CONTINUING EDUCATION PROGRAM: FOCUS...

CT-guided biopsies in lung infections in patients with haematological malignancies

C. de Bazelaire*, A. Coffin, S. Cohen-Zarade, C. de Margerie-Mellon, A. Scemama, F. Sabatier, R. Calmon, E. de Kerviler

Interventional radiology department, hôpital Saint-Louis, université Paris-7 René-Diderot, 1, avenue Claude-Vellefaux, 75010 Paris, France

KEYWORDS
Interventional radiology; Haematological malignancy; Lung biopsy; Infections

Abstract CT-guided transparietal lung biopsy in imaging makes it possible to find the pathogenic agent in half of all fungal infections and most bacterial infections (sensitivity = 55%, specificity = 100%). Performance is decreased in consolidations (50% of infections) compared to masses. Complications, pneumothorax, alveolar bleeding and hemoptysis are generally benign and rarely (< 5%) require specific treatment. On the other hand, the diagnostic performance increases significantly with the calibre of 18G co-axial systems compared to 20G. The risk is not related to the number of samples or platelet levels.

© 2013 Éditions françaises de radiologie. Published by Elsevier Masson SAS. All rights reserved.

The prognosis of patients being treated for haematological malignancies has clearly improved over the past decades. However, these patients develop numerous complications including relapse or a transformation of their haemopathy, a primary cancer, toxicity to treatments and infection. Haematological malignancies are often the cause of an immune deficiency that promotes the onset of pulmonary infections. This immune deficiency can be related to the tumoural disease of the patient or to the treatments he or she receives. Chemotherapies are responsible for variable haematological toxicities in terms of depth and duration. The risks of infection depend on the type of immune depression induced by the treatment and condition the risks of infection. Short-term neutropenia therefore promotes infections caused by Gram-negative bacilli or Gram-positive cocci while long-term neutropenia (acute leukaemia, chemotherapy) creates a receptive environment for fungal infections caused by Candida or Aspergillus. Cases of T lymphocytopenia observed, for example in

* Corresponding author.
E-mail address: cedric.de-bazelaire@sls.aphp.fr (C. de Bazelaire).

2211-5684/$ – see front matter © 2013 Éditions françaises de radiologie. Published by Elsevier Masson SAS. All rights reserved.
http://dx.doi.org/10.1016/j.diii.2012.12.008
patients with lymphoma or leukaemia, are responsible for a cell immune deficiency, which makes these patients more sensitive to viral infections (HSV, EBV, CMV, etc.), intracellular bacterial infections (mycobacteria, Nocardia, Legionella) and intracellular mycoses (pneumocystosis, toxoplasmosis, etc.). Humoral deficiencies related to cases of B lymphocytopenia are observed in patients with myeloma, Waldenström’s macroglobulinaemia, chronic lymphoid leukaemia and chemotherapy promote intracellular bacterial and viral infections and encapsulated bacterial infections (Staphylococcus pneumoniae, Haemophilus influenzae, Staphylococcus aureus).

Hospital-acquired infections can also occur, such as, for example, septic embolisms originating from central catheters (S. aureus, Pseudomonas aeruginosa or Candida) or aspiration pneumonia from mucitis or gastritis that promotes the colonisation of the oro-pharynx by Gram-negative bacilli (P aeruginosa, Enterobacter, Klebsiella, Escherichia coli and Acinetobacter) [1]. Finally, certain non infectious lung diseases can be distinguished from infectious lung diseases: tumoural progression, the onset of a broncho-pulmonary cancer, pulmonary infarction (septic or cronic infarctions), acute pulmonary oedema (cardiotoxicity of chemotherapy, overload), alveolar bleeding due to thrombocytopenia (allograft, chemotherapy, bone marrow insufficiency, etc.), diffuse alveolar damage (severe sepsis, toxicity) and alveolar proteinosis that promotes infections caused by Nocardia (myelodysplasia, immunoglobulin deficiency). Finally, lesions related to radiation (consolidation, organised lung disease) or drug-induced toxicity must also be considered. The time between complications and treatment is important data to be taken into account [2]. Therefore, during the neutropoenia of the first month, bacterial and fungal infections (aspergillusosis, candidiasis) will be encountered more frequently. Then, during the first 3 months, pneumocystosis and tuberculosis should be screened for. Patients can then develop tuberculosis, bacterial infections (S. pneumoniae, H. influenza), viral infections (VZV) that must be distinguished from interstitial pneumonia, obliterating bronchiolitis lesions and malignant lesions. In the same way, a prolonged corticosteroid treatment for more than 3 weeks during the last 2 months is a factor that promotes aspergilliosis.

