Histopathology of Respiratory System and Mediastinum

15

Rashida Ahmed and Qurratulain Chundriger

Abstract

Biopsies from respiratory system like bronchial and lung parenchymal are among the commonest ones. Besides conventional bronchoscopic biopsies, tiny CT-guided biopsies are also frequent. On the flip side, treating physicians require more and more information not only in terms of a definitive entity but also what therapy they are likely to respond. This puts immense pressure on the pathologists to be highly judicious in performing IHC markers to leave enough tissue for mutational analysis like EGFR, ALK, ROS1 and PD-L1. Among non-neoplastic lesions, 'interstitial lung diseases' are among the most demanding and challenging with subtle and overlapping features requiring quick revision of the subject. Pleural biopsies are also at times challenging. Mediastinal pathology is markedly diverse, and almost any kind of pathology may be seen in this region. In this chapter however our focus is on those entities which are indigenous to this region like various types of thymoma.

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Lung

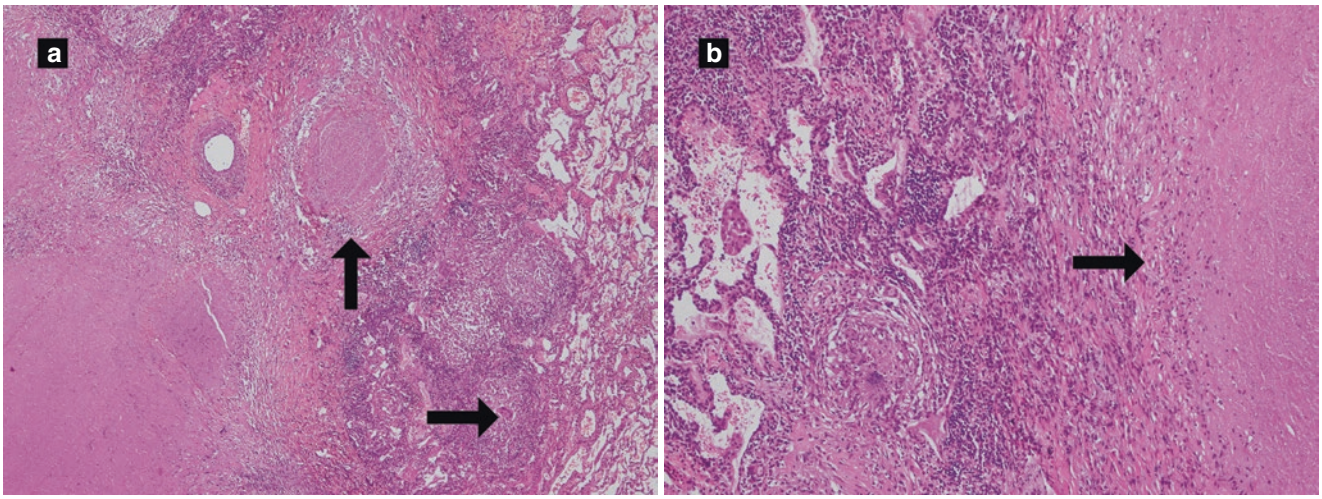

Fig. 15.1 (**a**, **b**) *Pulmonary tuberculosis (TB):* Pulmonary tuberculosis is still very common in third world low-income countries. On microscopy, epithelioid histiocytes form granulomas, typically with central caseous necrosis (**a**↑, **b**→). This necrotic debris is composed of dead histiocytes and mycobacteria, which have abundant lipid content in their cell membranes, resulting in caseous or cheesy type of necrosis. Multinucleated giant cells are commonly seen (**a**→)

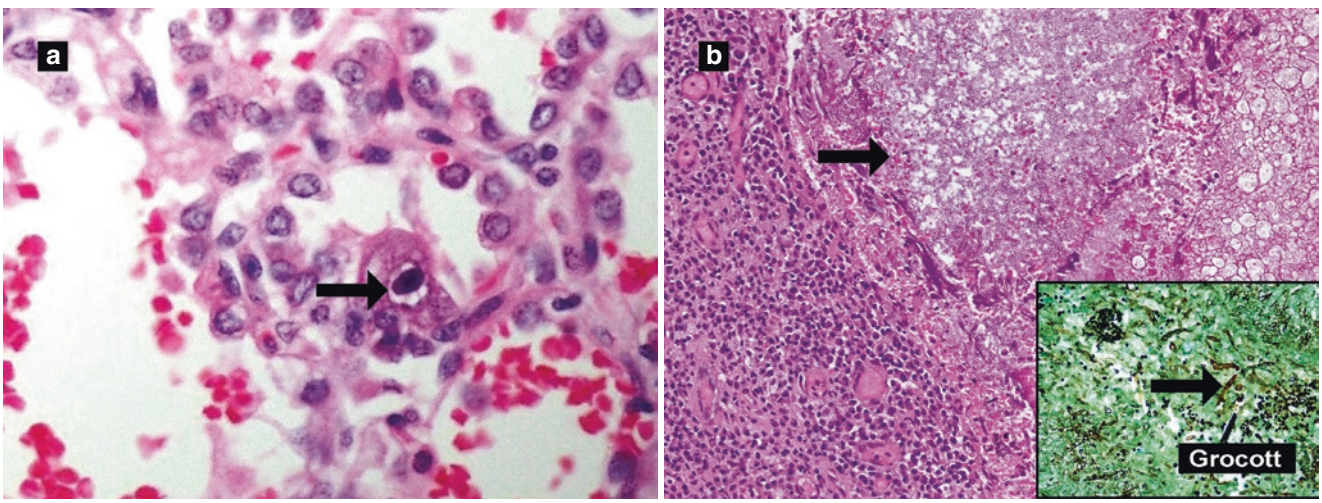

Fig. 15.2 (**a**, **b**) *Cytomegalovirus (CMV) and Aspergillus infection: Cytomegalovirus* (CMV) is a herpes virus which causes lung infection in immunocompromised patients particularly in lung transplant recipients. The immunocompetent individuals harbour asymptomatic latent infection. There is an infiltrate of mononuclear cells with mild edema and hyperplasia of type II pneumocytes. The infected cells are large and show intranuclear as well as intracytoplasmic inclusions. The intranuclear inclusions are eosinophilic, surrounded by a clear halo with peripheral margination of chromatin (**a**→). These characteristic inclusions may be seen in pneumocytes, endothelial cells, or histiocytes. *Aspergillus* is a commensal of the airways. It usually causes invasive infections in transplant recipients. In immunocompetent individuals, there is a preceding history of pulmonary tuberculosis in most cases, with resultant cavitary lesions colonized by aspergillus forming an aspergilloma. On H&E stained sections and special stain PAS and Grocott's, septate fungal hyphae are seen with dichotomous (45°) branching (**b**, inset→)

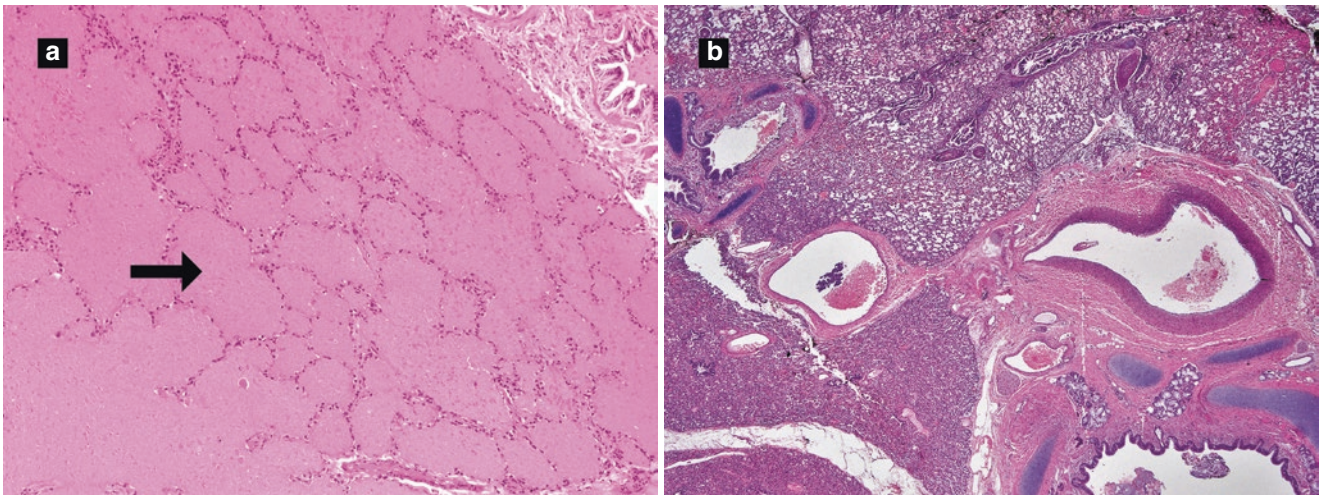

Fig. 15.3 (**a**, **b**) *Alveolar proteinosis and bronchopulmonary sequestration:* Alveolar proteinosis radiologically manifests as bilateral perihilar and peribasilar infiltration, which resembles pulmonary edema. On histology, there is accumulation of acellular, eosinophilic granular precipitate within the alveoli (**a**→), with occasional presence of cholesterol clefts. The alveolar septae are intact and may show mild inflammation. This material is the surfactant produced by type II pneumocytes. There is imbalance between the production and removal by alveolar macrophages. Majority of the affected patients are cigarette smokers but non-smokers, even children and adolescents may also be affected. It is usually treated by bronchoalveolar lavage. *Bronchopulmonary sequestration* also called *accessory lung* is a congenital abnormality of lung development in which there is non-functional lung tissue that does not communicate with normal tracheobronchial tree and, hence, does not participate in gaseous exchange. It presents with recurrent/chronic chest infections, cough, pneumonia, etc. On microscopic examination, it is composed of cystic lung tissue of embryonal origin (**b**)

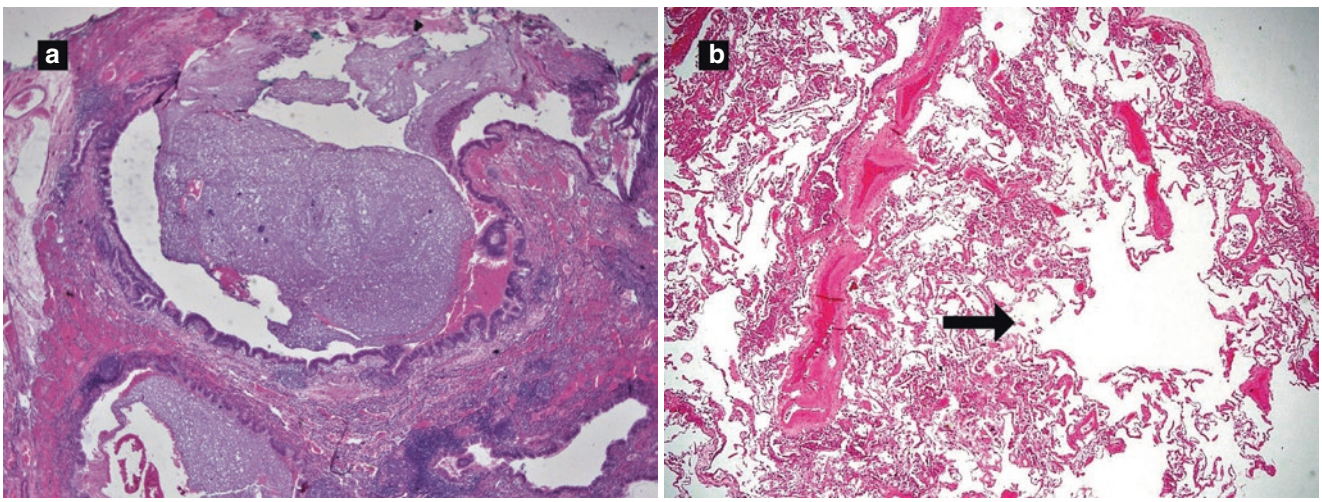

Fig. 15.4 (**a**, **b**) *Bronchiectasis and Emphysema:* Bronchiectasis is characterized by dilated airways, often accompanied by acute and chronic inflammation. It is the end result of a number of conditions that result in gradual weakening and ultimately permanent dilatation of airways. On histology, dilated airways with abundant mucus in the lumen and surrounding lymphoid aggregates are typically seen (**a**). *Emphysema* is characterized by destroyed alveolar walls with formation of bullae within the lung parenchyma (**b**→). It is caused by a number of etiological factors like *Alpha 1 antitrypsin* deficiency and smoking. There is destruction of elastin in the alveolar septae which is mediated by proteases. A number of causes can be attributed to emphysema including cigarette smoking and infections. It can be *centriacinar* involving the upper lobe, *panacinar* involving the lower lobe, or *paraseptal* which is sub-pleural in location

