with inadequate material in the palpation-guided group, especially for small nodules (10–15 mm). The increase in cost for the image-guided procedure of about $20 (US) was deemed acceptable, especially considering the improved sampling from small lesions [17]. The specialty of the person doing the ultrasound-guided FNAC seems less important. One study reported similar rates for diagnostic aspirations by radiologists and surgeons but with a significantly quicker turnaround time for a cytological diagnosis for the surgeon [20]. Ultrasound-guided biopsy should be directed to the periphery of the lesion in solid lesions and to solid areas of cystic lesions [19]. Both 23- and 27-gauge needles may be used. A study evaluating the yield from 23- to 27-gauge needles in ultrasound-guided FNAC found no significant difference in adequacy of sampling between the two needle sizes [18]. It was recommended, however, to use both sizes because the number of dry taps was lower with the larger needle, but the quality of samples was higher using the smaller needle [18].

Salivary Glands

FNAC has for many years been used as the initial biopsy in salivary gland lesions [21]. The literature reports highly variable results with a sensitivity for malignancy in some centers reaching 70–80% but with a nondiagnostic yield as high as 56% in some reports [21]. As in most other fields, the diagnostic yield is reported to increase with image guidance [21]. Ultrasound-guided core biopsy has been reported having higher sensitivity and specificity than non-guided FNAC [22] and should be at the forefront of salivary gland evaluation [22, 23].

Lung

With the introduction of multidetector CT and CT fluoroscopy, biopsy of lung nodules has become much easier. In many centers, a CT-guided biopsy is preferred for most lesions because CT gives excellent anatomical detail regarding surrounding tissue such as mediastinum, nerves, and vessels. The major complication, pneumothorax, has been

reported to be minimized by using fine needles, usually 21 or 22 gauge [24]. On the other hand, the incidence of pneumothorax has been reported to be similar for single-needle FNA, coaxial-needle FNA, and core biopsy [25]. Diagnostic success is higher in lesions close to the pleura and in lesions larger than 1 cm in diameter, in which ultrasound guidance can also be used [26]. With deeper lesions, the risk of pneumothorax also increases, especially if a fissure is traversed, which increases the number of pleural passages. CT guidance requires patients to be able to hold their breath for the time necessary for biopsy. This is a concern especially in the lower lung fields because the basilar parts of the lungs move the most with breathing. This is not of such great concern with fluoroscopy-guided biopsies, which may in these cases be preferred instead. For mediastinal masses, CT guidance can in many cases be applied, e.g. by using a posterior paravertebral approach under CT guidance [27] to approach subcarinal lymph nodes. Also, ultrasound-assisted transthoracic fine-needle aspirations with on-site evaluation followed by core biopsies where indicated are safe and have a high diagnostic yield [28]. Although ultrasound is cheaper than CT and is free from ionizing radiation, lesions obscured by aerated lung, small deep-seated lesions, and cavitary lesions cannot be biopsied with the use of ultrasound [29]. The precision of ultrasound guidance and CT guidance was reported similar in a study evaluating all lesions in the lung, thorax, and thoracic wall [29]. Prior pneumonectomy and other instances of a single lung are possibly the only absolute specific contraindication to image-guided lung biopsy [30]. Among relative contraindications to lung biopsy are suspected hydatid cyst or vascular malformation, significant pulmonary arterial hypertension, or severe obstructive lung disease (forced expiratory volume [FEV]1 < 1.1) [30]. Besides pneumothorax, hemoptysis and hemorrhage occur in up to 10% of patients after lung biopsy and are the major complications after biopsy. Needles larger than 18 gauge and cutting needles are associated with an increased risk for hemorrhage [30].

Abdomen

For most abdominal FNAC procedures, ultrasound guidance is the method of choice. Usually, a needle guide is used on the transducer. The method is quick, without radiation to the patient or examiner, and the complete mobility of the ultrasound probe will in most cases give clear access to the lesion, and the ultrasound probe can be used to displace the bowels. Thus, the liver [31], pancreas, kidneys, ovaries [32, 33], lymph nodes [34, 35], and spleen [36] are usually biopsied using ultrasound [37]. Deep-seated lymph nodes, both in the thorax and abdomen, may be biopsied under ultrasound guidance [34]. In some cases with hard-to-reach lesions, CT is preferred [38]. CT may also often be the modality of choice in biopsy of the adrenal glands [39] or the spleen [40]. For hard-to-reach masses in or around the pancreatic head, FNAC using a posterior transcaval approach with CT guidance has been described [41]. Serious complications of abdominal image-guided FNAC are comparatively rare, considering the longer access routes and larger amounts of tissue traversed compared with more superficial FNAC [37, 42, 43].

Musculoskeletal

Imaging in conjunction with FNAC may in special cases be diagnostic, obviating the need for a surgical biopsy [44]. For soft-tissue lesions, CT is the best guidance modality, giving excellent soft-tissue contrast to locate the target. Depending on the equipment used, the procedure may differ in detail, but the main procedure commonly involves acquiring a scout scan over the body part to be biopsied, after which a diagnostic CT examination is performed to locate the lesion. The section most optimal for biopsy is selected, and the angle and depth of the approach is determined. After antiseptic cleaning and local anesthesia, the lesion is biopsied. Preferably a coaxial technique is used to avoid multiple skin passages and to facilitate and expedite the procedure, especially if the approach is difficult. If a trocar is used for the coaxial approach, a core biopsy may be performed through the same trocar. The downside of using CT is that an oblique approach in the craniocaudal direction is difficult because, in most CT scanners, the CT gantry must remain perpendicular to the long axis of the body of the patient during the procedure. Superficial lesions or deep-seated lesions close to the muscular fascia may be biopsied with ultrasound guidance. Bony lesions are approached in the same way as soft-tissue lesions using CT, with the exception that a trocar with a drill in most cases is necessary to penetrate the cortical bone. Osteolytic lesions are then easily biopsied with FNAC. Densely sclerotic lesions may be very difficult to biopsy with FNAC [45]. A high rate of accuracy and clinical usefulness has been reported for image-guided needle biopsies of musculoskeletal lesions [46], where the authors emphasized the importance and benefit of referring patients with a possible musculoskeletal tumor to a specialized referral center. Mehrotra et al. [47] recommend the use of image-guided FNAC as the first diagnostic method for skeletal lesions of unknown origin. However, image-guided core biopsies have been reported to have a slightly higher accuracy than FNAC [48, 49].

