2 Missed Lung Lesions: Side-by-Side Comparison of Chest Radiography with MDCT

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Learning Objectives

- To be aware of the actual risks of misdiagnosis when reading chest radiographs
- To learn the best tips and tricks for reducing your error rate
- To understand the limitations of chest radiographs compared with multi-detector CT

2.1 Introduction

Missed lung lesions are one of the most frequent causes of malpractice issues [1–3]. Chest radiography plays an important role in the detection and management of patients with lung cancer, chronic airways disease, pneumonia and interstitial lung disease. Amongst all diagnostic tests, chest radiography is essential for confirming or excluding the diagnosis of most chest diseases. However, numerous lesions of a wide variety of disease processes affecting the thorax may be missed on a chest radiograph. For example, the frequency of missed lung carcinoma on chest radiographs can vary from 12 to 90%, depending on study design [4]. Despite the lack of convincing evidence that screening for lung cancer with the chest radiograph improves mortality, chest radiography is still requested for this purpose. The chest radiograph will also help narrow a differential diagnosis, help to direct additional diagnostic measures and serve during follow-up. The diagnostic usefulness of the radiograph will be maximized by the integration of the radiological findings with the clinical features of the individual patient. In this chapter, we will review the more important radiological principles regarding missed lung lesions in a variety of common chest diseases, with a special focus on how correlation with multi-detector CT (MDCT) of missed lung lesions can help improve interpretation of the plain chest radiograph.

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2.2 Reasons for Missed Lung Lesions

Conditions contributing to missed lung lesions, especially carcinomas, have been extensively studied [2, 4–6]. Poor viewing conditions, hasty visual tracking, interruptions, inadequate image quality and observer inexperience are amongst the most important [5, 7, 8]. Features of lesions themselves, when faced with nodules, such as location, size, border characteristics and conspicuity, also play a role [5]. Missed lung nodules during initial reading of a chest radiograph are not uncommon. Missing a nodule which may represent malignancy will have adverse consequences on patient management, essentially through delayed diagnosis, which may carry medicolegal implications. A number of authors have explored the reasons why lesions are overlooked [9–14]. Specific studies have focussed on size [7], contrast gradient [15], conspicuity [16] and anatomic noise [17]. Importantly, other types of errors, named systemic errors, can also occur [18] and include inappropriate orders or imaging utilization, procedure phase errors (patient identification, laterality, technique) and post-procedure phase errors (lighting conditions, transcription errors, communication failures).

One interesting study [19] examined the imaging features of non-small-cell lung carcinoma overlooked at digital chest radiography and compared general and thoracic radiologists' performance for lung carcinoma detection. Frontal and lateral chest radiographs from 30 consecutive patients with lung carcinoma overlooked during initial reading and 30 normal controls were submitted to two blinded thoracic radiologists and three blinded general radiologists for retrospective review. The location, size, histopathology, borders, presence

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of superimposed structures and lesion opacity were recorded. Interobserver agreement was calculated, and detection performance between thoracic and general radiologists was compared. The average size of carcinomas missed by the thoracic radiologists was 18.1 mm (range 10–32 mm). The average size missed by general radiologists was 27.7 mm (range 12–60 mm). Seventy-one percent (5/7) of missed lesions were obscured by anatomical superimposition. Forty-three percent of lesions were located in the upper lobes, and 63% were adenocarcinomas. Compared with general radiologists, the lesions missed by thoracic radiologists tended to be smaller but also had significantly lower CT density measurements and more commonly had an ill-defined margin. The clinical stage of the overlooked lesions did not differ between the two groups ($p = 0.480$). The authors concluded that the lesion size, location, conspicuity and histopathology of lesions overlooked on digital chest radiography were similar to those missed on conventional film screen techniques.

The detection of carcinoma on a chest radiograph remains difficult with implications on patient management. Nowadays, it is still by far the most frequent cause of malpractice suits (42% of cases) [3]. Whereas overlooking chronic airways disease, pneumonia and interstitial lung disease may not have the same potential medicolegal implications, the consequences for patient care could be critical.

We propose to review how correlation with multi-detector computerized tomography (MDCT) of missed lung lesions can help improve interpretation of the plain chest radiograph. During the course of clinical work, when reporting chest CT, whenever available, every effort should be made to review previous chest radiographs and their reports, thereby providing one of the best learning tools for chest radiograph interpretation.

Artificial intelligence will probably replace or modify our work as chest radiologists, minimizing detection errors and helping us to reduce our error rate. Convolutional neural networks have already been reported to provide a sensitivity of 97.3% and specificity of 100% in the detection of tuberculosis on chest X-rays [20].

A CT scan can be performed in patients with a negative chest radiograph when there is a high clinical suspicion of chest disease. CT scan, especially MDCT reconstructed with high-resolution algorithm and iterative reconstruction, is more sensitive than plain films for the evaluation of interstitial disease, bilateral disease, cavitation, empyema and hilar adenopathy. CT is not generally recommended for routine use because the data for its use in chronic airways disease and pneumonia are limited, the cost is high, and there is no evidence that outcome is improved. Thus, a chest radiograph is the preferred method for initial imaging, with CT scan reserved for further characterization (e.g., evaluation of pattern and distribution, detecting of cavitation, adenopathy, mass lesions or collections).