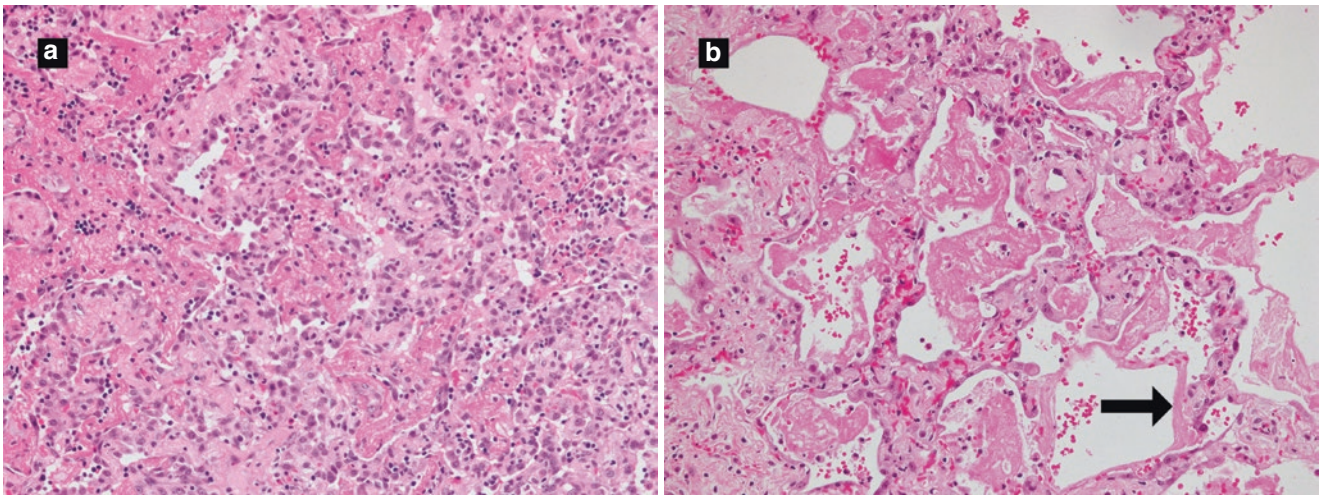

Fig. 15.5 (**a**, **b**) *Diffuse alveolar damage (DAD):* Diffuse alveolar damage (DAD) is the prototypical manifestation of acute lung injury leading to acute respiratory distress (ARDS) with formation of hyaline membranes (**b**→) within alveolar spaces. There is minimal mononuclear inflammatory cell infiltrate in the interstitium. These hyaline membranes resolve completely in most cases. In other cases, there can be fibrosis and structural remodelling of the lung parenchyma with honeycombing

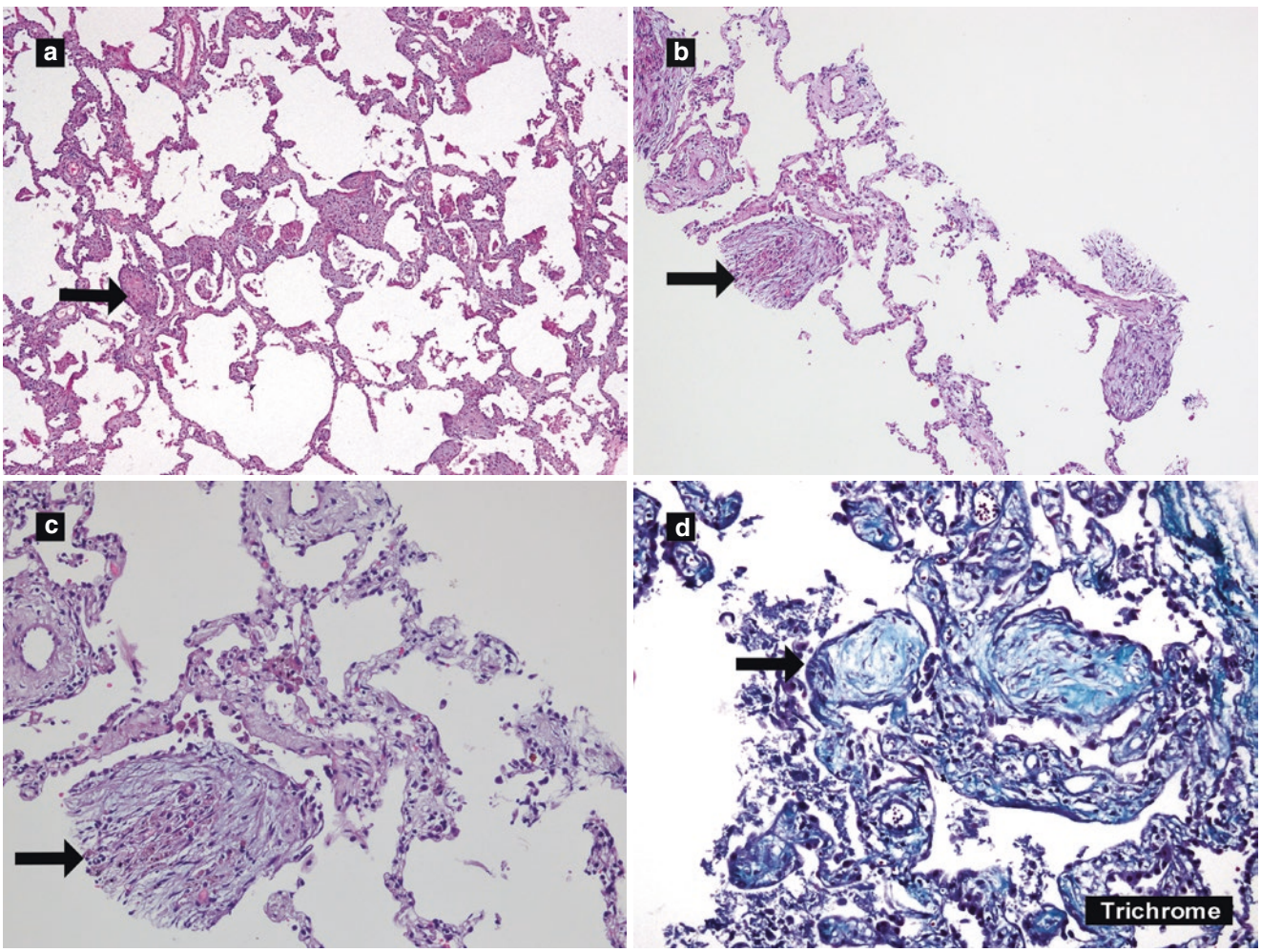

Fig. 15.6 (**a**–**d**) *Organizing pneumonia (cryptogenic organizing pneumonia):* Organizing pneumonia, previously called *cryptogenic organizing pneumonia (COP)* or *bronchiolitis obliterans with organizing pneumonia (BOOP)* is characterized by plugs of loose organizing connective tissue (**a**→, **b**→, **c**→) in small airways and alveolar ducts. The plugs comprise of fibroblasts in pale staining immature loose collagen matrix and may have polypoid shape (Masson body) elongated or serpiginous in form. The collagen in these connective tissue plugs is highlighted on special stain trichrome (**d**→)

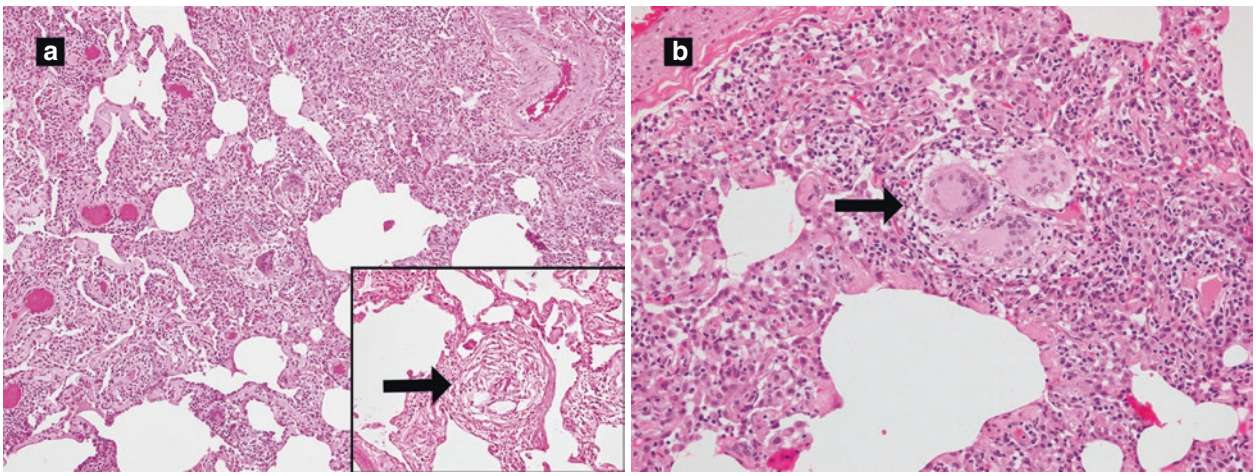

Fig. 15.7 (**a**, **b**) *Hypersensitivity pneumonitis:* Hypersensitivity pneumonitis is characterized by non-necrotizing interstitial granulomas around terminal bronchioles, comprising of giant cells, lymphocytes and plasma cells (**b**→). There is lymphoplasmacytic infiltrate surrounding small bronchioles. Cholesterol granulomas may also be seen, comprising of epithelioid histiocytes and cholesterol clefts (**a**, inset→). It may be seen due to inhaled dust, molds and chemicals