Special Techniques

To obtain samples from the bone, the cortical bone must be penetrated by drilling unless there is cortical destruction or softening from the lesion in question. There are several alternatives on the market using a cannula with a trocar and/or a drill [3]. After cortical penetration, FNAC samples may be acquired from the target lesion using a coaxial technique. The technique can even be used to traverse intact bone to biopsy a soft-tissue lesion in an otherwise inaccessible location [1, 2]. Other ways to reach "inaccessible" lesions include a selection of the proper imaging modality and to consider alternate biopsy routes such as transgluteal, transvaginal, and other transorgan approaches [25, 28]. Another approach is to consider an out-of-plane approach in the CT-guided biopsy, whereby the target is reached by a craniad or caudad approach toward the selected slice. The CT gantry may also be angled to provide an alternate path [37]. Special needles, designed to better reflect the sound waves, may be used for ultrasound biopsies. When losing track of the needle in an ultrasound procedure, it is best to keep the transducer locked on the target lesion and redirect the needle. The next best approach is to keep the needle still and locate it by slightly redirecting the transducers. One should never manipulate the transducer and needle simultaneously. Biopsy needles will deviate in harder tissues, with less deviation with thinner needles. The degree of deviation for core biopsy using 2.1 mm needles has been evaluated using butter blocks at different temperatures to simulate tissue of different hardness in the human breast [38].

Safety

With deep-seated intrapulmonary, intra-abdominal, or musculoskeletal lesions, post-biopsy bleeding becomes more important because hemorrhages are harder or virtually impossible to control. If the patient is taking acetylic acid, bleeding time should be checked [17]. If prolonged, the procedure may have to be postponed until the bleeding time has been normalized to avoid the risk of bleeding complications. For patients on anticoagulants such as warfarin, the prothrombin time (PT) or the international normalized ratio (INR) should be checked before the procedure and, with help of the treating physician, the PT should be reduced to a manageable level. This level depends on which tissue will be sampled, the depth and accessibility for manual compression, the surrounding anatomical structures, and possible complications. Besides a bleeding diathesis or anticoagulant therapy, inability of the patient to cooperate is also a relative contraindication to needle biopsy [20], also depending on the situation. In general, FNAC is a safe procedure with few complications reported [39].

Results

In order to obtain optimal results, it is probably irrelevant whether a radiologist, cytologist, or another physician performs the actual biopsy [20]. The radiologist should have adequate training in aspiration technique. The most important factor achieving a high success rate is probably the assistance of on-site cytopathology to help with smearing the samples and providing a preliminary evaluation of the FNA quality [50, 51]. When performing image-guided FNAC, it is in many cases reasonable to perform a core biopsy simultaneously [5, 52].

Illustrative Cases

Case 1

A 63-year-old woman with a history of breast carcinoma 10 years ago and squamous cell carcinoma in the gingiva 2 months ago. A single suspect metastatic lesion in the sacral bone was detected with positron emission tomography (PET)/CT. A single focus of hypermetabolism in the right ischial tuberosity is shown on a coronal section (*arrow*; see Fig. 2.1). Diagnostic CT before biopsy confirmed the lesion shown as a diffusely sclerotic area in the ischial tuberosity (*arrows*; see Fig. 2.2). In the prone position, the lesion was biopsied through a trocar to obtain multiple fine-needle samples as well as a core biopsy (see Fig. 2.3). The tip of the drill can be seen in the medullary bone, whereas the trocar is anchored in the cortical bone. FNAC of the sacral lesion shows clusters of the atypical epithelial cells consistent with metastatic carcinoma from the breast (see Fig. 2.4a). Positive results of immunostaining with antibodies against estrogen receptor (ER) confirmed the diagnosis (see Fig. 2.4b).

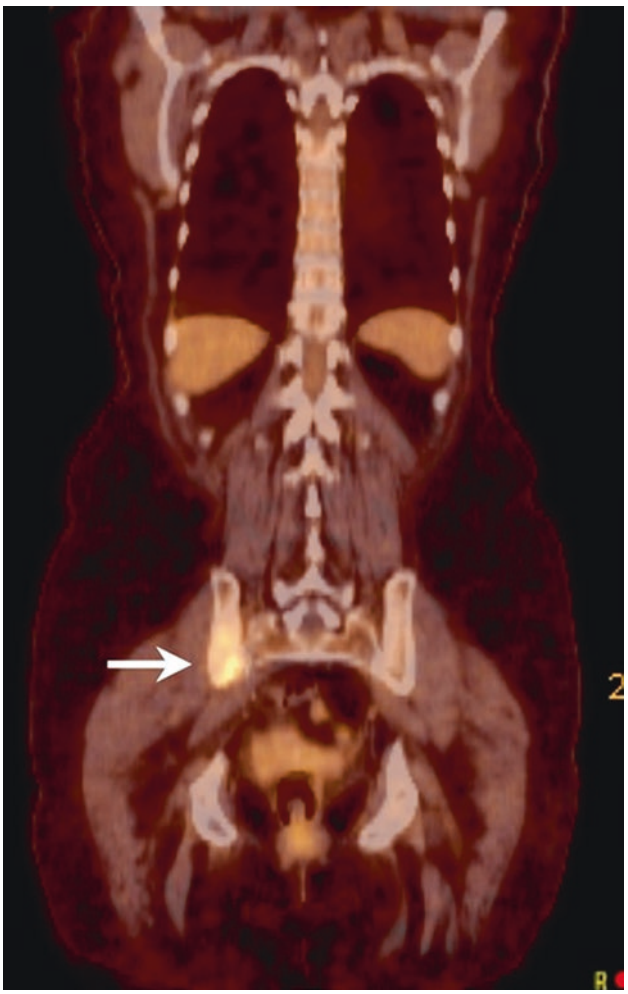

Fig. 2.1 Metastatic carcinoma from the breast. PET/CT: a single focus of hypermetabolism in the right ischial tuberosity on a coronal section (*arrow*)