The high resolution scan, the clinical data and the laboratory samples (blood samples, broncho-alveolar lavage, transbronchial biopsies) make it possible to obtain the aetiological diagnosis of the pneumopathy in more than 70% of cases. On the other hand, for the remaining patients, the scan images are not specific, the test treatments are ineffective and the samples turn out to be sterile or inconclusive (Fig. 1). In addition, several complications can develop at the same time and must be recognized. For these patients, percutaneous lung biopsy (PLB) guided using a scan is an absolutely necessary diagnostic tool. Since 1976, many publications have shown that PLB is a simple and effective technique [3–10]. It makes it possible to screen for infectious lung disease and to rule out other diagnoses. However, the use of PLB is often impeded by the fragile condition of the patients, who often have haemostasis disorders (thrombocytopenia, anticoagulant treatment). In the same way, the respiratory “reserve” of these patients is often limited due to underlying parenchymatous lesions (sequela of radiotherapy, infections, drug toxicity) and the onset of pneumothorax during or after the biopsy can considerably worsen respiratory insufficiency.

The objective of this review is to present the important technical points that could improve the performance of PLB by limiting the risk of complications.

Preparation of the patient

CT-guided punctures are carried out under local anaesthesia. First, it is absolutely necessary to explain to the patient what is at stake with the biopsy, while insisting on his or her role and the importance of his or her cooperation. It is also recommended to have the patient sign an informed consent form after having given him or her fair and appropriate explanations. The fasting condition of patients is controversial. If there is an exceptional haemorrhagic complication, it makes easier surgical or resuscitation treatment possible. However, it promotes the onset of vasovagal syncope, or hypoglycaemia in diabetic patients, much more frequently. An approach via the venous route is absolutely necessary for lung biopsies. It is exceptionally used due to uncontrolled bleeding, but it can be very useful in cases of pain or vasovagal syncope. An emergency cart or an oxygen tank must be rapidly accessible in order to be able to carry out emergency first aid. In the same way, a monitoring system for saturation and blood pressure and a scope must be close at hand.

Haemostasis can be controlled using different tests: the prothrombin time (PT) calculated using the Quick time (QT) and the International Normalized Ratio (INR), (QTpatient / QTcontrol) make it possible to control the extrinsic route of coagulation (factors II, V, VII and X). PT is reduced in patients being treated with vitamin K antagonists or those with hepatocellular insufficiency or DIC. The PT is normally between 70 and 100%. Normal INR values are between 0.8 and 1.2. The INR must be systematically checked before conducting a lung biopsy and corrected if it exceeds 1.5 [11]. The PTT (partial thromboplastin time) explores the intrinsic route of coagulation (factors VIII, IX, XI and XII), which is increased in patients being treated with heparin, vitamin K antagonists, circulating antiphospholipid antibodies (lupus) or those with hepatocellular insufficiency, DIC, von Willebrand disease and haemophilia. The PTT must be measured in all of these clinical situations. A normal PTT varies between 25 and 39 s. The PTT ratio (PTT patient / PTT control) must be less than 1.2. On the other hand, there is no consensus on systematic use of PTT [11]. Fibrinogen (factor I) increases in cases of infection or inflammation and decreases in cases of DIC. In risky situations, it must be measured, and its concentration should be between 1.8 and 4 g/L. Platelet levels must be controlled routinely before conducting a biopsy in this at risk population and corrected by transfusion if the levels are below 50,000/μL. Treatments with Plavix and aspirin must be suspended 5 days before the procedure. Low molecular weight heparins must be stopped 24 h ahead of time.