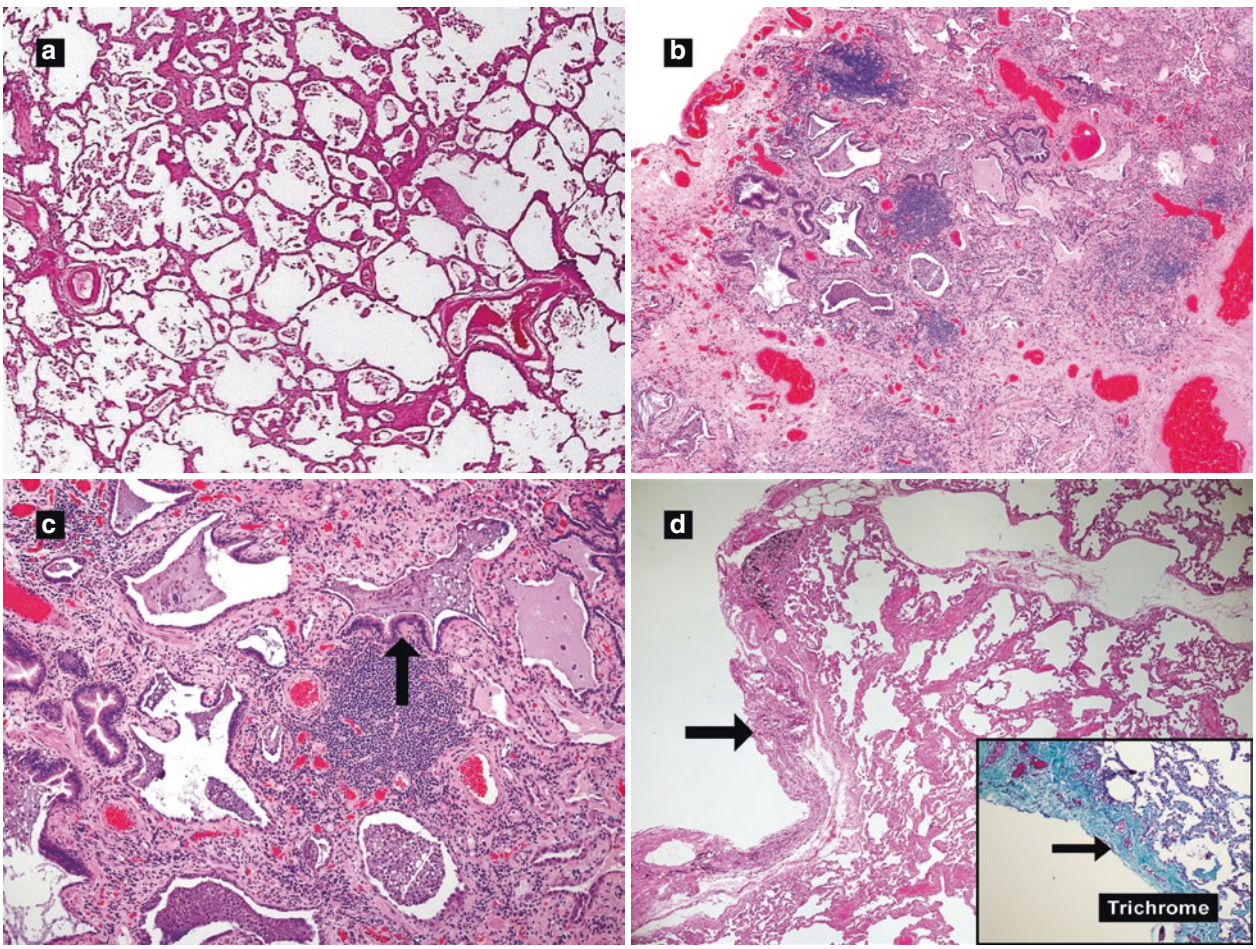

Fig. 15.8 (**a**–**d**) *Usual interstitial pneumonia (UIP) and sub-pleural fibrosis:* Usual interstitial pneumonia (UIP) is the histologic pattern of fibrosis seen in idiopathic pulmonary fibrosis (IPF). It is a disease of older patients. Although exact cause is unknown, several factors have been implicated in the pathogenesis of UIP, cigarette smoking being the most important. It presents characteristically with cough and worsening dyspnoea. This process is patchy and involves peripheral portions of the lung lobule, hence cannot be diagnosed on core biopsies or endobronchial biopsy specimen. Histologically, patchy areas of ongoing pneumocyte injury as well as interstitial fibrosis and remodelled lung with honeycombing are seen (**a**, **b**). Honeycombing shows cystic spaces lined by ciliated columnar epithelium and filled with mucus (**c**↑). Inflammatory infiltrate is seen in the adjacent tissue. Late stages result in s*ub-pleural fibrosis* (**d**→). Special stain trichrome highlights fibrotic area (**d**, inset→)

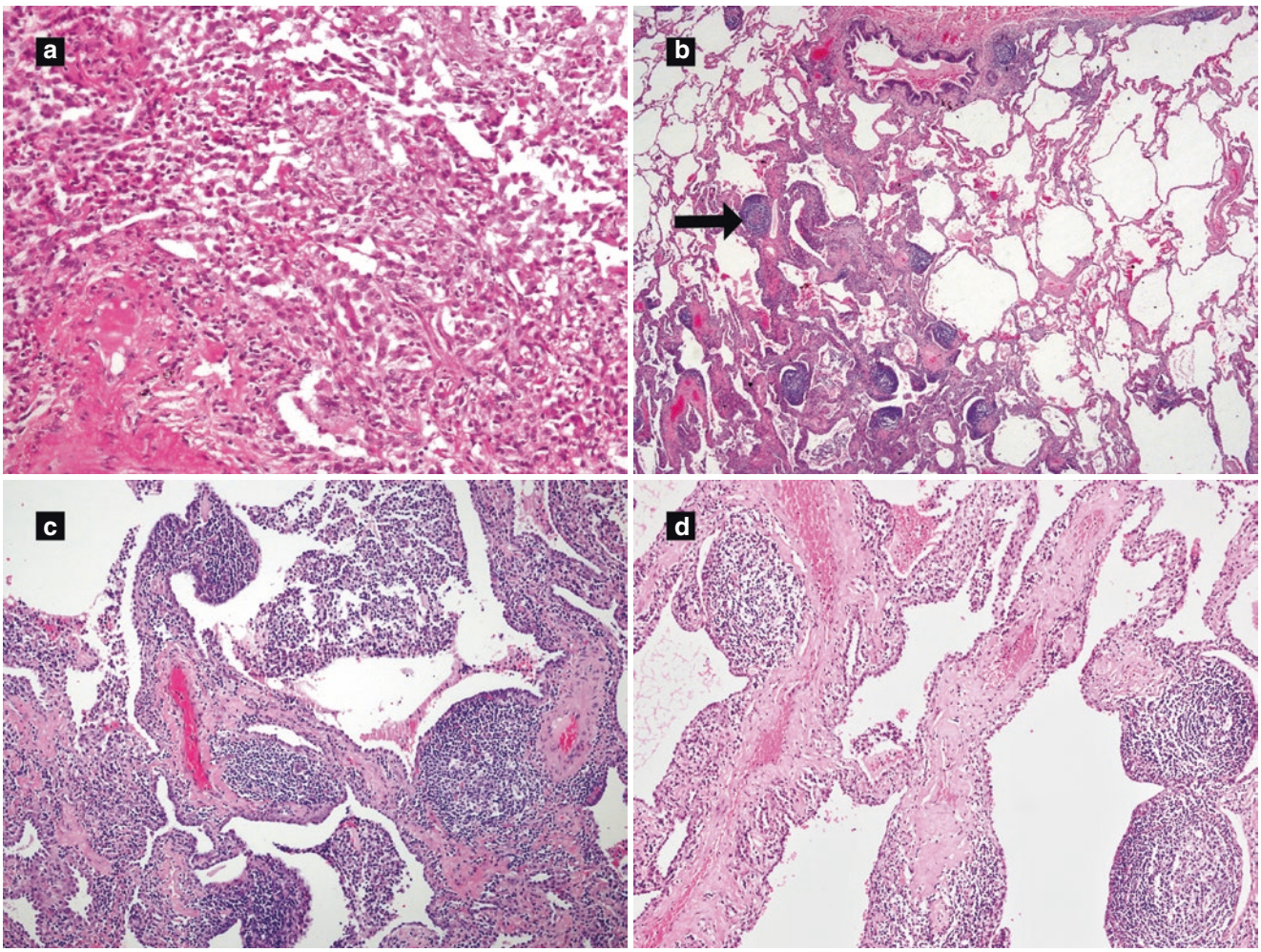

Fig. 15.9 (**a**–**d**) *Desquamative interstitial pneumonia (DIP) and follicular bronchiolitis:* Desquamative interstitial pneumonia is a classic but rare manifestation of smoking-related interstitial diseases. Non-smokers have a history of either passive smoking or exposure to dust or chemical fumes. It is characterized by massive accumulation of macrophages within the alveoli (**a**). *Follicular bronchiolitis* is the primary hyperplasia of bronchus-associated lymphoid tissue (BALT). BALT is not a normal finding and is presumed to result from chronic antigen exposure. It is characterized by lymphoid follicles and plasma cells around distal bronchi and bronchioles (**b**→, **c**, **d**), infiltrating fibromuscular wall and may compress the lumen. It is usually associated with autoimmune diseases/connective tissue disorders like Rheumatoid arthritis and Sjogren's syndrome as well as congenital and acquired immunodeficiency conditions like AIDs

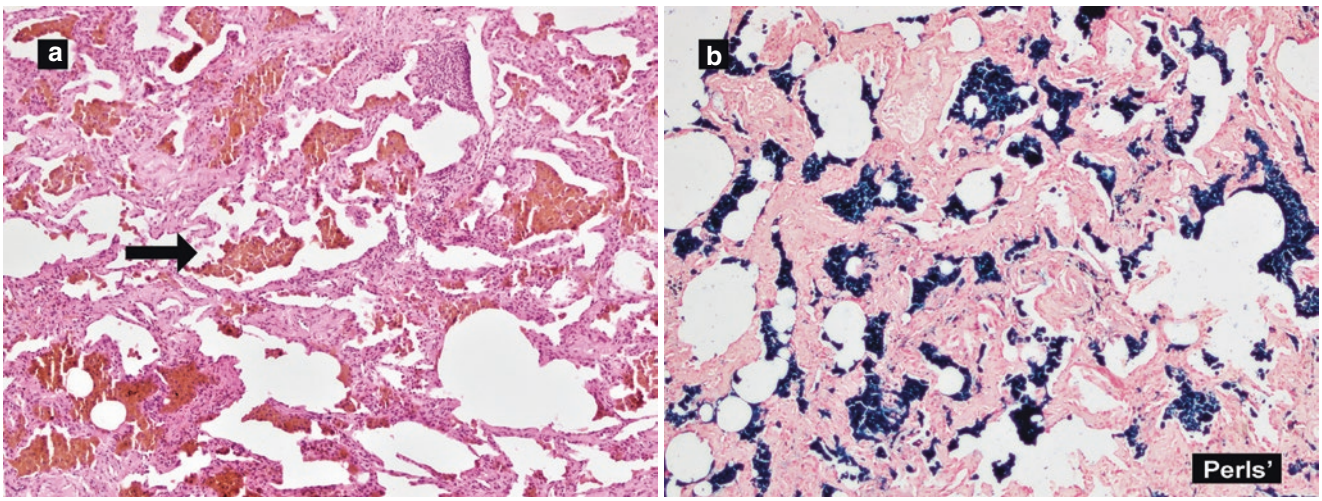

Fig. 15.10 (**a**, **b**) *Pulmonary haemosiderosis:* Pulmonary haemosiderosis may be primary or secondary. It is characterized by aggregates of haemosiderin-laden macrophages in the alveoli (**a**→), highlighted by Perls' Prussian blue stain for iron (**b**)