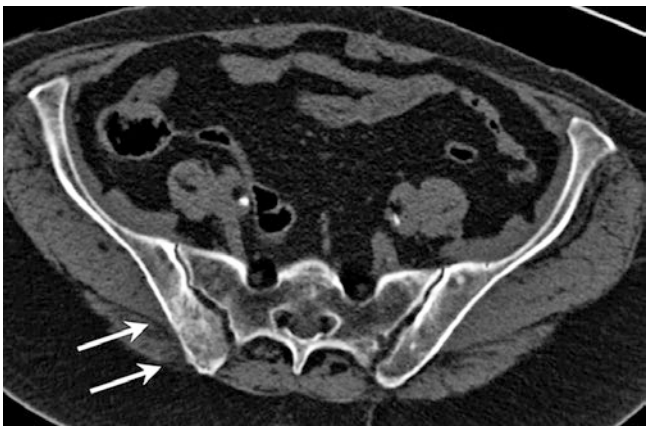

Fig. 2.2 Metastatic carcinoma from the breast. Diagnostic CT before biopsy shows a diffusely sclerotic area in the ischial tuberosity (*arrows*)

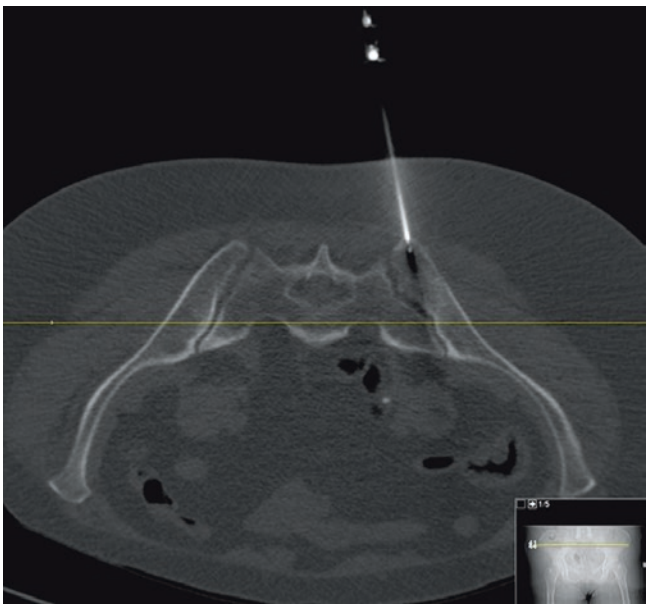

Fig. 2.3 Metastatic carcinoma from the breast. In the prone position, the tip of the drill can be seen in the medullary bone, while the trocar is anchored in the cortical bone