Many methods have been suggested for correct interpretation of the chest radiograph. There is no preferred scheme or recommended system. The clinical question should always be addressed. An inquisitive approach is always helpful and being aware of the areas where mistakes are made is essential. Hidden abnormalities can thus be looked for. The difficult "hidden areas" which must be checked are the lung apex, superimposed over the heart, around each hilum and below the diaphragm. We will concentrate on difficult areas such as lesions at the lung apices or bases or lesions adjacent to or obscured by the hila or heart. For a systematic approach, we will divide the review into three sections representing specific problems: missed nodules, missed consolidation and missed interstitial lung disease. Finally, we will illustrate some of the common signs that may help to detect lesions located in difficult anatomical areas of the chest.

Key Points

- Missing lesions is frequent.
- Hidden areas are at highest risks for missing lesions.
- Missing lesions is a frequent cause of medicolegal issues.

2.3 Specific Problems

Specific problems of missed lung lesions can be divided into missed nodules, missed consolidation and missed interstitial lung disease. In cases of a missed nodule or missed consolidation, the overlooked pathology may have been detected if special attention were paid to known "difficult areas". The examples which follow will show how a side-by-side comparison of the chest radiograph and CT images improves our understanding of the overlooked lesion. There is no harm done by learning from one's mistakes!

2.4 Missed Nodules

2.4.1 Nodular Lesions: Tumours

Nodular lesions are frequently due to lung cancer, which may be primary or secondary. Lung cancer is probably one of the most common lung diseases that radiologists encounter in practice. Berbaum formulated the concept that perception is better if you know where to look and what to look for [21]. Our first example is that of a 53-year-old man who complained of pain in the right axilla for 4 months and underwent chest radiography. The postero-anterior and lateral radiographs were interpreted showing normal findings (Fig. 2.1a and b). The subsequent MDCT showed a right