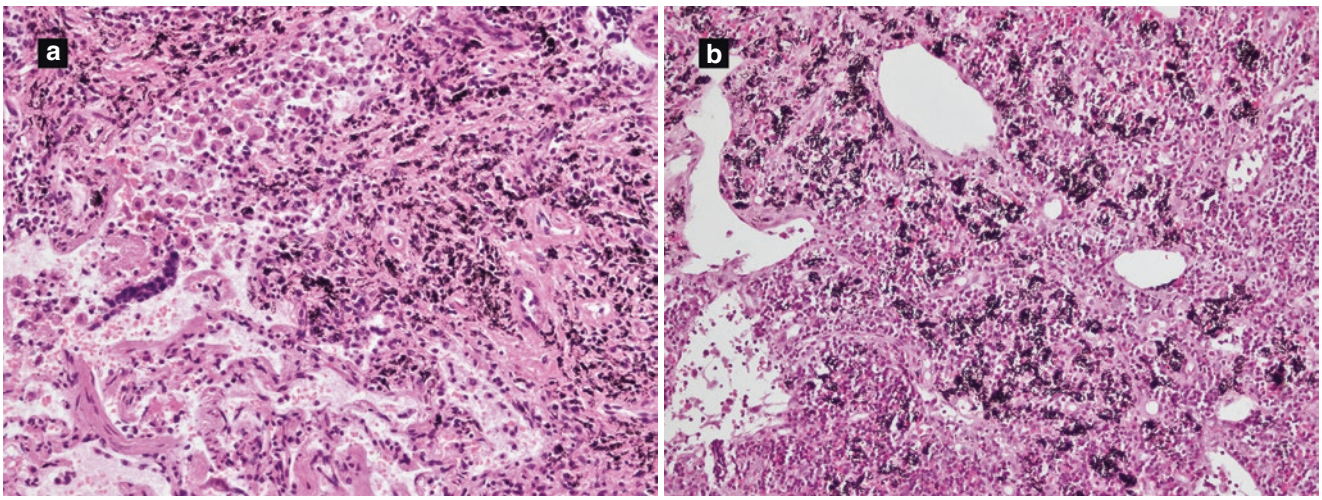

Fig. 15.11 (**a**, **b**) *Anthracosis:* Anthracosis refers to deposition of black carbon pigment. It is commonly seen in perihilar lymph nodes as well as within lung parenchyma (**a**, **b**). There can be prominent storiforming of histiocytes, to such an extent as to mimic a neoplastic lesion histologically. It is a common finding in smokers and polluted city dwellers

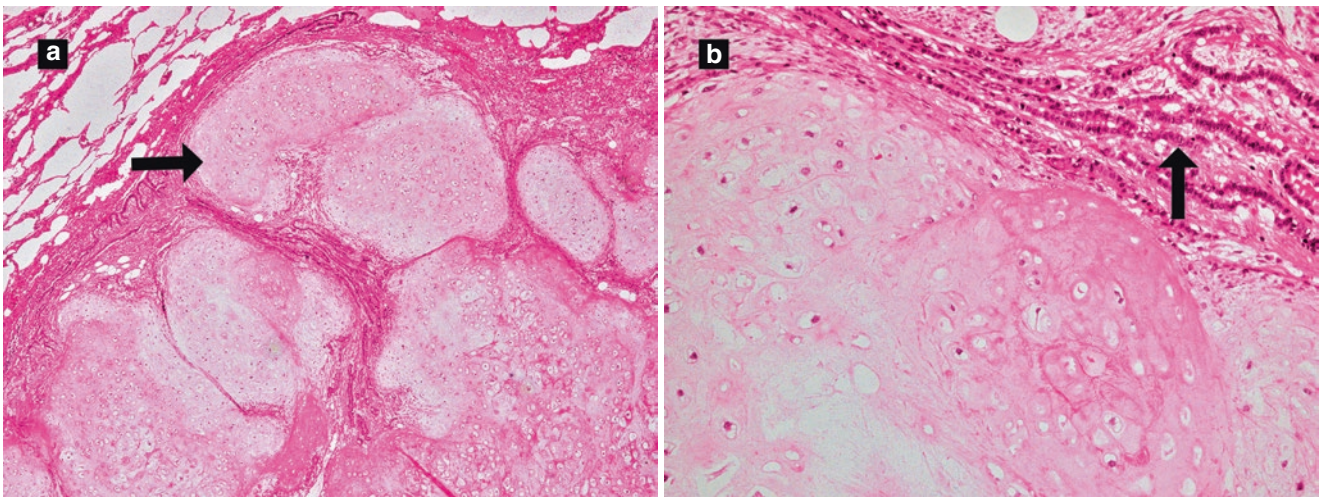

Fig. 15.12 (**a**, **b**) *Bronchial hamartoma:* Hamartoma is a developmental malformation, which comprises of tissues that are native to a particular organ but have disorganized arrangement. Bronchial hamartoma mostly presents as a solitary pulmonary nodule in the peripheral lung, with a characteristic popcorn pattern of calcification on radiology. Rarely, it may present as an endobronchial mass. It comprises of abnormal mixture of mature epithelial and mesenchymal tissue with latter usually dominated by lobules of mature cartilage (**a**→). Epithelial component is present in the form of clefts, which are lined by ciliated or non-ciliated respiratory epithelium (**b**↑)

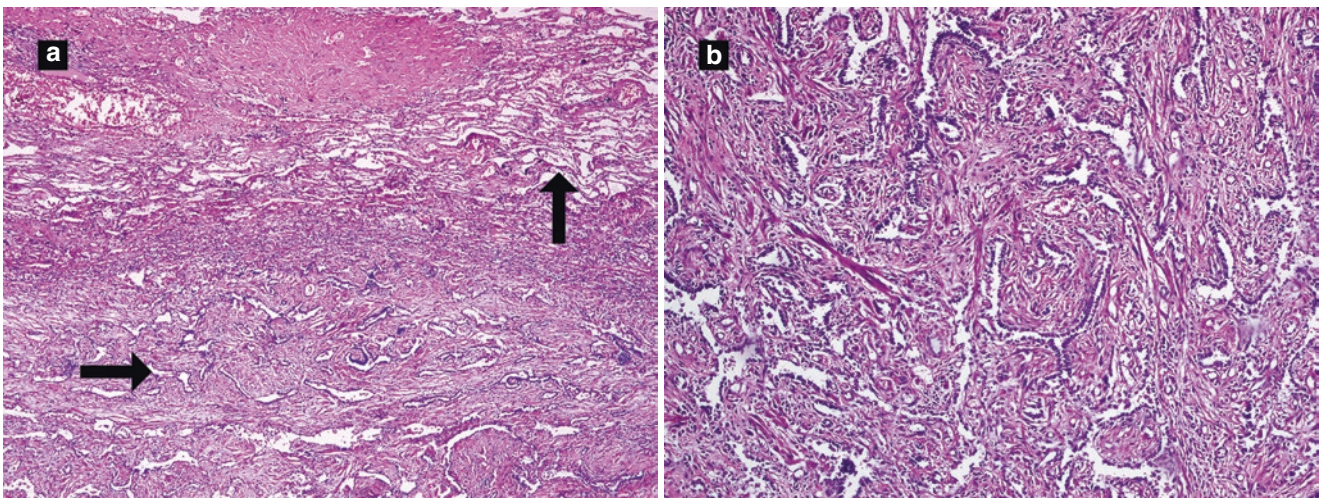

Fig. 15.13 (**a**, **b**) *Pulmonary sclerosing pneumocytoma:* Pulmonary sclerosing pneumocytoma previously known as pulmonary sclerosing haemangioma is a neoplasm of middle-aged females. It is presumed to originate from primitive respiratory epithelium. It comprises of epithelial and stromal cells. Epithelial cells resemble type II pneumocytes and have immunohistochemical profiles similar to them. The stromal cells are small, round with well-defined borders, central nuclei and finely dispersed chromatin. Epithelial cells are arranged in irregular tubular structures (**a**→, **b**); adjacent lung parenchyma may be seen at the upper half (**a**↑). Sclerosing pneumocytoma is a great mimicker of malignant tumours of lung

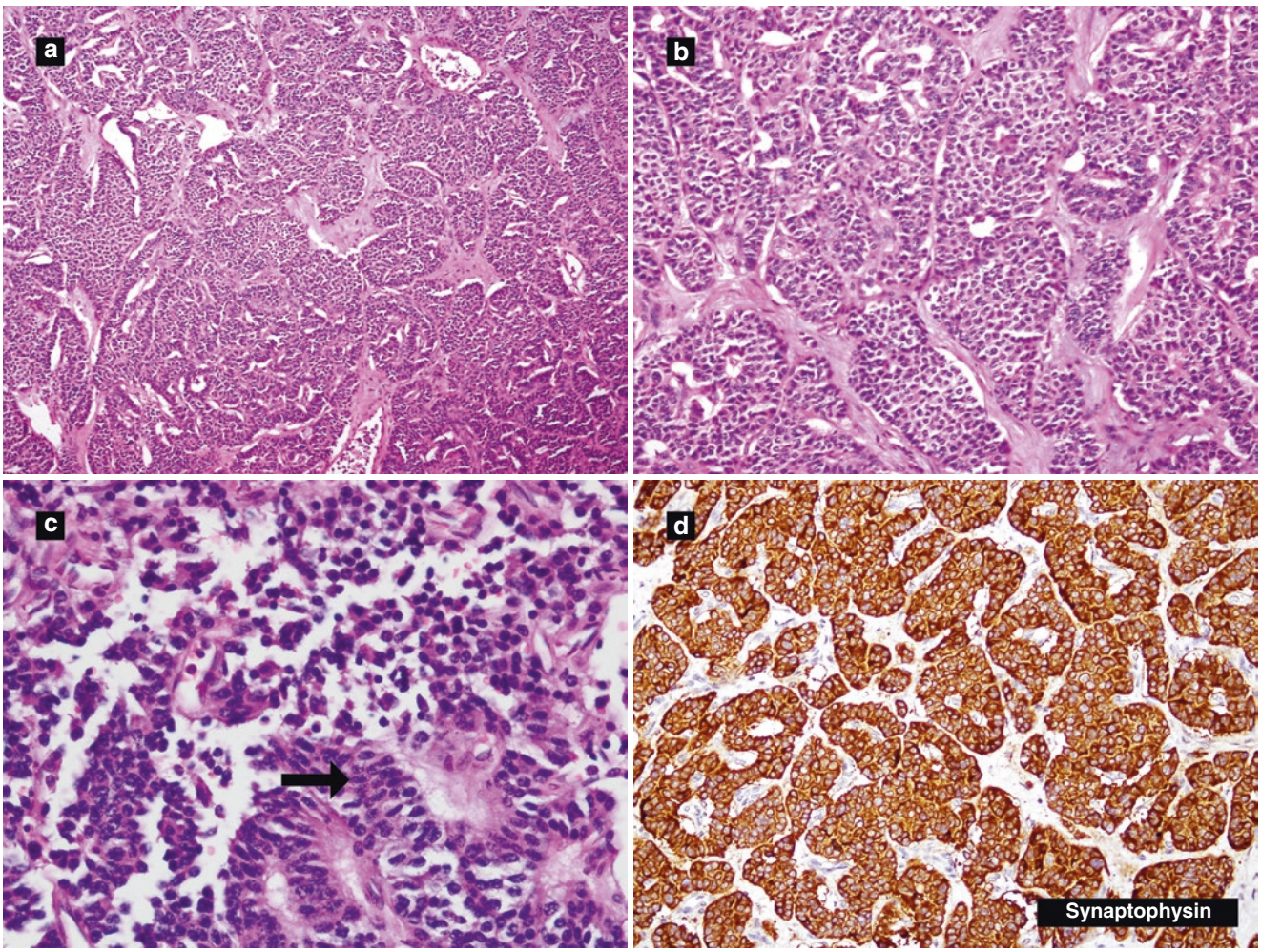

Fig. 15.14 (**a**–**d**) *Carcinoid tumour of the lung:* Carcinoid tumour belongs to the epithelial neuroendocrine lung neoplasms. It is divided into typical carcinoid and atypical carcinoid. The typical carcinoid tumour comprises of trabeculae or nests of uniform-appearing cells (**a**, **b**) with characteristic salt-and-pepper-like chromatin pattern (**c**→). In some cases, scattered prominently pleomorphic cells may be present, but they should not be considered significant in isolation. Carcinoids show reactivity for pan-endocrine immunohistochemical markers like synaptophysin (**d**) and chromogranin A. Mitoses are <2/10 HPFs, and there is no necrosis in these tumours