There are no recommendations concerning respiratory treatment, which is the framework for the PLB. However, most practitioners recommend not biopsying patients with
Figure 1. CT-scans in high diagnostic resolution (a, b and c) and CT-guided scan of percutaneous lung biopsies (d, e and f) in three patients treated for haematological malignancies. The poorly delimited, spiculated, consolidating mass-type lesions are not specific. The percutaneous biopsies found tuberculosis (a and d), mucormycosis (b and e) and MALT lymphoma (c and f).
Diagnostic hypotheses

Interventional radiologists and clinical practitioners must discuss the diagnostic hypotheses before the procedure and define the diagnoses to be screened for first in order to limit the number of samples to be taken. The conditioning of the samples must be suited to the diagnostic hypotheses. Three types of conditioning are predominant: fixation in all cases, freezing in case of a suspected solid cancer or haemopathy and fresh samples to screen for bacterial, viral or fungal infections (Fig. 2).

Fixation

Fixed samples allow for morphological (histological) and immunohistochemical study. The biopsy fragments must be immediately immerged in a fixing liquid such as 10% buffered formaldehyde or a mix of alcohol, formaldehyde and acetic acid. They are then sent to the anatomical pathology lab. The immunohistochemistry makes it possible, thanks to the use of monoclonal antibodies, to detect membrane antigens (ex: CD20 marker for B lymphocytes), cytoplasm antigens (ex: CD79a) or nuclear antigens (ex: P53, cyclin D1 or Ki67). Immunohistochemical studies can be carried out on fixed or frozen samples. They have a preponderant role for the diagnosis and treatment, as they make it possible to prescribe targeted treatments for which the efficacy has been proven.

Freezing

Often, the samples are put on a compress soaked in normal saline and rapidly sent to the anatomical pathology lab where they are frozen. There are two disadvantages:

• the time for transfer to the laboratory is variable;
• this conditions the time the biopsy is carried out.

We recommend direct freezing in the radiology department. The sample must be frozen quickly, as the half-life of RNA is 10 min under the effect of RNAases. Each biopsy core is placed on a thin sterile slide made of transparent plastic, then inserted into an identified tube. Then, this tube is placed in a canister and immersed in a tank of nitrogen at −80 °C. Freezing is immediate.

Freezing makes it possible to conduct molecular biology analyses. They are useful for determining the type of lymphoma: screening for Bcl2 transcription (B lymphoma), Bcl1 (mantle cell lymphoma) or Akl (anaplastic lymphoma). Screening for B or T clonality is also possible. The new methods of molecular biology by microarray applied to human tissues (DNA array, proteomic and protein array, CGH array, tissue microarray, etc.) theoretically make it possible to identify several thousand biological markers on the scale of the genome, transcriptome and proteome. These frozen cores are also a reserve to complete the examinations when morphology and immunohistochemistry turn out to be insufficient. In the same way, it is possible to resuscitate bacteria.
using frozen samples when cultures turn out to be insufficient for diagnosis.

**Fresh samples**

The obtaining of fresh samples is reserved in particular for screening for pathogenic agents. The two key points are the use of sterile tubes and a time of transfer to the laboratory that is as short as possible. The samples for virological study are rarely taken and must be interpreted along with the markers for blood replication. If there is a risk of late transfer of the sample (laboratory far away from the sampling site), it is possible to use specific viral transport media. Then, the identification of the different viruses is carried out after grinding of the sample by cell culture or by identification of nucleic acids in molecular biology.

**Appositions**

In emergency situations, it is possible to carry out appositions. A core sample is placed directly on a slide, rolled, and then removed before being fixed. The cells located at the surface of the core sample are transferred to the slide and leave an imprint of the tissue like a stamp would after inking. It is therefore a cytological study with a certain degree of information concerning the tissue architecture.

**Choice of the target**

A thoracic CT-scan must be carried out before every biopsy. This examination makes it possible to direct the fibroscopy, thus improving its performance. The scan can also show peripheral lesions that are inaccessible by fibroscopy and can encourage the clinical practitioner to do a PLB directly. On the other hand, the scan can find diffuse consolidations or areas with a ground-glass appearance that are better analysed by bronco-alveolar lavage than by biopsy. There should be no hesitation with regard to repeating the thoracic CT-scan and discussing the indication of the PLB again if the clinical course of the patient makes it seem that the pulmonary lesions could have changed before the biopsy. The thoracic CT-scan is also used to guide the procedure. The trajectory of the puncture must be as short as possible and avoid crossing fissures, emphysema bubbles, bronchial tubes and blood vessels. The internal thoracic vessels must be located and avoided in anterior approaches. The position of the patient in the CT-scan should be adjusted to the approach: procubitus for posterior approaches, decubitus for anterior approaches and lateral decubitus for lateral approaches.