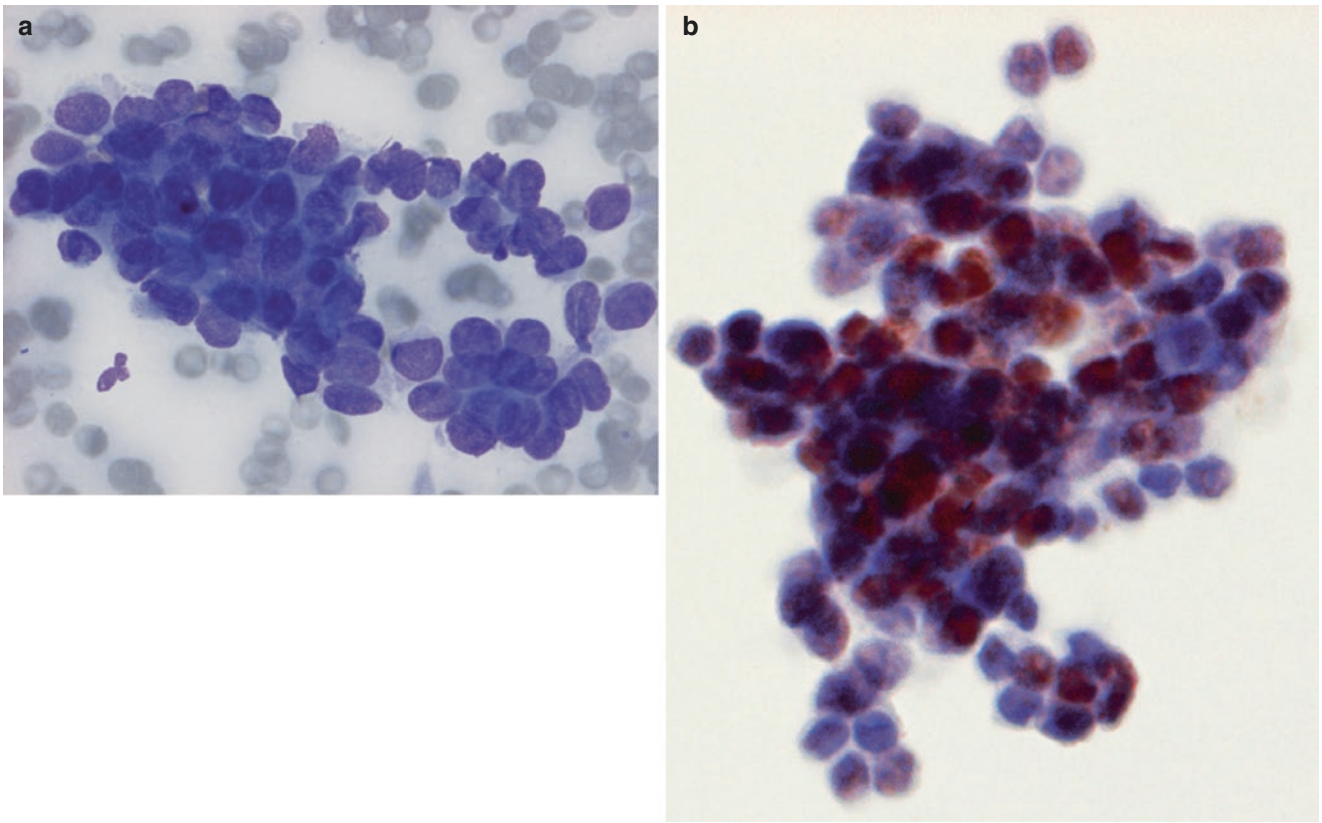

Fig. 2.4 Metastatic carcinoma from the breast. (**a**) FNAC showing clusters of the malignant epithelial cells (May-Grünwald Giemsa [MGG]). (**b**) Positive results of immunostaining with antibodies against ER confirmed the diagnosis (ThinPrep; Hologic; Bedford, MA, USA)

Case 2

A 13-year-old girl with a 3-month history of left hip pain. Radiography showed an irregular bone structure in the left supra-acetabular area. MRI showed an osteolytic tumor in the supra-acetabular area (*arrow*) with soft-tissue extension through the quadrilateral plate into the pelvis (*arrowheads*), with suspicion of Ewing sarcoma (see Fig. 2.5). A diagnostic CT before biopsy confirmed the osteolytic destruction (*arrows*; see Fig. 2.6a). The soft-tissue extension can be appreciated also with CT (*arrowheads*; see Fig. 2.6b). With the patient in the prone position, the lesion was biopsied through a trocar to obtain multiple fine-needle samples and a core biopsy (see Fig. 2.6b). FNA smears were hypercellular (see Fig. 2.7a). In high-power view, there was a mixture of small dark cells and larger light cells with occasionally moderate to abundant cytoplasm with characteristic vacuolization/empty spaces after glycogen (see Fig. 2.7b). Ancillary tests confirmed the diagnosis of Ewing sarcoma.

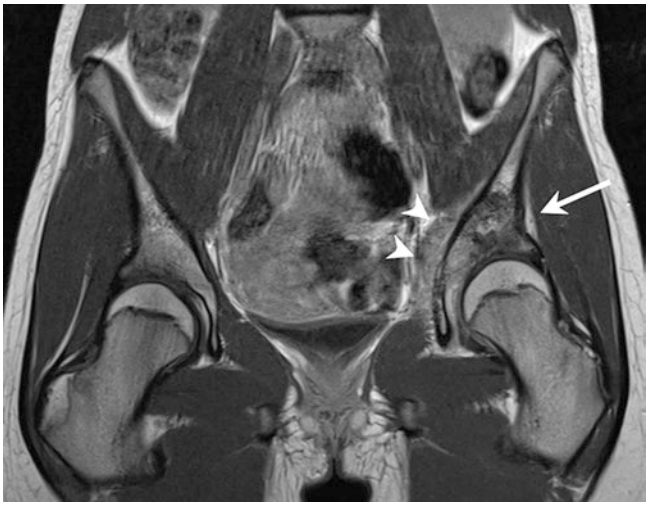

Fig. 2.5 Ewing sarcoma. MRI showing an osteolytic tumor in the supra-acetabular area (*arrow*) with soft-tissue extension through the quadrilateral plate into the pelvis (*arrowheads*)

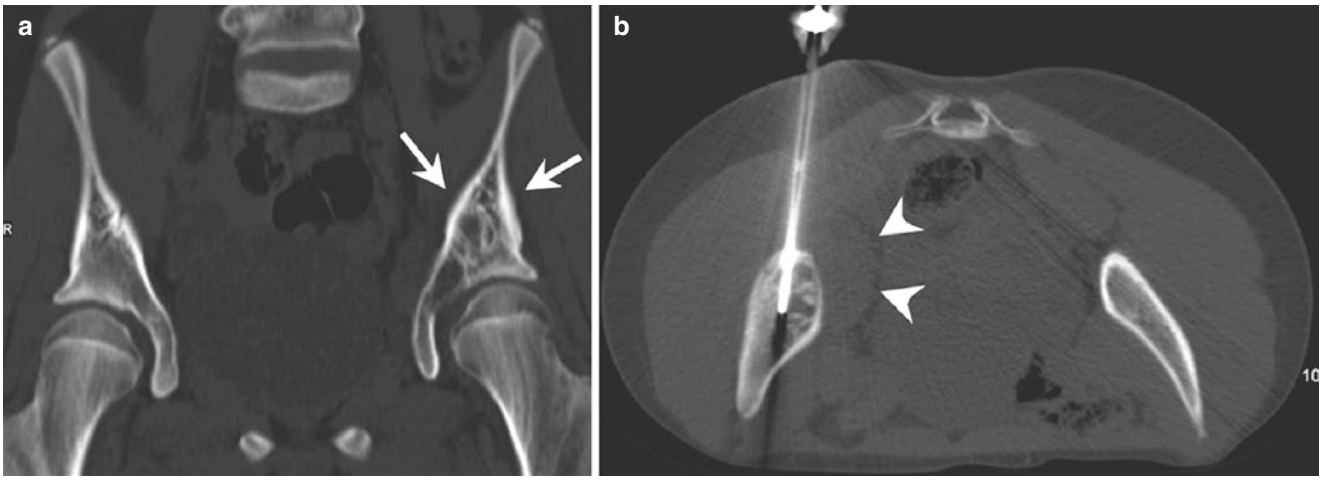

Fig. 2.6 Ewing sarcoma. (**a**) Diagnostic CT before biopsy confirmed the osteolytic destruction (*arrows*). (**b**) The soft-tissue extension can be appreciated also with CT (*arrowheads*). In the prone position, the lesion was biopsied through a trocar