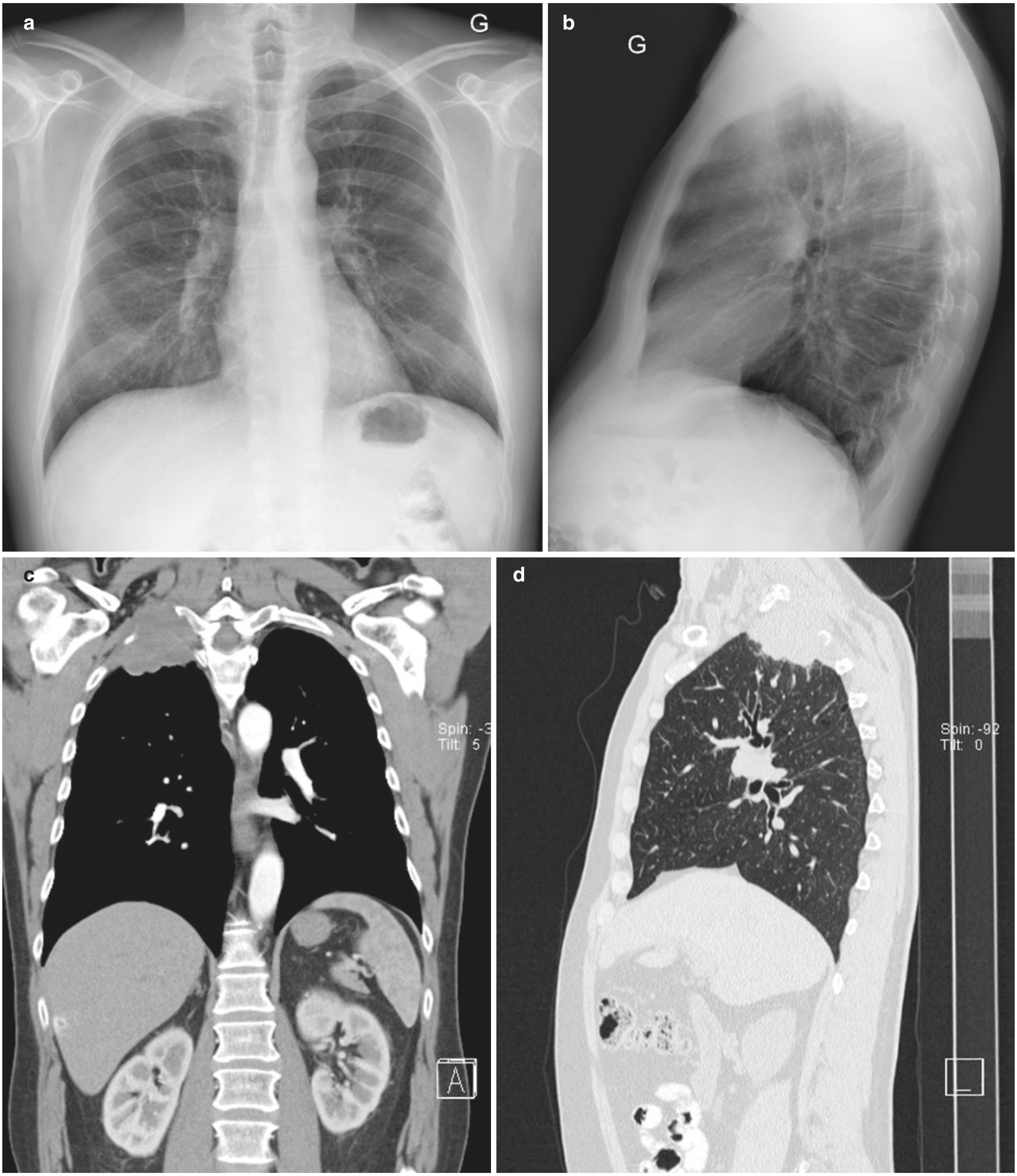

Fig. 2.1 A 53-year-old man who underwent chest radiography for pain in the right axilla. Postero-anterior (**a**) and lateral (**b**) radiographs interpreted as normal. With hindsight bias from MDCT the right apical mass is obvious. MDCT coronal and sagittal images with soft tissue (**c**) and bone (**d**) windows showing a right apical mass with bone destruction

superior sulcus mass with rib destruction (Fig. 2.1c and d). Needle biopsy established a diagnosis of bronchogenic carcinoma (adenocarcinoma). Hindsight bias [22] with the information available from the MDCT makes the initial lesion extremely obvious. Careful scrutiny of both apices is essential when reporting a frontal chest radiograph.

Radiologic errors can be divided into two types [23]: cognitive, in which an abnormality is seen but its nature is misinterpreted, and perceptual or the "miss", in which a radiologic abnormality is not seen by the radiologist on initial interpretation. The perceptual type is estimated to account for approximately 80% of radiologic errors [24].

Our second patient illustrates the complexity of the detection of a lung nodule close to the hilum. A 77-year-old man with known prostate cancer underwent chest radiography for right upper quadrant abdominal pain (Fig. 2.2a and b). The