It is preferable to biopsy masses and nodules rather than consolidations (Fig. 3). Lung biopsies are in fact more effective in the nodules (57%) and masses (71%) than in the consolidations (50%) [12]. The poor performance of biopsies in consolidations is due on one hand to the aetiologies responsible for consolidations and on the other hand, to the physiology of the lung. Consolidations are a type of presentation that is commonly found in infections. However, the positive diagnosis of infection is more complex than that of tumours due to the limited performance of bacterial culture, which depends on the entire chain of events: the PLB, the type of conditioning, the duration of transport and the culturing process. Certain teams propose culturing immediately after sampling, but the strictly aseptic conditions necessary at the time of culture limit the use of this method. The radiological semiology explained by the physiology of the lung makes the biopsy more complex. The areas of consolidation

![Figure 3](image_url)

**Figure 3.** High resolution CT-scans. a: the biopsy made it possible to diagnose organized pneumopathy in a 65-year-old patient being treated for non-Hodgkin’s lymphoma; b: discovery of an adenocarcinoma by percutaneous lung biopsy in a 63-year-old patient being treated for non-Hodgkin’s lymphoma. The diagnostic performance of the biopsy of the alveolar consolidation of the patient in (a) is theoretically lower than for the mass of the patient in (b). The risk of pneumothorax in the patient in (a) is higher, as the lesion is located less than 2 cm from the pleural cavity. On the other hand, the risk of complications is the same for consolidation as for a mass.
on the CT-scan are in fact made up of an infectious or tumoural area and a peripheral region of reactive inflammatory tissue or atelectasis. The limit between these different entities is usually not visible and many puncture are negatives because they are made in the atelectasis. It is possible to use a PET-scan for assistance in guiding the biopsy in the hyper-fixing pathological area [13–15]. However, a PET-scan is not always available before biopsy. Qi et al. propose distinguishing between pathological areas that have restricted diffusion on the MRI and areas of atelectasis characterised by free diffusion (Fig. 4) [16]. Finally, for Hur et al., the overall sensitivity and the precision of the PLB in lesions with a ground-glass appearance are 71% and 82%, respectively [17].

The precision of the diagnosis depends on the size of the lesion [18,19]. It is preferable to aim for voluminous lesions to improve the diagnostic performance [18–23]. However, certain operators find no significant difference in terms of diagnostic performance between lesions superior and inferior to 2 cm in diameter (Fig. 5) [24,25]. The precision and sensitivity of the CT-guided PLB for large nodules (> 15 mm) are 91% and 94%, respectively, while the precision and sensitivity decrease for small nodules (< 10 mm) to 88% and 82%, respectively [26]. When the target is smaller than the sampling window (20 mm), a puncture trajectory that makes it possible to sample the largest amount of abnormal tissue should be used. A biopsy trajectory parallel to the largest axis of the target should therefore be favoured in order to place the largest possible part of the sampling window in the pathological tissue and reduce as much as possible the taking of healthy tissue that has no diagnostic interest located around the target. During the biopsy, it is useful to control the position of the sampling window compared to the target with scan cuts without injection. The control cuts make it possible to position things so that the target is at the centre of the sampling window in order to sample the most pathological tissue possible (Fig. 6). In the same way, the diagnostic precision is better for short puncture trajectories (90% if the trajectory is less than 40 mm) than for long trajectories (56% if the trajectory is greater than 40 mm) (Fig. 6) [26].

In cases of infectious multifocal pulmonary lesions, micro-abscesses are often found in other organs such as the liver or the spleen. Targeted liver biopsy on micro-abscesses can be an interesting alternative to PLB that is still effective on infra-centimetric nodules (Fig. 7). The diagnostic performance of liver biopsies to screen for infection is comparable to that of lung biopsies [27].

Quantity of sampled material

Calibre of the guns

Anatomical pathologists are more efficient when they interpret samples taken with an 18-gauge (diameter = 1.2 mm) gun than with a 20-gauge (diameter = 0.8 mm) gun [28]. They obtain approximately two times more material per core sample with the 18 G than with the 20 G. The overall diagnostic precision of the biopsies is 96% with needles with a calibre of 18 G and 92% with needles with a calibre of 19 G, with sensitivities of 95% and 89% and specificities of 100% and 99%, respectively [29].