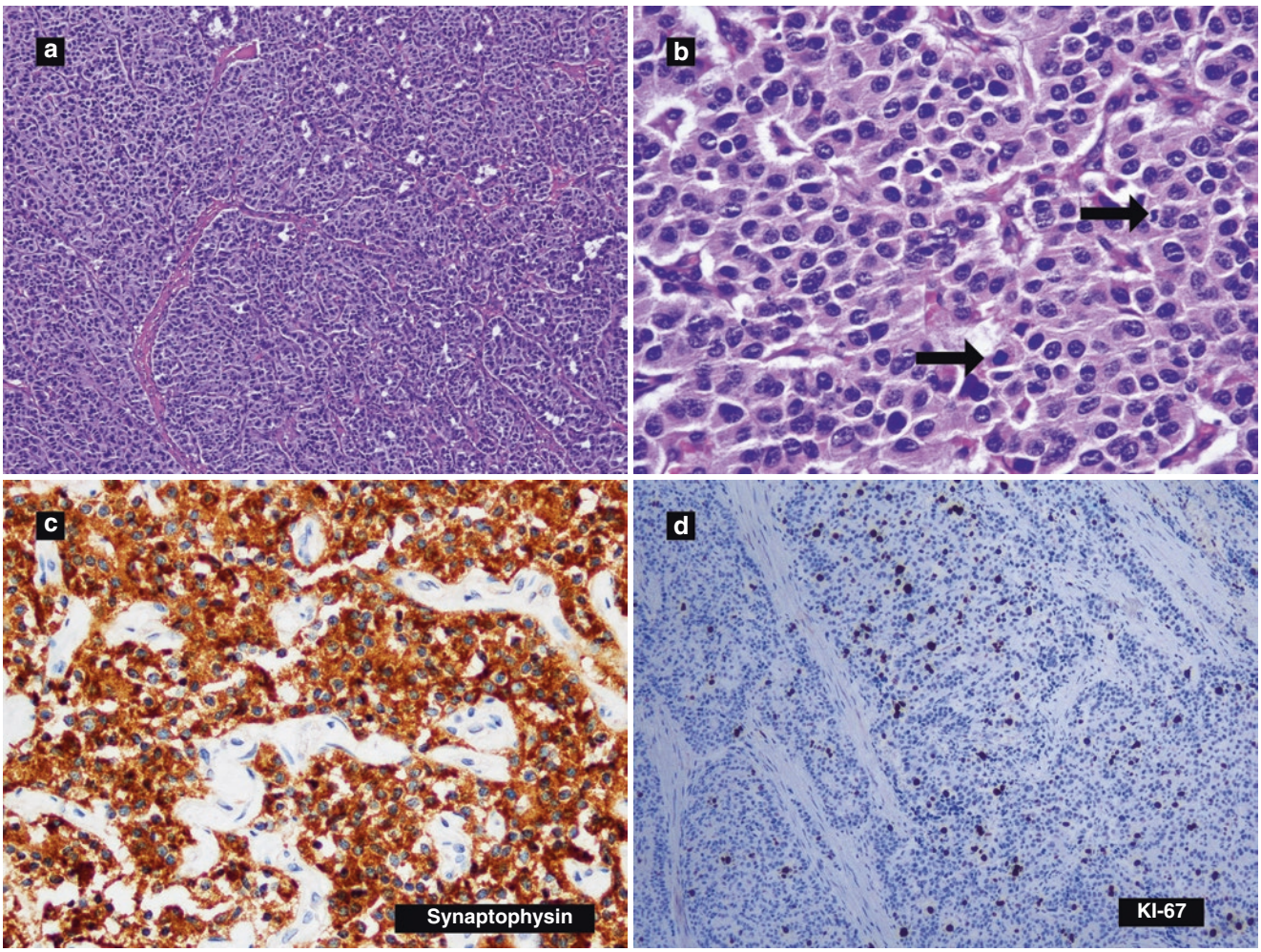

Fig. 15.15 (**a**–**d**) *Atypical carcinoid tumour of the lung:* These tumours, in contrast to typical carcinoids, show increased mitotic activity (**a**, **b**→) and/or necrosis. As per WHO criteria, atypical carcinoid shows 2–10 mitoses per 10 HPFs. Reactivity to pan-endocrine markers like synaptophysin is also consistent (**c**). The utility of Ki-67 proliferative index has not been established yet to differentiate between typical and atypical carcinoids in the lung. Ki-67 labelling in an atypical carcinoid tumour is shown in panel (**d**)

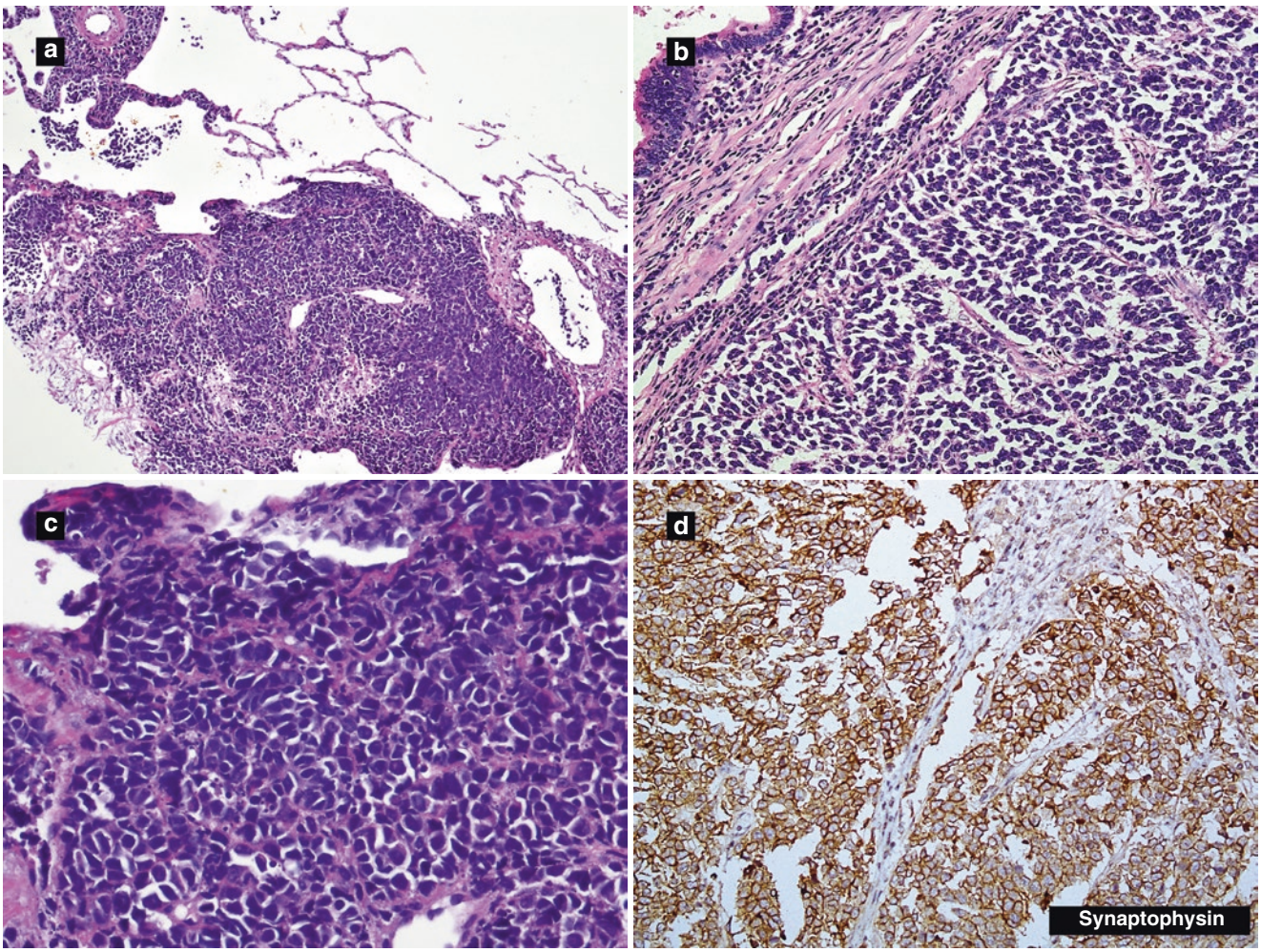

Fig. 15.16 (**a**–**d**) *Small cell carcinoma of the lung:* Small cell carcinoma typically grows in the perihilar region. It comprises of sheets and nests of small-sized cells with crushing artefact in most cases (**a**, **b**). These cells tend to have scant cytoplasm, nuclear moulding and inconspicuous nucleoli (**c**). The nuclear chromatin is finely dispersed (salt-and-pepper like). These tumours show positive staining with epithelial markers, TTF1, synaptophysin (**d**), chromogranin A and CD56. Ki-67 proliferative index is high. These tumours may show reactivity with p63

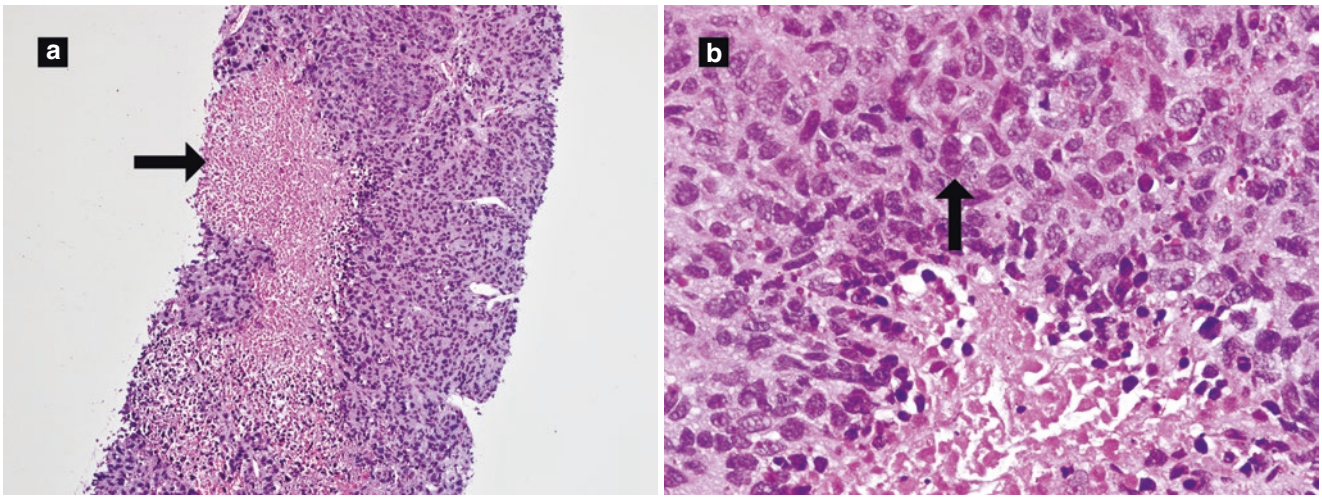

Fig. 15.17 (**a**, **b**) *Large cell neuroendocrine carcinoma of the lung:* Large-cell neuroendocrine carcinoma is a non-small cell lung carcinoma which is mostly located peripherally. It shows neuroendocrine growth patterns, i.e. rosette formation and peripheral palisading. Areas of necrosis are also common (**a**→). Mitotic activity is high. The cells are larger than those of small cell carcinoma and contain appreciable amount of eosinophilic cytoplasm with vesicular nuclei having prominent nucleoli (**b**↑). Immunohistochemical profile is similar to small cell carcinoma of lung