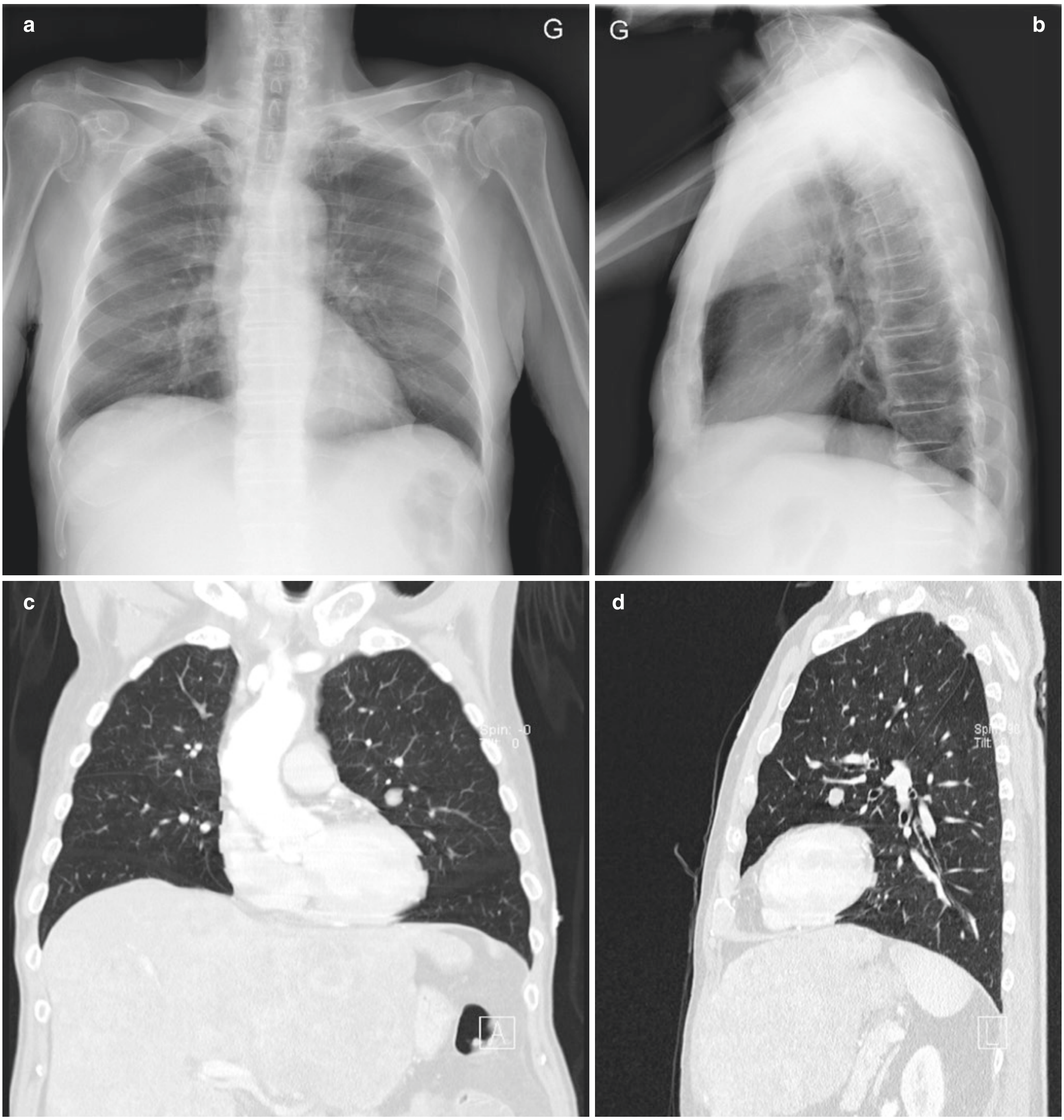

Fig. 2.2 A 77-year-old man with right upper quadrant pain. Posteroanterior (**a**) and lateral (**b**) radiographs interpreted as normal. With hindsight, the 13 mm nodule in the superior segment of the lingula can be seen. Coronal (**c**) and sagittal (**d**) reformats (lung window) show the position of the lingular nodule, close to the hilum

radiographs were reported as normal. The coronal and sagittal reformats demonstrate the position of the nodule (Fig. 2.2c and d), which can be seen clearly with hindsight on the postero-anterior and lateral chest radiographs.

2.4.2 Nodular Lesions: Infections

Nodular lesions attributed to pulmonary infections are most often seen in nosocomial pneumonias and in immunocompromised patients. They may be caused by bacteria such as *Nocardia asteroides* and *M. tuberculosis*, septic emboli and fungi. *Nocardia asteroides* causes single or nodular infiltrates with or without cavitation. Invasive pulmonary aspergillosis (IPA), *mucor* and C*ryptococcus neoformans* may present with single or multiple nodular infiltrates, which often progress to wedge-shaped areas of consolidation. Cavitation (the "crescent sign") is common later in the course of the infiltrate. In the appropriate clinical setting, CT may aid in the diagnosis of IPA by demonstrating the so-called halo sign. Figure 2.3 shows a 43-year-old woman with fever after a bone marrow transplant. The postero-anterior radiograph was interpreted as normal (Fig. 2.3a). With hindsight, a subtle infiltrate can be seen at the left apex. Conspicuity is lessened by the overlying clavicle and first rib. Axial CT image (Fig. 2.3b) shows nodular consolidation