Number of samples

To our knowledge, there are no particular recommendations for the number of samples to be taken during PLBs in patients being treated for haematological malignancies. In our
experience, it appears that the optimal number of samples to be taken is between three and four (personal non-published data). The increase in the number of samples beyond four does not increase diagnostic performance. It is therefore important to define the diagnostic hypotheses with the clinical practitioner and to agree on two or three differential diagnoses that are to be favoured. In this way, if there is a suspected fungal infection in an immune depressed subject during treatment for a haematological malignancy, a first sample must be placed in a dry tube and quickly cultured in order to confirm colonisation. The presence of fungal filaments can also be found in histological cuts, which requires a second sample to be fixed and stained (Grocott). The invasive character of a fungal infection is confirmed in the fixed samples [30–32]. A third sample must systematically be fixed in the AFA and stained with HES to rule out a specific lesion of the haematological disease. Finally, a fourth frozen sample is recommended in our example. This frozen sample will be absolutely necessary if there is a haematological lesion for the characterisation of the disease (lymphoma, for example) or could be used in histology or bacteriology depending on the needs (Fig. 8). During the biopsy, samples must be taken using the sextant technique by inclining the gun in the target before pushing the trigger in a different direction for each sample so as not to biopsy the cavity left by the preceding biopsies. The quality of the biopsy core samples is improved when the tissue is pushed down in the sample window before selecting it. To do this, the gun simply needs to be inclined again by approximately 10 degrees [15].

Complications

The complications occurring during lung biopsies in patients being treated for a haematological disease are largely the same as in the general population, though these patients more often have hemostasis disorders. The operators must check their practice and calculate the rate of complications. The risks should be clearly explained to the patients in order for them to be able to give their informed consent before the procedure. The complication rates of lung biopsies accepted in the literature are, for example, 20.5% of pneumothorax,
CT-guided biopsies in lung infections

3.1% of which require the insertion of a thoracic drain, and 5.3% of hemoptysis.

Serious complications

The risk of death caused by lung biopsy is exceptional (<0.15%) [33]. Serious complications requiring a specific treatment are rare and include drained pneumothorax, haemopericardium, hemothorax, hemoptysis and intense pain [4,34–36]. The rates of the main complications are summarized in Table 1. The rate of complications during PLB does not depend on the appearance of the lesion on the scan [12].

Pneumothorax

The insertion of a thoracic drain to treat iatrogenic pneumothorax occurs in 3 to 15% of all biopsies [25]. The risk generally occurs for lesions located less than 2 cm from the pleural cavity [37]. In the majority of cases, the thoracic drain can be withdrawn within 48 h. When the pulmonary parenchyma is destroyed (emphysema, GVH lesions, etc.), the thoracic drain can be left in place for a longer period of time.

Figure 6. Biopsy of a centimetric nodule of the lower left lobe in a patient being followed for non-Hodgkin’s lymphoma. The lung biopsy revealed a bronchial adenocarcinoma. The control cuts made it possible to get into a position so that the target is at the centre of the sampling window in order to take the most abnormal tissue possible.

Figure 7. Infection caused by Geotrichum clavatum diagnosed via ultrasound-guided liver biopsy in a febrile patient being treated for acute myeloid leukaemia. In cases of infectious lesions with hematogenic dissemination, micro-abscesses are often found in other organs than the lungs, such as the liver or the spleen. The targeted liver biopsy of the micro-abscesses can be an interesting alternative to percutaneous lung biopsy that is less efficient on infra-centimetric nodules.
Figure 8. Percutaneous lung biopsy in a 73-year-old patient treated for lymphoplasmocytary non-Hodgkin’s lymphoma in 2002, and secondary myelodysplasia in 2010 with pancytopenia (30,000 platelets). The nodules with a ground-glass halo and the clinical history are suggestive of fungal infection, bacterial infection or progression of the lymphoma. Three samples were taken: the sample fixed in AFA and the freezing made it possible to establish EBV-induced lymphoproliferation confirmed by EBV PCR measured at 7.07 log.
Table 1 Complication CT-scan guided percutaneous lung biopsies in the general population.