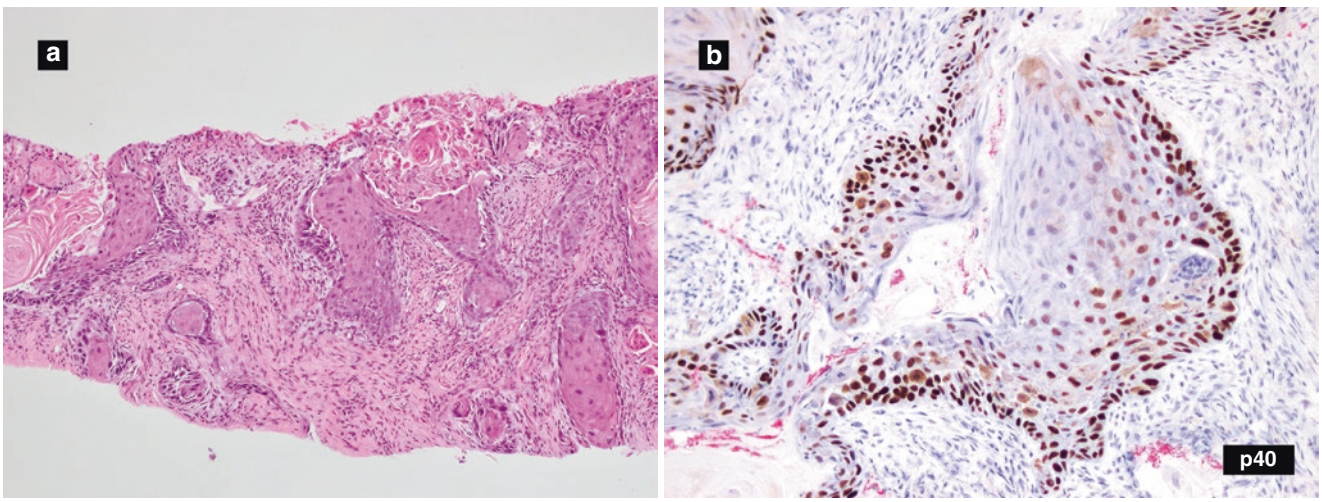

Fig. 15.18 (**a**, **b**) *Squamous cell carcinoma of the lung:* Squamous cell carcinoma shows evidence of keratinization and/or the presence of intercellular bridges (**a**). It usually grows within the bronchus and may cavitate due to necrosis. Non-keratinizing variants are diagnosed with the help of immunohistochemistry by expression of markers of squamous differentiation such as p40 (**b**), p63 and high molecular weight cytokeratins like CK5/CK6

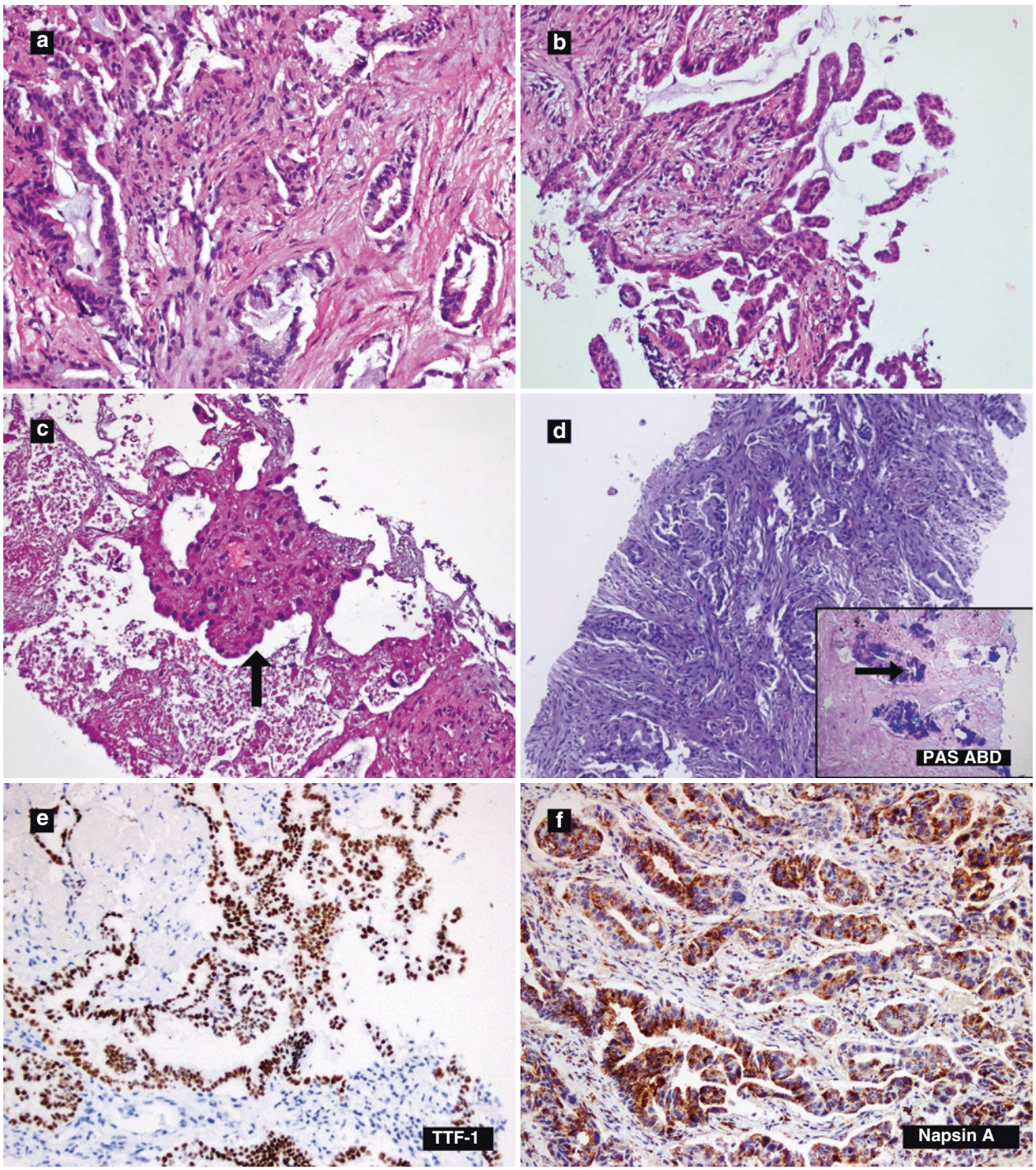

Fig. 15.19 (**a**–**f**) *Adenocarcinoma of the lung:* Adenocarcinoma of the lung is diagnosed on the basis of glandular differentiation, mucin production and expression of pneumocyte markers. It shows a variety of growth patterns

(**a**) shows *acinar* pattern in which gland formation is seen with a central lumen. Cribriform arrangement may also be seen

(**b**) shows *papillary* growth pattern, which is characterized by well-formed papillary structures with a fibrovascular core, covered by tumour cells. Driving EGFR mutations are more frequent in tumours with this pattern of growth. Another variation to this is micropapillary pattern which lacks fibrovascular cores and comprises of loose tufts of tumour cells. This pattern is also associated with psammomatous calcifications and has poor prognosis

(**c**) shows *lepidic* growth, which is the new terminology for non-invasive bronchioloalveolar carcinoma. It shows growth of bland-looking tumour cells along the alveolar walls (**c**↑). In order to make a diagnosis of lepidic predominant adenocarcinoma, presence of an invasive component of more than 5 mm is a prerequisite. This invasive component may show any pattern of growth. Another variant is *solid* adenocarcinoma, which comprises of majority of tumour growing in solid sheets and lacking any of the patterns described above. If the tumour is 100% solid, in order to call it an adenocarcinoma, there should be intracellular mucin in more than five tumour cells in each of two high-power fields along with positive immunohistochemical stains for mucin, as per WHO guidelines

(**d**) shows intracellular mucin (**d**, inset→), demonstrated on special stain PAS Alcian blue with diastase

(**e**, **f**) shows positive nuclear staining for TTF-1 and positive granular cytoplasmic staining for napsin A, respectively

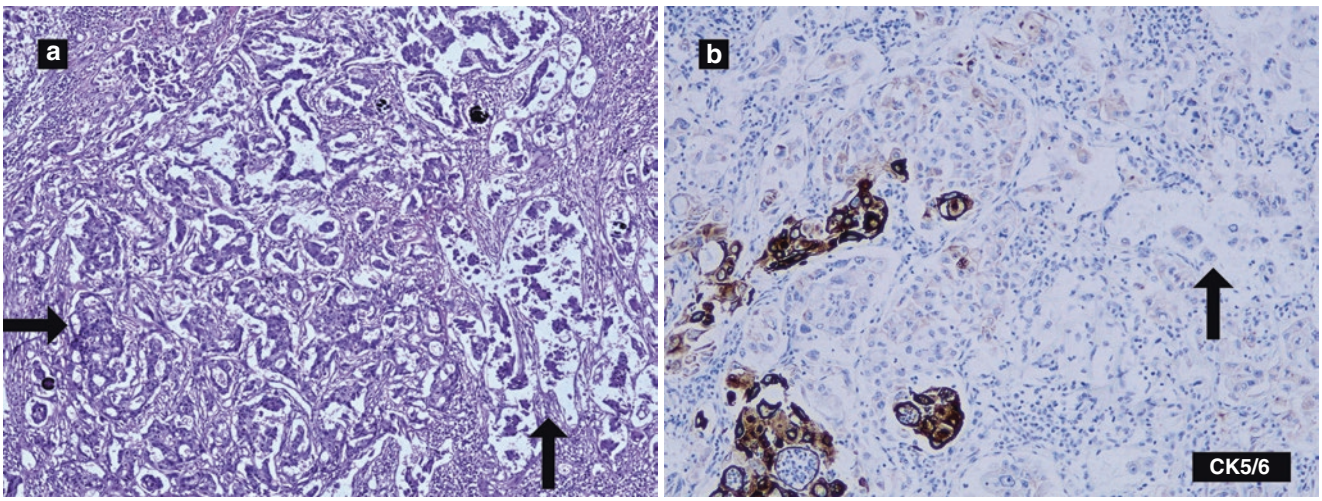

Fig. 15.20 (**a**, **b**) *Adenosquamous carcinoma:* Adenosquamous carcinoma comprises both adenocarcinoma and squamous cell carcinoma components, each constituting at least 10% of the tumour. The squamous cell carcinoma shows either intercellular bridges or keratinization (**a**→). The adenocarcinoma may show any of the growth patterns. Panel (**a**) shows an adenosquamous carcinoma with a prominent micropapillary growth in adenocarcinoma component (↑). Panel (**b**) shows positive staining for CK5/CK6 in squamous areas and negative staining in adenocarcinoma component (↑)