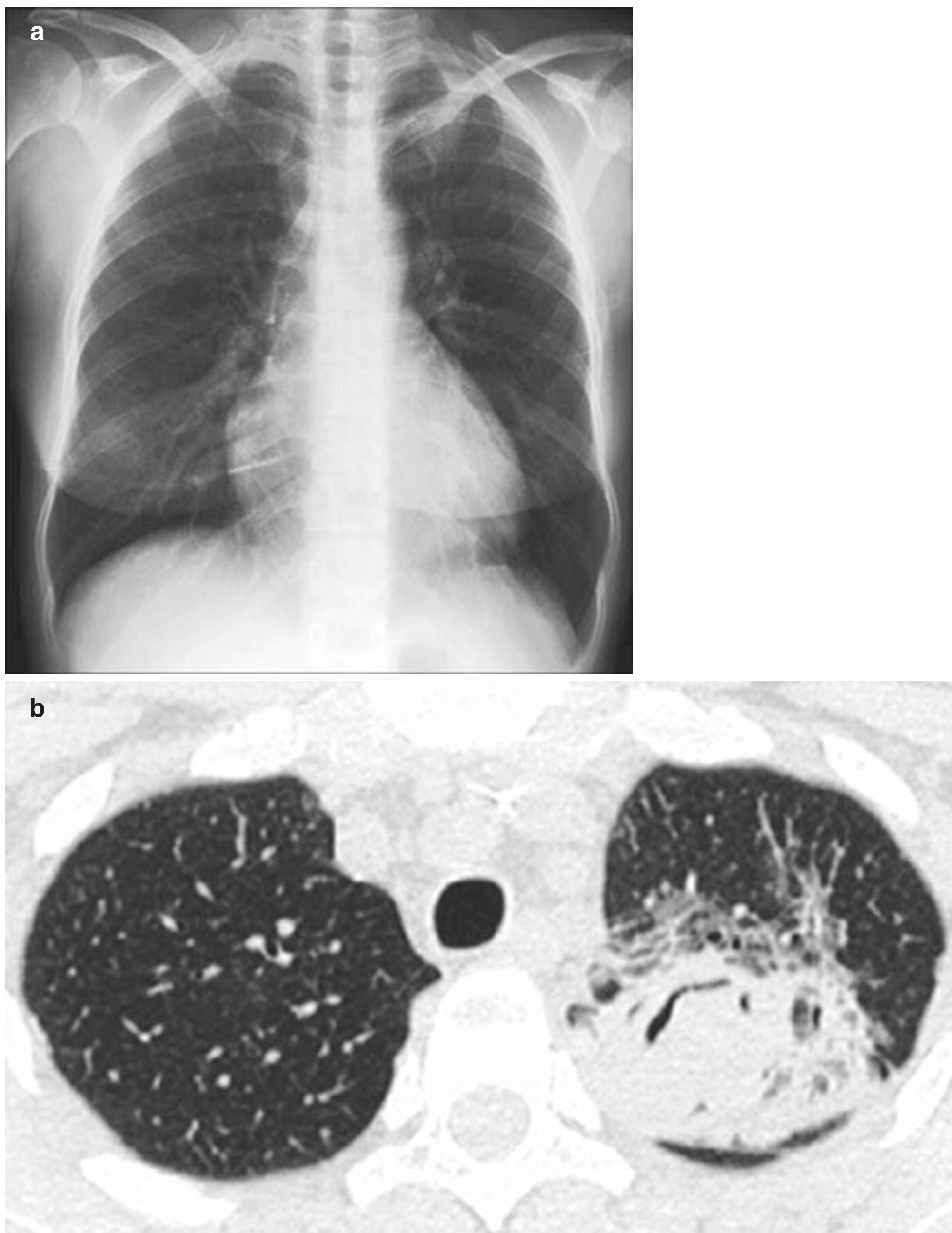

Fig. 2.3 A 43-year-old woman with fever after a bone marrow transplant. Postero-anterior radiograph interpreted as normal (**a**). With hindsight, a subtle infiltrate can be seen at the left apex. Conspicuity is lessened by the overlying clavicle and first rib. Also note the indwelling catheter from the left brachial vein to the superior vena cava. Axial CT image (lung window) shows nodular consolidation with crescentic cavitation (air-crescent sign) and surrounding ground-glass infiltrate (halo sign) (**b**)

with crescentic cavitation (the "crescent sign") and surrounding ground-glass infiltrate (the "halo sign"). These characteristic findings of IPA are best identified on CT.

> **Key Points**
> - Nodule location in hidden areas is the most frequent cause for missing nodules
> - Low nodule attenuation favours missing the lesion
> - Calcified nodules are easiest to detect but not clinically relevant

2.5 Missed Consolidation

2.5.1 Airspace Disease

Airspace disease is usually caused by bacterial infections. However, airspace disease can be seen in viral, protozoal, fungal infections and malignancy, typically brochioloalveolar carcinoma. Acute airspace pneumonia is characterized by a mostly homogeneous consolidation of lung parenchyma, well-defined borders, and does not typically respect segmental boundaries. An air bronchogram is very common. Progression to lobar consolidation may occur. As with lung nodules, whether consolidation is detected or missed on the plain chest radiograph may be determined by any combination the same factors of size, density, location and overlying structures. Location is a significant factor for missed consolidation. Consolidation in the middle lobe and both lower lobes can be difficult to diagnose, especially when only the postero-anterior view is obtained. Figure 2.4 shows a 46-year-old woman with cough and right-sided chest pain. The postero-anterior radiograph was interpreted as normal (Fig. 2.4a). Due to a clinical suspicion of pulmonary embolism, MDCT was requested, showing consolidation in the anterior segment of the right lower lobe. The coronal and sagittal reformats demonstrate the extent of the consolidation (Fig. 2.4b and c). There were no signs of pulmonary embolism on the contrast media study. A diagnosis of right lower lobe pneumonia was established, and the patient was treated successfully with antibiotics.

Chest radiography is the first recommended imaging test for the diagnosis of pneumonia. Chest radiography can diagnose pneumonia when an infiltrate is present and differentiate pneumonia from other conditions that may present with similar symptoms, such as acute bronchitis. The results of the chest radiograph may occasionally suggest a specific aetiology (e.g., a lung abscess) and identify a complication (empyema) or coexisting abnormalities (bronchiectasis, bronchial obstruction, interstitial lung disease). Chest radiography remains a valuable diagnostic tool in primary care patients with a clinical suspicion of pneumonia to substantially reduce the number of patients misdiagnosed. MDCT imaging is useful in patients with community-acquired pneumonia when there is an unresolving or complicated chest radiograph and at times in immunocompromised patients with suspected pulmonary infections. MDCT can help in differentiating infectious from non-infectious abnormalities. MDCT may detect empyema, cavitation and lymphadenopathy when the chest radiograph cannot. MDCT should be performed in immunocompromised patients with a clinical suspicion of pneumonia when the chest radiograph is normal. This is especially true when the early diagnosis of pneumonia is critical, as is the case with immunocompromised and severely ill patients.

> **Key Points**
> - Chest radiography is the first imaging test for the diagnosis of pneumonia.
> - Chest radiographs may help identify complications of pneumonia.
> - Hidden areas are the most frequent reasons for missing pneumonia.