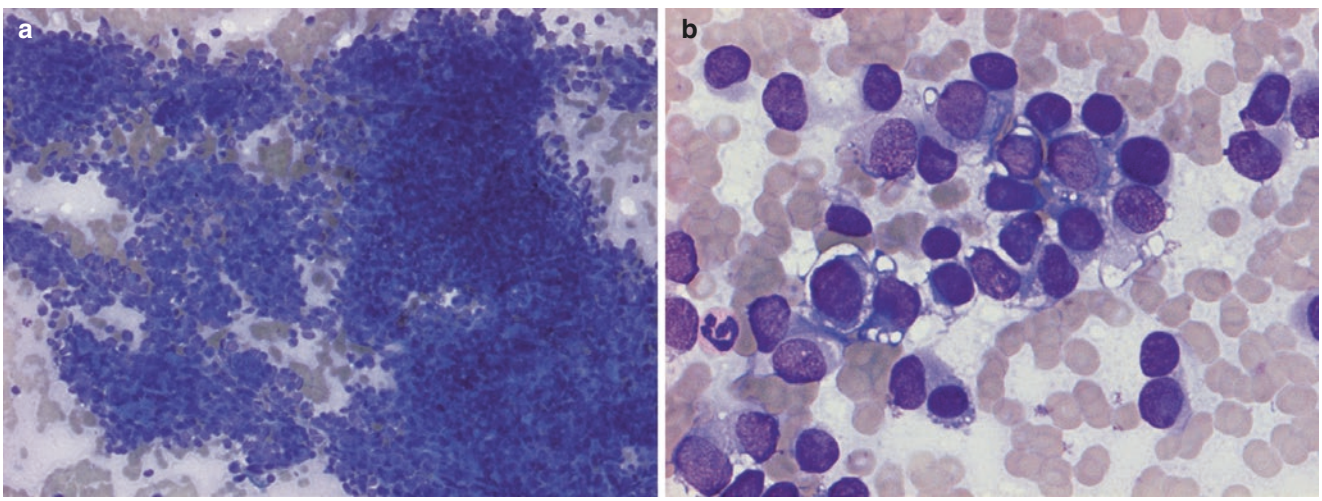

Fig. 2.7 Ewing sarcoma. (**a**) Hypercellular FNA smears. (**b**) In high-power view, a mixture of small dark cells and larger light cells with moderate to abundant cytoplasm and characteristic vacuolization/empty spaces after glycogen (MGG)

Case 3

A 72-year-old overweight man with renal failure and chronic heart failure on antithrombotic treatment with warfarin for previous left ventricle thrombus. Chest radiography had revealed a suspicious lesion in the left lung, which was confirmed with PET/CT (see Fig. 2.8a). The same PET/CT also revealed a single suspect metastasis in the right acetabular medial wall (see Fig. 2.8b). Because the patient's coagulation status could not be restored to normal, it was decided to first biopsy the suspect metastasis instead of the presumed primary lung tumor. The patient's general poor health made a biopsy from posterior using a prone position unsuitable. From anterior, the direct approach to the tumor (*arrow*) was obstructed by the femoral vessels (*star*) and the funicle (*rhombus*; see Fig. 2.9). By using an indirect lateral oblique approach, a 0.9 mm needle was anchored in the pectineus muscle between the funicle and the vessels (see Fig. 2.10a). The needle was then redirected toward the lesion in the acetabular wall and advanced to its full length (9 cm; see Fig. 2.10b). Coaxial fine-needle aspirations were performed using 15 cm long 0.7 mm needles (*arrow* indicates outer needle, *arrowhead* indicates biopsy needle; see Fig. 2.10c). Core biopsy was not performed due to the poor coagulant status. FNA smears were hypercellular showing multiple cohesive sheets and papillary clusters (see Fig. 2.11a) of slight-to-moderate pleomorphic tumor cells with abundant cytoplasm, round nuclei, and inconspicuous nucleoli (see Fig. 2.11b). Positive results of immunostaining with antibody to TTF-1 confirmed the diagnosis of metastatic adenocarcinoma from the lung.

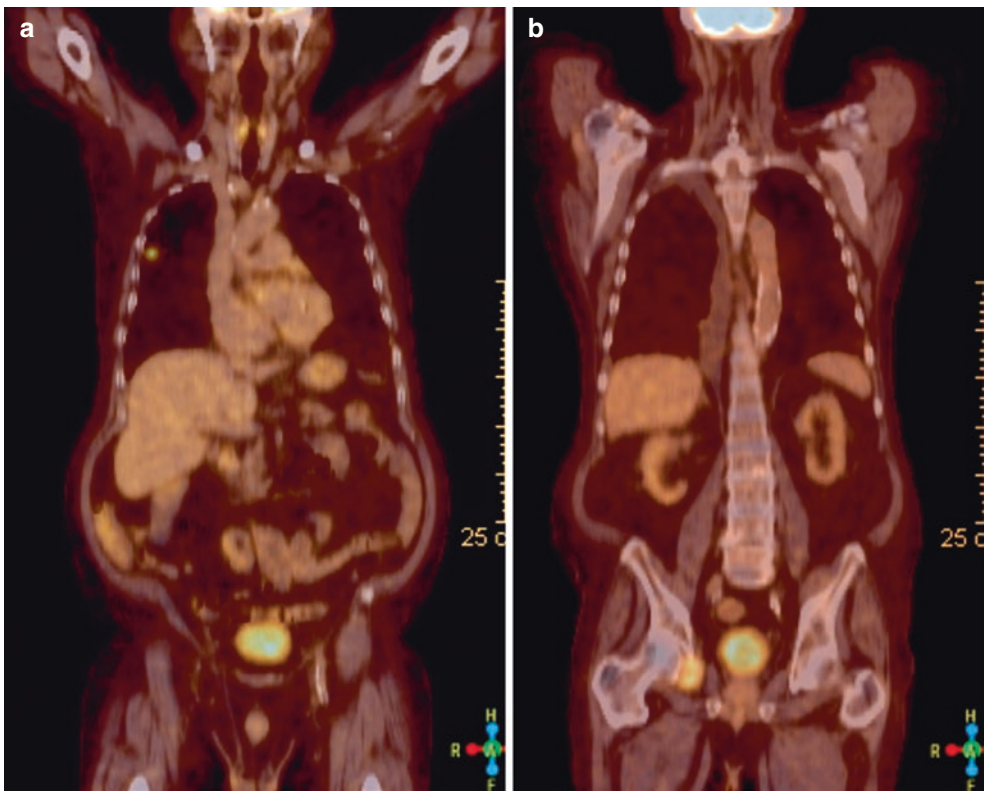

Fig. 2.8 Metastatic adenocarcinoma from the lung. (**a**) PET/CT showing a suspicious lesion in the left lung. (**b**) A single suspect metastasis in the right acetabular medial wall