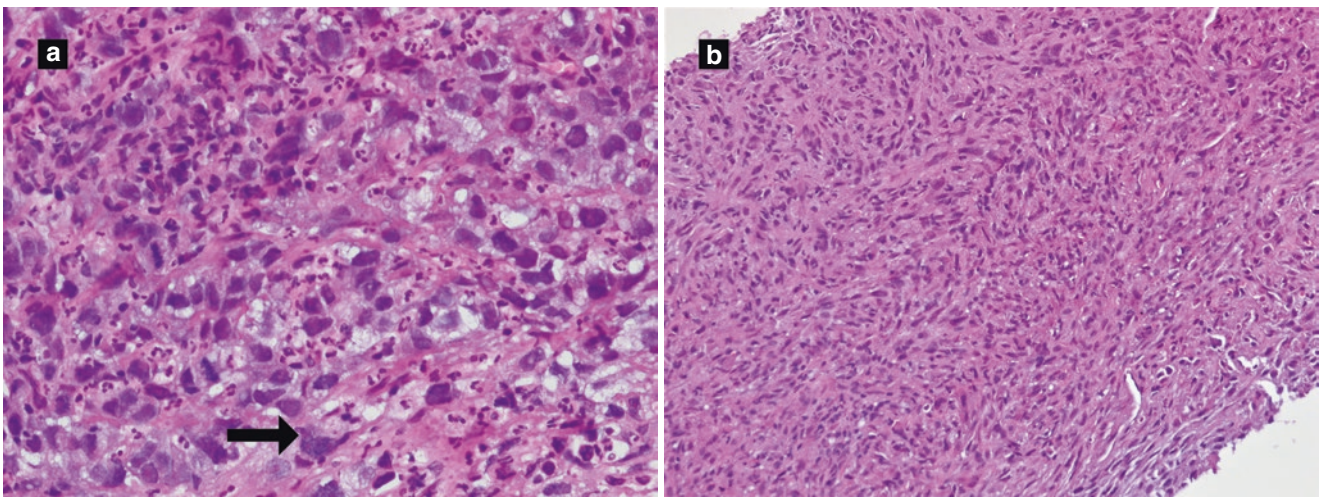

Fig. 15.21 (**a**, **b**) *Pleomorphic carcinoma and spindle cell carcinoma:* Pleomorphic carcinoma is a poorly differentiated carcinoma which either comprises squamous cell carcinoma, adenocarcinoma, or undifferentiated non-small cell carcinoma with at least 10% spindle and/or giant cell component (**a**→). Some of the cells are binucleated as well. Immunohistochemical stains can be helpful only to highlight the differentiated components of the tumour. These tumours show poor prognosis. *Spindle cell carcinoma* comprises of pure population of only spindle cells (**b**). Identifiable epithelial components are not seen in these tumours. The tumour cells show positive staining with vimentin and fascin. Markers of differentiation like cytokeratins may be variably expressed

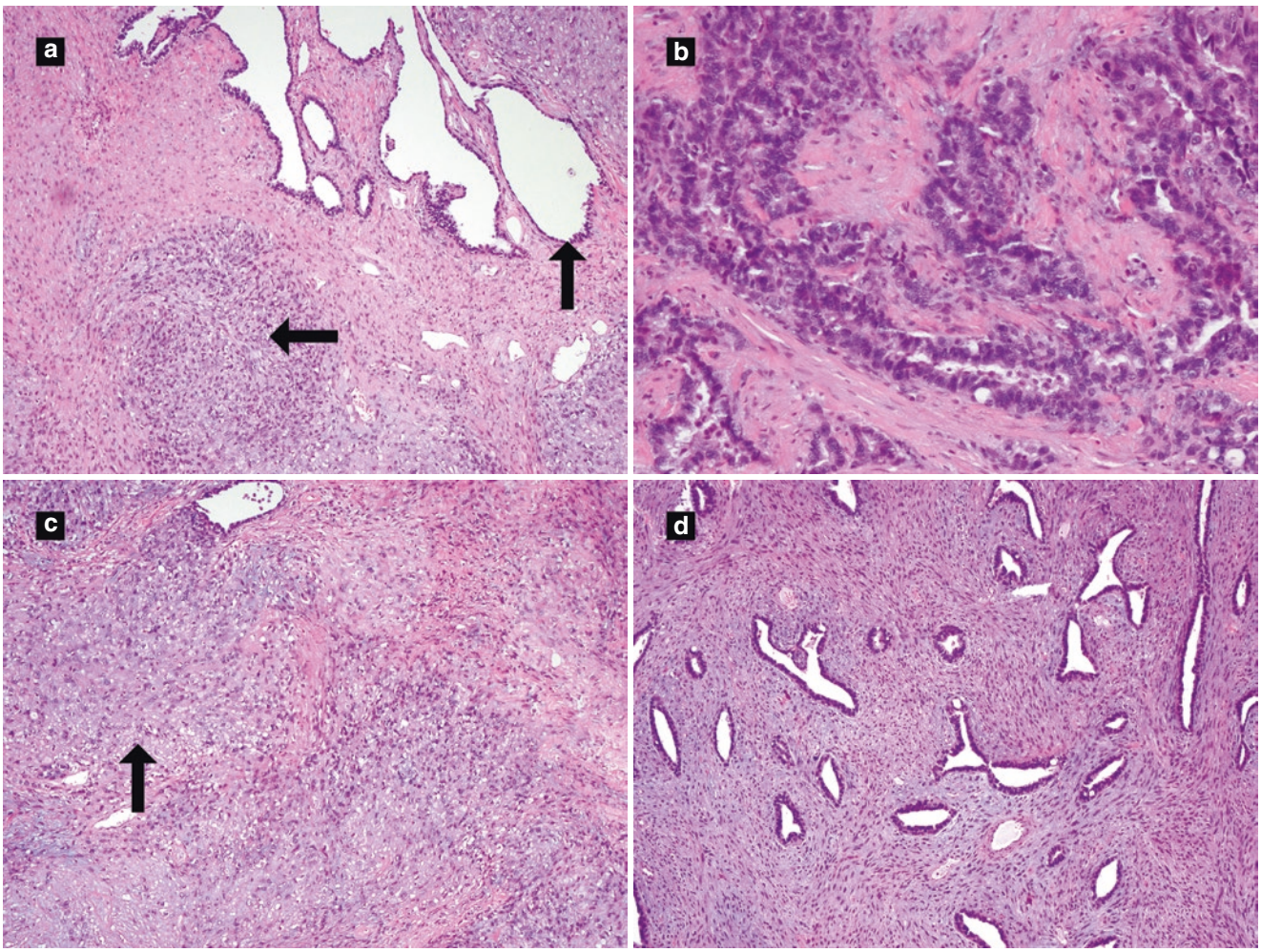

Fig. 15.22 (**a**–**d**) *Pulmonary blastoma:* Pulmonary blastoma is a biphasic tumour that comprises of low-grade foetal adenocarcinoma with primitive mesenchymal stroma. Panel (**a**) shows a low-power view of the tumour with both components. Glandular structures lined by cuboidal cells with low-grade morphology are seen at the upper part of the image (↑), while the mesenchymal component is present in the lower left field, comprising of a nodule of primitive-appearing cells (←). Panel (**b**) shows high-power view of the glandular elements, with mild nuclear hyperchromasia. These areas may resemble fetal lung tissue (**d**). Panel (**c**) shows primitive cells with a high nuclear to cytoplasmic ratio growing in a myxoid background (↑). Not found in this case, there can be areas of heterologous differentiation such as chondrosarcoma, osteosarcoma, or rhabdomyosarcoma in up to 25% of cases. Unusual elements like yolk sac and other germ cell tumours may also be seen rarely

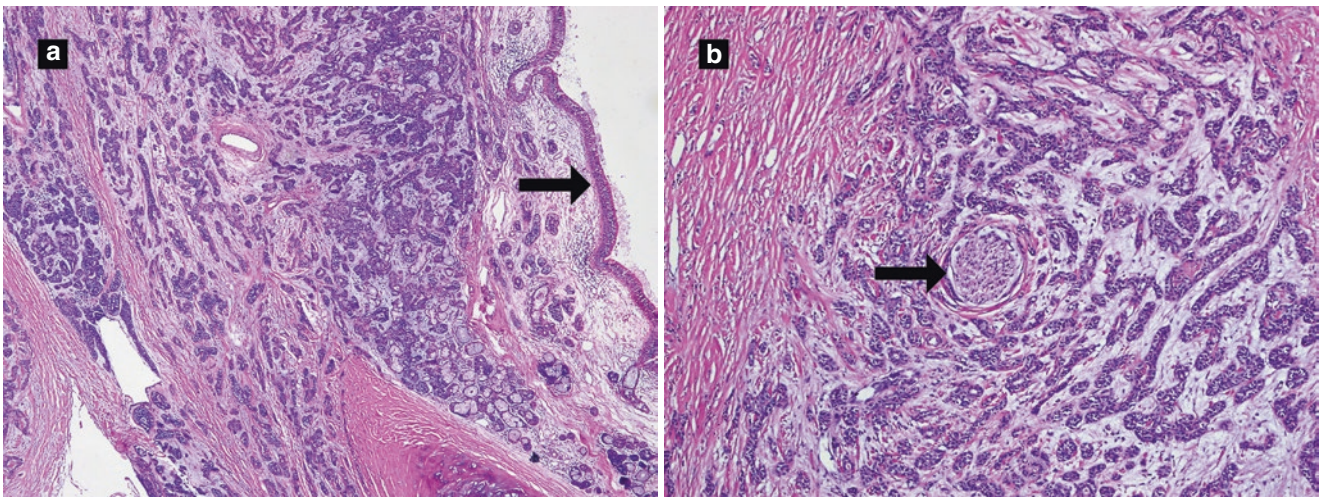

Fig. 15.23 (**a**, **b**) *Adenoid cystic carcinoma of the lung:* Adenoid cystic carcinoma is a salivary gland-type tumour, which is almost always localized to the tracheobronchial tree. Normal-appearing respiratory-type epithelium may be seen (**a**→). The morphology is essentially the same as when they arise in a salivary gland. On microscopy, infiltrative growth is seen, comprising of small cells with uniform hyperchromatic nuclei growing in tubules and cribriform areas, forming cylindrical structures with myxoid and hyalinized material (**a**, **b**). Perineural invasion is frequently seen (**b**→)