2.6 Missed Interstitial Lung Disease

2.6.1 Diffuse (Interstitial or Mixed Alveolar-Interstitial) Lung Disease

Diffuse lung disease presenting with widely distributed patchy infiltrates or interstitial reticular or nodular abnormalities can be produced by a number of disease entities. An attempt is usually made to separate the group of idiopathic interstitial pneumonias from known causes, such as infections, associated systemic disease or drug related. The most common infectious organisms are viruses and protozoa. In general, the aetiology of an underlying pneumonia cannot be specifically diagnosed because the patterns overlap. It is beyond the aim of this chapter to discuss in detail the contribution of MDCT to the diagnosis of diffuse infiltrative lung disease. For over three decades, the development and then refinement of high-resolution computed tomography (HRCT) have resulted in markedly improved diagnostic accuracy in acute and chronic diffuse infiltrative lung disease. The chest radiograph remains the preliminary radiological investigation of patients with diffuse lung disease but is often non-specific. Pattern recognition in diffuse lung disease has been the subject of controversy for many years. Extensive disease may be required before an appreciable

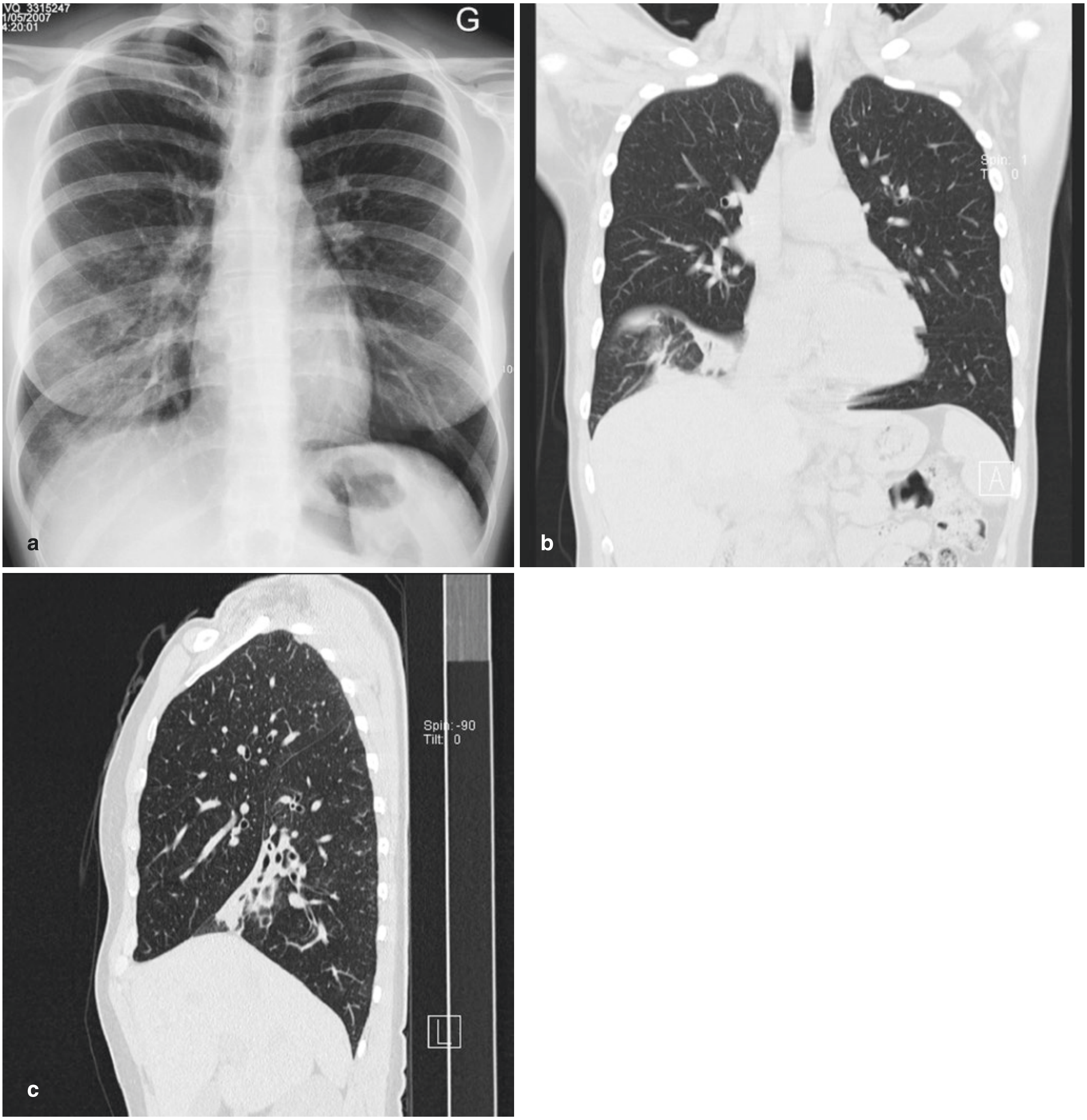

Fig. 2.4 A 46-year-old woman with cough and right-sided chest pain. Postero-anterior radiograph interpreted as normal (**a**). Coronal (**b**) and sagittal (**c**) reformats showing consolidation in the anterior segment of the right lower lobe

change in radiographic density, or an abnormal radiographic pattern can be detected on the plain chest radiograph. At least 10% of patients who are ultimately found to have biopsy-proven diffuse lung disease have an apparently normal chest radiograph. HRCT and now MDCT have become an integral component of the clinical investigation of patients with suspected or established interstitial lung disease. These techniques have had a major impact on clinical practice.

Key Points

- Chest radiography is less sensitive and less specific than MDCT.
- If the chest radiograph is normal, MDCT may be indicated.
- Chest radiographs may be helpful for the follow-up of ILD.