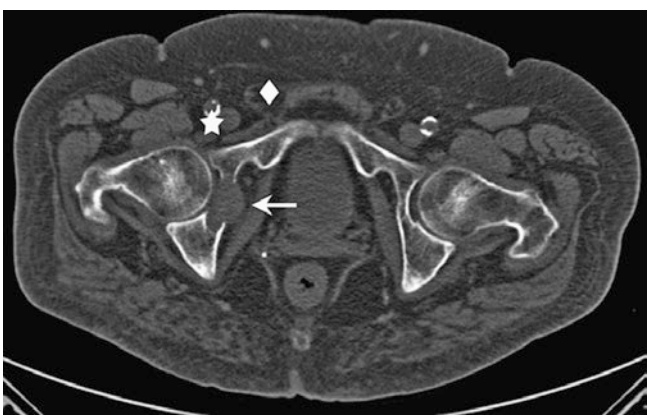

Fig. 2.9 Metastatic adenocarcinoma from the lung. Diagnostic CT before biopsy. The direct approach to the metastasis (*arrow*) was obstructed by the femoral vessels (*star*) and the funicle (*rhombus*)

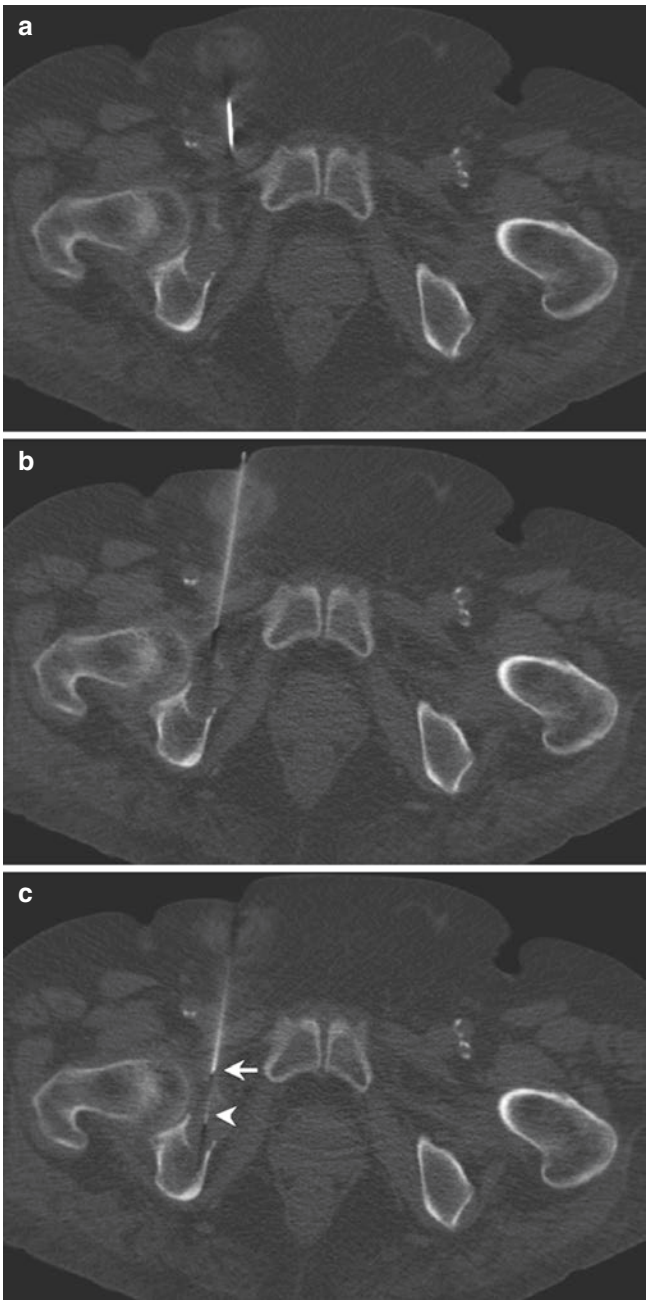

Fig. 2.10 Metastatic adenocarcinoma from the lung. (**a**) By using an indirect lateral oblique approach, a 0.9 mm needle was anchored in the pectineus muscle between the funicle and the vessels. (**b**) The needle was then redirected toward the lesion in the acetabular wall and advanced to its full length. (**c**) Coaxial FNA was performed using 15-cm-long 0.7 mm needles (*arrow* outer needle, *arrowhead* biopsy needle)