<table>
<thead>
<tr>
<th>Complication</th>
<th>Risk (%)</th>
<th>Number of procedures</th>
<th>Calibre</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumothorax (total/chest tube)</td>
<td>23/5</td>
<td>660</td>
<td>19G CNB</td>
<td>[51]</td>
</tr>
<tr>
<td></td>
<td>62/31</td>
<td>61</td>
<td>18G PNAB</td>
<td>[26]</td>
</tr>
<tr>
<td></td>
<td>28/2.5</td>
<td>162</td>
<td>22G PNAB</td>
<td>[19]</td>
</tr>
<tr>
<td></td>
<td>26/8</td>
<td>846</td>
<td>19G PNAB</td>
<td>[29]</td>
</tr>
<tr>
<td></td>
<td>21/2</td>
<td>97</td>
<td>19G PNAB</td>
<td>[8]</td>
</tr>
<tr>
<td></td>
<td>17/2</td>
<td>135</td>
<td>17G CNB</td>
<td>[37]</td>
</tr>
<tr>
<td></td>
<td>17/0.5</td>
<td>605</td>
<td>19G CNB</td>
<td>[52]</td>
</tr>
<tr>
<td>Bleeding (total/haemoptysis)</td>
<td>30/4</td>
<td>660</td>
<td>19G CNB</td>
<td>[51]</td>
</tr>
<tr>
<td></td>
<td>1/2</td>
<td>846</td>
<td>19G PNAB</td>
<td>[29]</td>
</tr>
<tr>
<td></td>
<td>27/6</td>
<td>135</td>
<td>17G CNB</td>
<td>[37]</td>
</tr>
<tr>
<td></td>
<td>20/3.8</td>
<td>604</td>
<td>19G CNB</td>
<td>[52]</td>
</tr>
<tr>
<td>Vasovagal syncope</td>
<td>0.3</td>
<td>846</td>
<td>19G PNAB</td>
<td>[29]</td>
</tr>
</tbody>
</table>

Bleeding

Alveolar bleeding is observed in 5 to 30% of patients and haemoptysis in between 1.25 and 5% of cases [33,38]. The depth of the lesion (> 2 cm from the pleural cavity) has been identified as the most important risk factor for alveolar bleeding [39]. The hemothorax rate is low and is estimated to be 1.5%. Haemothorax can result from the accidental puncture of the internal thoracic or intercostal blood vessels [40]. The rate of complications during PLB does not increase in patients with thrombocytopoenia [41].

Pain

Pain is a rare complication (0.3% of patients) and can occur despite local anaesthesia without any cause being identified [29]. The pain can be accompanied by vasovagal syncope, a desaturation in oxygen or a drop in blood pressure. All of these symptoms generally regress spontaneously. However, this acute pain should result in screening for a complication and requires monitoring. Therefore, after the procedure, the patients are generally monitored in the day hospital for a few hours.

Minor complications

Minor complications are common (30 to 60%) of procedures and include pneumothorax of low abundance (17 to 60%) and alveolar bleeding (5 to 30%) [37]. Generally, these complications are asymptomatic and regress spontaneously. The risk of pneumothorax or bleeding increases with targets of less than 2 cm. The risk of pneumothorax increases for peripheral lesions located less than 2 cm from the chest wall (Fig. 9). Long trajectories for intra-pulmonary punctures (> 4 cm) are also associated with a larger number of cases of alveolar bleeding and pneumothorax. The risk of bleeding and pneumothorax also increases with the pleural cavity is crossed several times during the puncture. The duration of the procedure must also be as short as possible in order to reduce the rate of pneumothorax [37].

Performance

The number of lung biopsies has increased considerably over the course of the last decade. Several large studies have shown that the sensitivity and precision of PLB were greater than 80% (Table 2). The rate of false positives is generally less than 1% [42,43] and the rate of false negatives is less than 5 to 10% [44–46].