2.7 Key Signs for Reducing the Risk of Errors in CXRs

2.7.1 Deep Sulcus Sign

The deep sulcus sign (Fig. 2.5) is seen on chest radiographs obtained with the patient in the supine position [25]. It represents lucency of the lateral costophrenic angle extending toward the abdomen. The abnormal deepened lateral costophrenic angle may have a sharp, angular appearance. When the patient is in the supine position, air in the pleural space (pneumothorax) collects anteriorly and basally within the nondependent portions of the pleural space; when the patient is upright, the air collects in the apicolateral location. If air collects laterally rather than medially, it deepens the lateral costophrenic angle and produces the deep sulcus sign. In Fig. 2.5, a deep sulcus sign is seen on the left, in addition to a continuous diaphragmatic sign, seen when air is seen between the diaphragm and the heart.

2.7.2 Spine Sign

On the normal lateral chest radiograph, the attenuation decreases (the lucency increases) as one progresses down the thoracic vertebral bodies. If the attenuation increases, locally or diffusely, there must be a posterior located lesion (Fig. 2.6). This lesion might not be seen on the frontal view, hidden by the heart or the hila. Interestingly, the positive predictive value of the spine sign is high (up to 97%) [26].

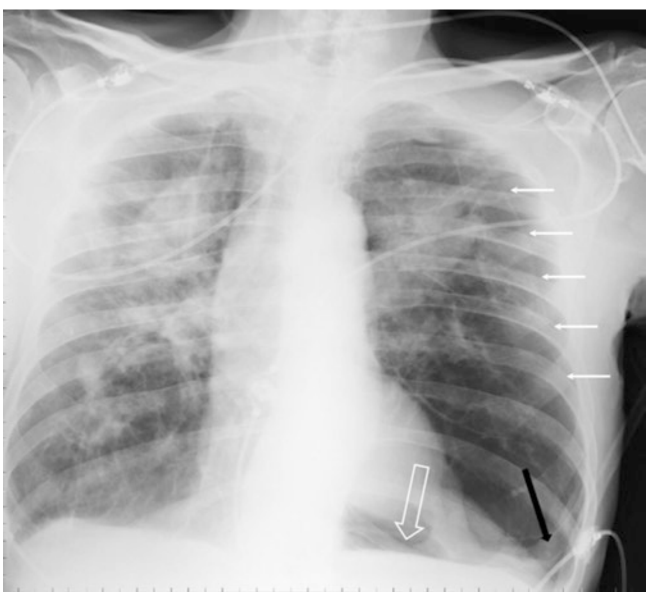

Fig. 2.5 A 78-year-old man with acute left chest pain and previous history of pneumoconiosis. Bedside chest radiograph showing a thin white line near the left chest wall (white arrows), corresponding to the left lung visceral pleura and indicating a pneumothorax. The deep lucency of the left lateral costophrenic angle extending towards the abdomen is an indirect sign of pneumothorax (black arrow). The continuous diaphragmatic sign is also seen as air separating the diaphragm from the heart (white hollow arrow)

2.7.3 Silhouette Sign

In a chest X-ray, non-visualization of the border of an anatomical structure that is normally visualized shows that the area neighbouring this margin is filled with tissue or material of the same density (Fig. 2.6) [27]. The silhouette sign is an important sign indicating the presence and the localization of a lesion.

2.8 Concluding Remarks

Despite the increasing use of CT imaging in the diagnosis of patients with chest disorders, chest radiography is still the primary imaging method in patients with suspected chest disease. The presence of an infiltrate on a chest radiograph is considered the “gold standard” for diagnosing pneumonia. Extensive knowledge of the radiographic appearance of pulmonary disorders is essential when diagnosing pulmonary disease. Chest radiography is also the imaging tool of choice in the assessment of complications and in the follow-up of patients with pulmonary diseases.

MDCT plays an increasing role in the diagnosis of chest diseases, especially in patients with unresolving symptoms. CT will aid in the differentiation of infection and non-infectious disorders. The role of CT in suspected or proven chest disease can be summarized as follows:

1. CT is valuable in the early diagnosis of chest disease, especially in patient groups in which an early diagnosis is important (immunocompromised patients, critically ill patients).
2. CT may help with the characterization of pulmonary disorders.
3. CT is an excellent tool in assessing complications of chest disease.
4. CT is required in the investigation patients with a persistent or recurrent pulmonary infiltrate.

A side-by-side comparison between the chest radiograph and MDCT when confronted with a missed lung lesion is very instructive. The radiologist should be able to understand the reasons for missing certain lesions. By adopting this inquisitive approach, both our cognitive and perceptual errors could be reduced.