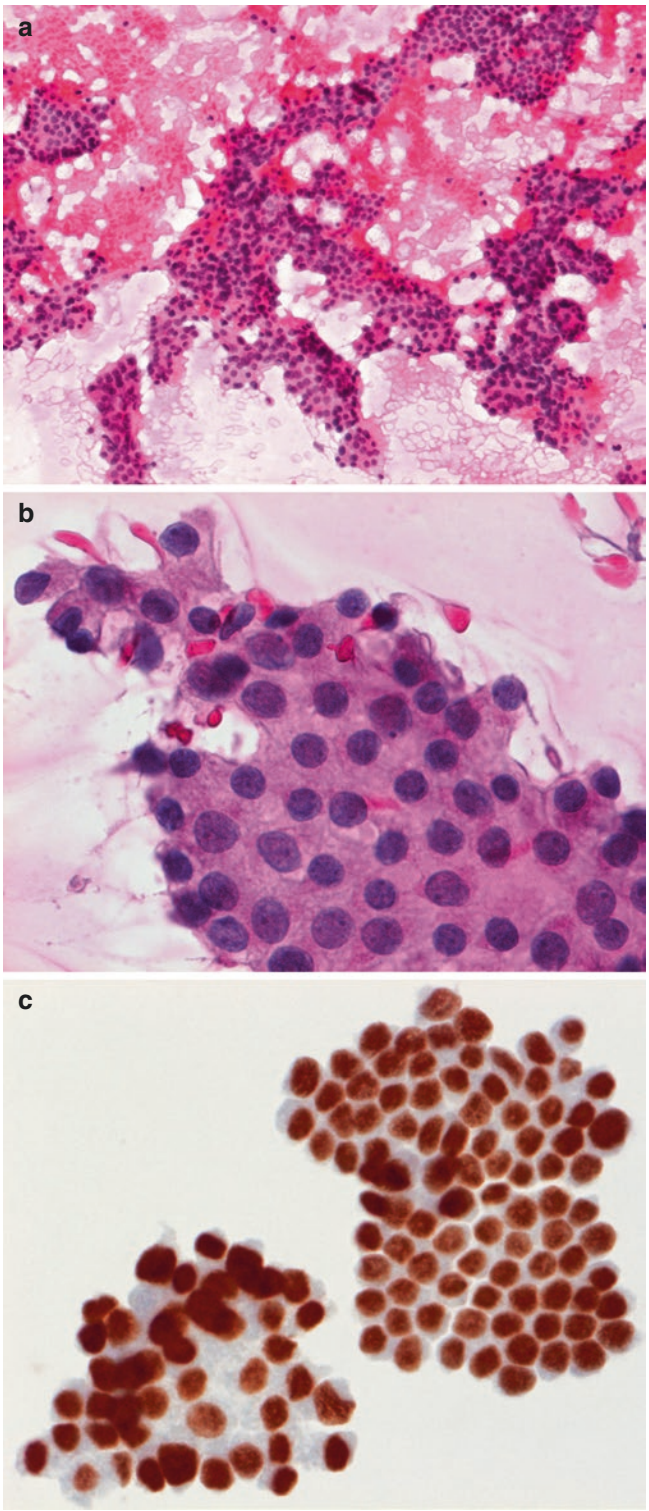

Fig. 2.11 Metastatic adenocarcinoma from the lungs. (**a**) Hypercellular FNA smears showing multiple cohesive sheets and papillary clusters of (**b**) slight-to-moderate pleomorphic tumor cells with abundant cytoplasm, round nuclei, and inconspicuous nucleoli (H&E). (**c**) Positive results of immunostaining with antibody to TTF-1 confirmed the diagnosis of metastatic adenocarcinoma from the lung (ThinPrep; Hologic; Bedford, MA, USA)

Case 4

A 20-year-old male with an almost 1-year history of low back pain and loss of the left patellar reflex. MRI (see Fig. 2.12a) showed a large tumor destroying a large part of the S1 and S2 vertebral bodies and most of the left lateral mass, with extension into the anterior and posterior soft tissues, as well as the spinal canal (see Fig. 2.12b). CT-guided biopsy in the prone position allowed for exact needle placement, thus avoiding the presumed location of the spinal canal and sacral nerve roots (see Fig. 2.13). FNA smears were hypercellular and showed clusters of uniform spindle cells embedded within a collagenous and slightly myxoid matrix (see Fig. 2.14a). Nuclear palisading and cell-poor areas in the cell clusters consisted of Verocay bodies (see Fig. 2.14b). Alcohol-fixed smears showed cohesive clusters of relatively uniformed spindle cells with indistinct cytoplasm and elongated nuclei, some with pointed ends (see Fig. 2.14c). Tumor cells expressed diffuse S-100 positivity (see Fig. 2.14d). FNA diagnosis was benign schwannoma, confirmed by examination of a surgical specimen from the removed mass.

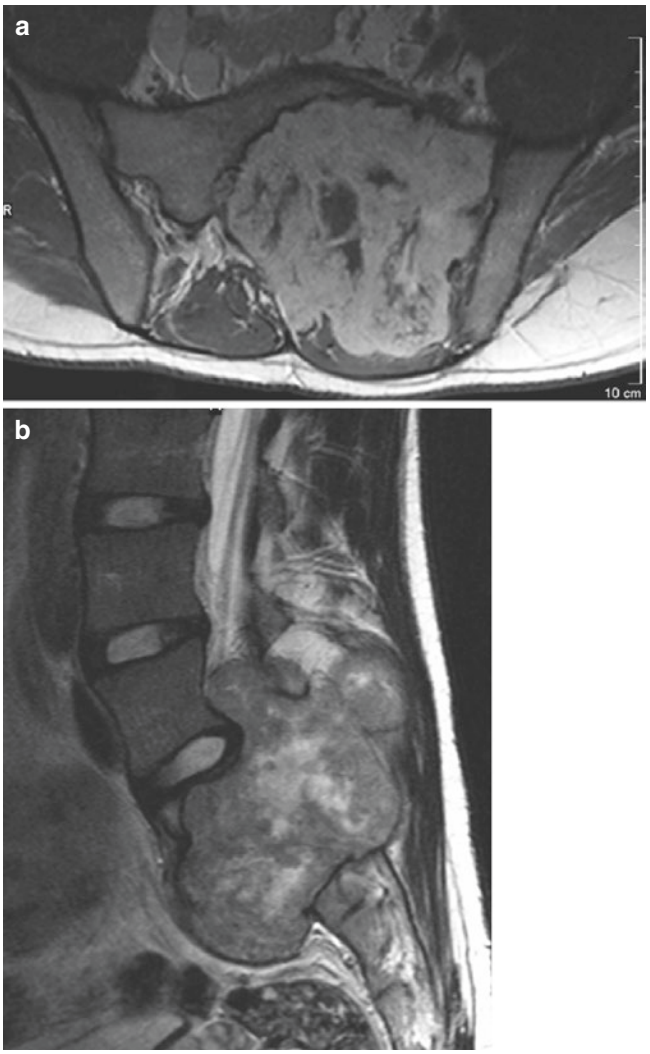

Fig. 2.12 Schwannoma. (**a**) MRI showing a large tumor destroying a large part of the S1 and S2 vertebral bodies and most of the left lateral mass. (**b**) Tumor extension into the anterior and posterior soft tissues, as well as the spinal canal