Lung biopsy makes it possible to diagnose up to 70% of infections with a sensitivity of 70% and a positive predictive value of 100% [47,48]. Lung biopsy is more effective for bacterial infections (100%) than for fungal infections (30 to 70%). The usual techniques such as thoracic CT-scan, BAL and cultures rarely make it possible to establish a diagnosis of fungal infection. BAL is usually carried out in patients with neutropenia if the imaging suggests a fungal infection, but this method has a sensitivity of 50% for aspergillosis [30–32]. Endoscopic procedures can detect a colonisation, but cannot demonstrate the invasive nature of the infection. Transbronchial biopsies, carried out when the platelet count is greater than 50 × 10⁹/L only slightly improve the precision of the diagnosis compared to exploratory fibroscopy without biopsy [30]. The histological results are often more effective than cultures for the diagnosis of bacterial and fungal infections. Cultures are positive in less than 40% of patients with aspergillosis or a mucormycosis [48]. The cultures are negative or late, particularly in patients with neutropenia due to an empirical antibacterial or antifungal treatment administered before the biopsy [49]. False positives for fungal or bacterial infection are also possible with cultures. Aspergillus is a common saprophyte and a positive culture is not proof of an infection. The diagnosis is therefore based on the demonstration of histological signs of tissue invasion. The biopsy makes it possible to distinguish aspergillosis and mucormycosis. This histological distinction is very important, as mucorales are generally resistant to azole derivatives and echinocandins, so that only amphotericin B can be used as treatment or secondary prophylaxis during transplants (Fig. 10). In addition, the histological results allow for an immediate diagnosis by showing necrosis containing numerous filamental fungi in case of fungal
infection. If there is a bacterial infection, the histology shows granulomas and infiltrates composed of neutrophil granulocytes or histiocytes.

CT-scan guided PLB is a reliable method for distinguishing malignant lesions of pulmonary infections. The diagnostic performance is well documented, with precision greater than 93% [21,50] and sensitivity greater than 95% [25,34,50]. The diagnosis of lymphoma is generally established by biopsy in 90% of patients. In cases of primary cancer in patients being treated for haematological malignancies, the PLB makes it possible to establish the diagnosis nine times out of 10 [29]. False negatives are generally explained by samples

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Performance of CT-scan guided percutaneous lung biopsies in the general population.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sensitivity (%)</td>
</tr>
<tr>
<td>Total</td>
<td>82</td>
</tr>
<tr>
<td></td>
<td>87</td>
</tr>
<tr>
<td></td>
<td>91</td>
</tr>
<tr>
<td>Cancers</td>
<td>89</td>
</tr>
<tr>
<td>&lt; 10 mm</td>
<td>88</td>
</tr>
<tr>
<td>&lt; 10 mm</td>
<td>67</td>
</tr>
<tr>
<td>&lt; 15 mm</td>
<td>72</td>
</tr>
<tr>
<td>&gt; 15 mm</td>
<td>94</td>
</tr>
<tr>
<td>&gt; 20 mm</td>
<td>75</td>
</tr>
<tr>
<td>Infections</td>
<td></td>
</tr>
<tr>
<td>Fungal</td>
<td>70.6</td>
</tr>
</tbody>
</table>
CT-guided biopsies in lung infections

Figure 10. Percutaneous lung biopsy in a patient being treated for acute myeloblastic leukaemia with febrile neutropoenia. a: suspicion of aspergillosis on the high resolution lung CT-scan performed in January 2007; b: the control scan after 1 month of treatment with voriconazole showed an unfavourable course. The clinical practitioner then suspected progression of the haemopathy, fungal infection and a bacterial infection. Three samples were taken: the sample fixed in AFA and the cultures made it possible to establish a diagnosis of mucormycosis infection. The freezing was carried out for the characterisation of any lymphoma.

taken in zones of inflammatory reorganization or necrosis. The biopsies also make it possible to diagnose organized pneumopathy, GVH and benign tumours.

PLB seems to have a benefit in patients who are severely immune depressed, but the rate of precise diagnoses is generally lower in immune depressed patients (40%) than in the immune competent group (90%). Missed diagnoses are generally fungal infections confirmed later on. However, PLB appears to contribute in half of these patients and generally shows an infection. The other diagnoses include GVH, organized pneumonia and lymphoma.

Conclusion

CT-scan guided percutaneous lung biopsies in patients being treated for haematological malignancies are useful for the diagnosis of pulmonary infection and make it possible to rule out a malignant tumoural lesion with great precision. The performance of the percutaneous lung biopsies is related to the size and the appearance of the lesion as well as the calibre of the samples. The risks of percutaneous lung biopsy are limited and the complications are generally benign, including alveolar bleeding and pneumothorax. These complications are associated with the size of the lesion and the depth. The discussion between the haematologist, pneumologists, pathologist and interventional radiologist is essential to establish the indications for the biopsy, select the best target and define the diagnostic hypotheses.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References