Awareness of the dangers of systemic errors has become of upmost concern, as a result of the high examination volume

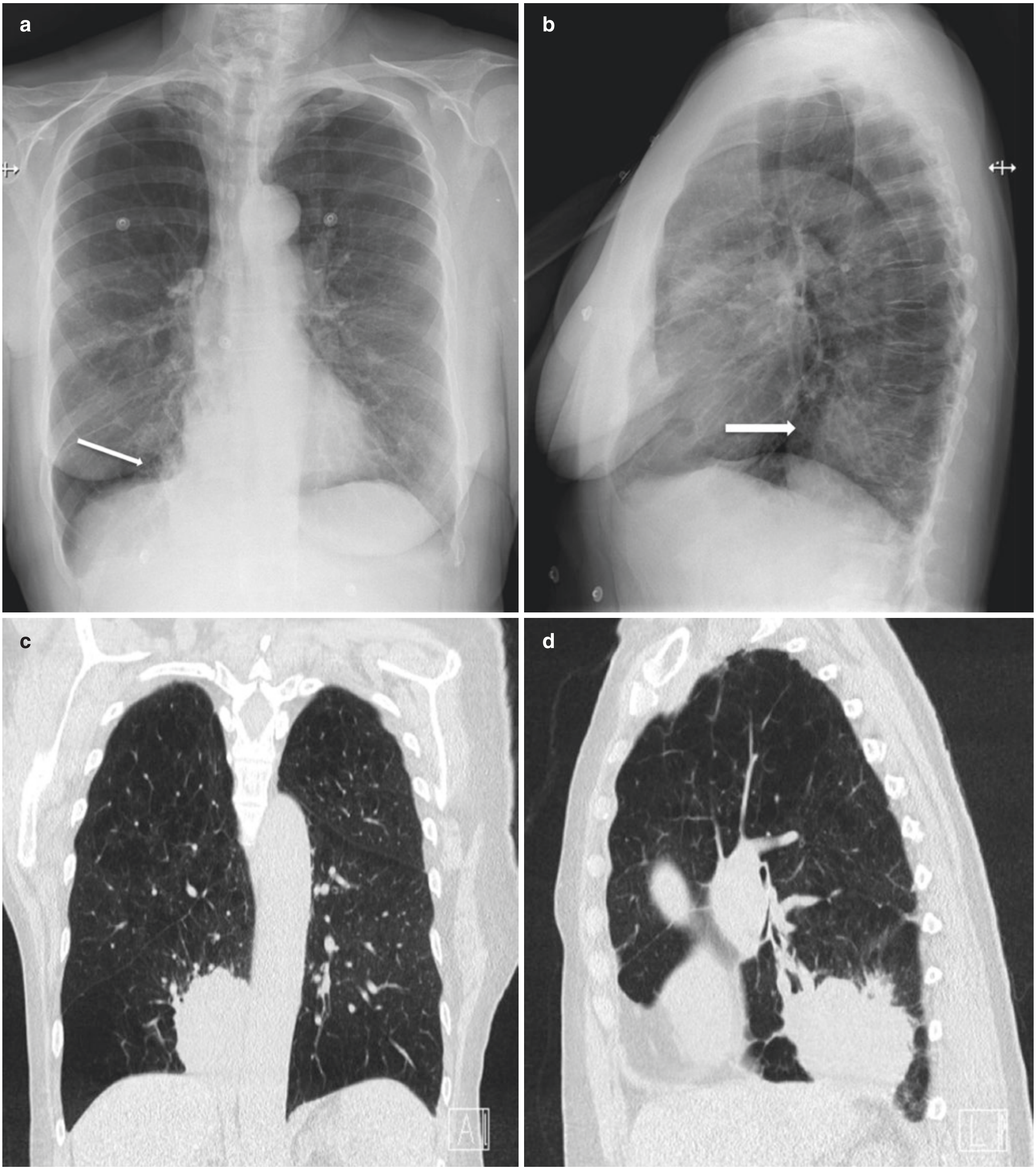

Fig. 2.6 A 69-year-old woman with COPD and haemoptysis. Posteroanterior chest radiograph (**a**) showing an opacity next to the right border of the heart (arrow) and obliterating the right side of the spine. This silhouette sign of the right posterior mediastinal border indicates that the lesion is in a posterior location in the right lower lobe. Lateral view (**b**) showing an increased density (arrow) of the lower spine compared with the upper and middle thoracic spine (spine sign). This increased density is due to a large mass in the right lower lobe. Coronal CT image (**c**) showing the right lower lobe mass obliterating the border of the mediastinum. Sagittal CT image (**d**) showing the posterior location of the mass

and long shifts experienced by radiologists [28]. Double readings and subsequent readings by subspecialists may become common practice, especially if medicine shifts toward physician payment based on quality or outcomes, rather than volume [29]. Artificial intelligence will undoubtedly offer opportunities to improve our diagnostic accuracy, as systems will be developed as adjuncts to human cognition and perception [30].

Artificial intelligence generates fear about the future role of radiologists and their employment. Let us remember that although we analyse many images, we still decide on what imaging examinations should be prescribed and how they are performed best, we confer on difficult diagnoses, we discuss treatment plans with patients and we translate the conclusions of the research literature into real-life practice. If some of the more repetitive tasks can be handled safely by a computerized helper, radiologists will be able to focus on the rewarding ones, improving patient care and safety.

Take-Home Messages
- Be aware that missing lesions is frequent.
- Always look at hidden areas.
- Beware of satisfaction of search.
- Take time to read the lateral view of the chest.
- Learn the key radiologic signs to reduce your error rate.

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