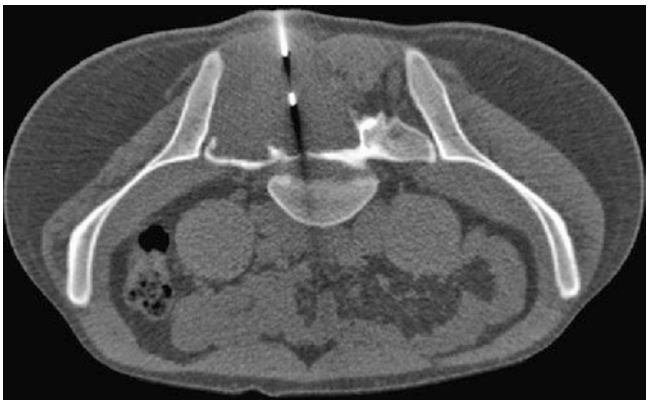

Fig. 2.13 Schwannoma. CT-guided biopsy in the prone position allowing for exact needle placement, thus avoiding the presumed location of the spinal canal and sacral nerve roots

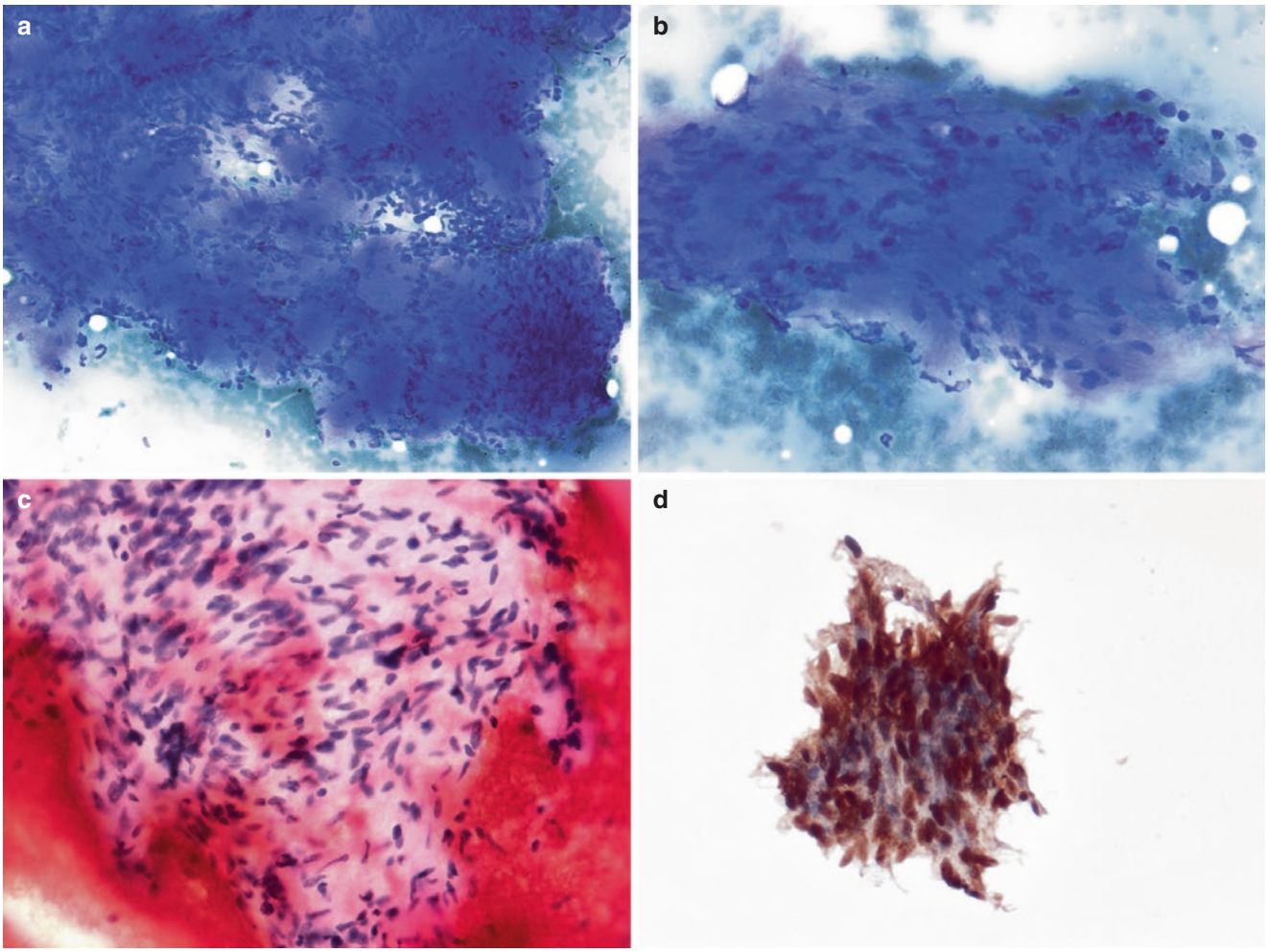

Fig. 2.14 Schwannoma. (**a**) Hypercellular FNA smears showing clusters of uniform spindle cells embedded within a collagenous and slightly myxoid matrix. (**b**) Nuclear palisading and cell-poor areas in the cell clusters consisted of Verocay bodies (MGG). (**c**) Alcohol-fixed smears showing cohesive clusters of relatively uniformed spindle cells with indistinct cytoplasm and elongated nuclei, some with pointed ends (H&E). (**d**) Diffuse S-100 positivity confirms a diagnosis of schwannoma (ThinPrep; Hologic; Bedford, MA, USA)

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