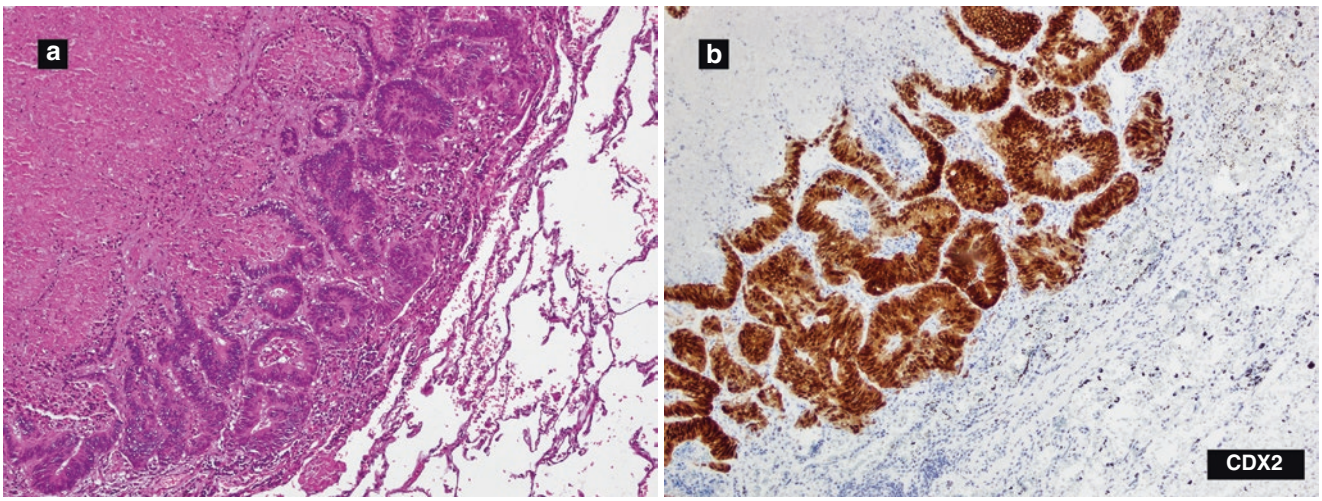

Fig. 15.24 (**a**, **b**) *Pulmonary metastases:* Pulmonary metastases arising from extra-pulmonary sites usually show multiple and bilateral parenchymal nodules on radiological studies. Carcinomas are the most common followed by sarcomas, melanomas and germ cell tumours. Gastrointestinal tract is one of the most common sites of origin for a metastatic carcinoma. Panel (**a**) shows a metastatic adenocarcinoma comprising of malignant glands with a characteristic pattern of festoon-like necrosis. Origin from the gastrointestinal tract is confirmed by positive staining for immunohistochemical marker CDX2 (**b**)

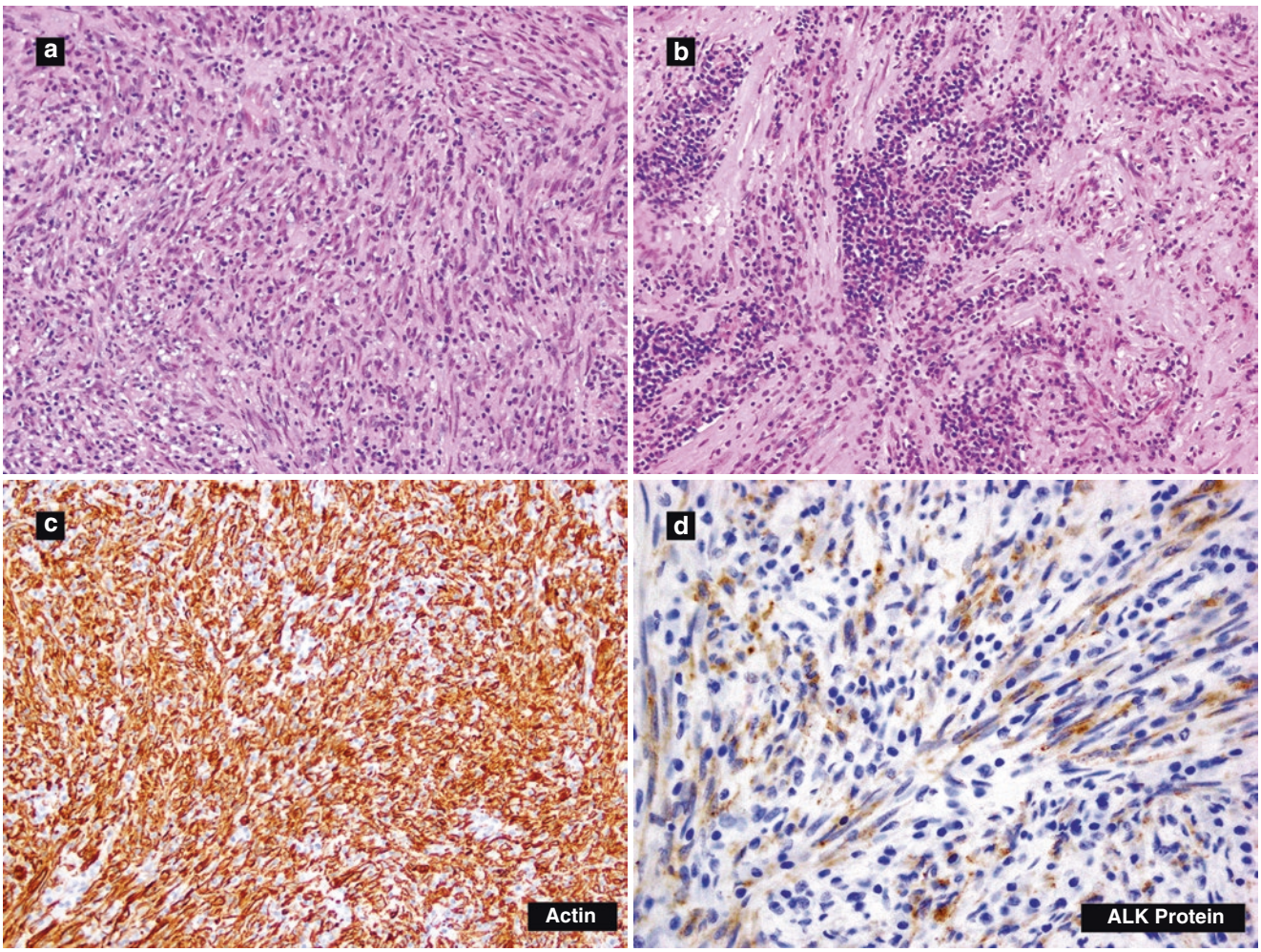

Fig. 15.25 (**a**–**d**) *Inflammatory myofibroblastic tumour (IMT):* Inflammatory myofibroblastic tumour (IMT) is predominantly seen in children and young adults, commonly arising in extra-pleural/extra-pulmonary sites. It is composed of myofibroblasts and fibroblasts with bland morphology (**a**), growing in fascicles amidst a population of inflammatory cells including lymphocytes, plasma cells, eosinophils (**b**). There can be variable myxoid or collagenous scar-like background. Mitotic activity is usually low. There is positive staining for immunohistochemical marker α-smooth muscle actin (**c**) and weak cytoplasmic staining for ALK protein (**d**). This tumour shows genetic heterogeneity. The ALK gene may fuse with several partners like TPM3, TPM4, CLTC, RANBP4 and CTIC. ALK-negative tumours have an aggressive behaviour with a higher rate of metastasis

Pleura

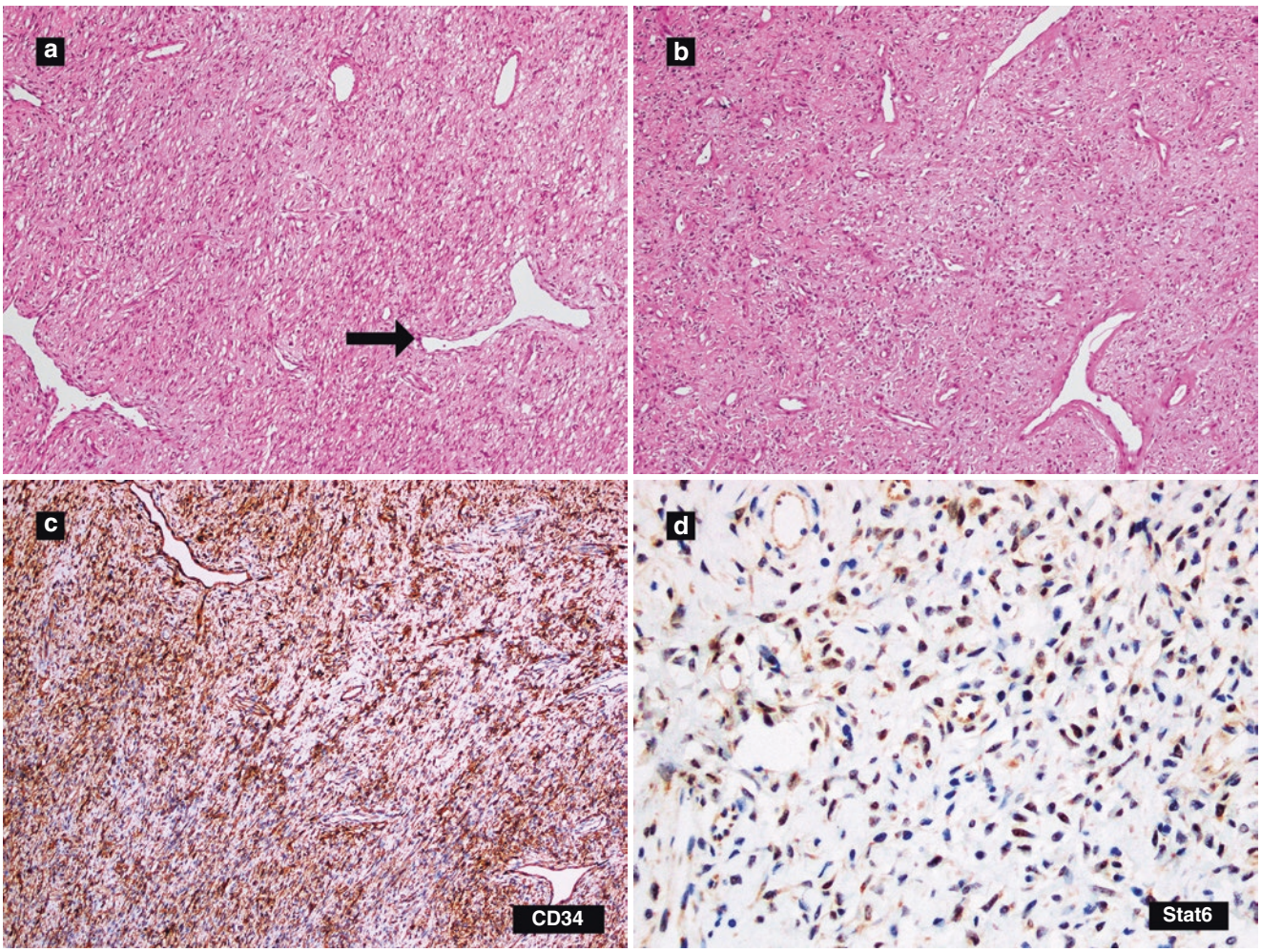

Fig. 15.26 (**a**–**d**) *Solitary fibrous tumour (SFT):* Solitary fibrous tumour (SFT) is a slow-growing tumour with a characteristic vascular pattern, comprising of branching, hemangiopericytoma-like or staghorn-like ectatic blood vessels (**a**→, **b**). The tumour cells are short spindly with bland-appearing tapering nuclei and pale cytoplasm. Focal storiform growth may be seen with a collagenous or sometimes myxoid background. Mitoses tend to be scanty. On immunohistochemistry, CD34 positivity is consistent (**c**). Diffuse nuclear positivity for Stat6 is also characteristic (**d**). Local recurrence may be seen in up to 15% of cases

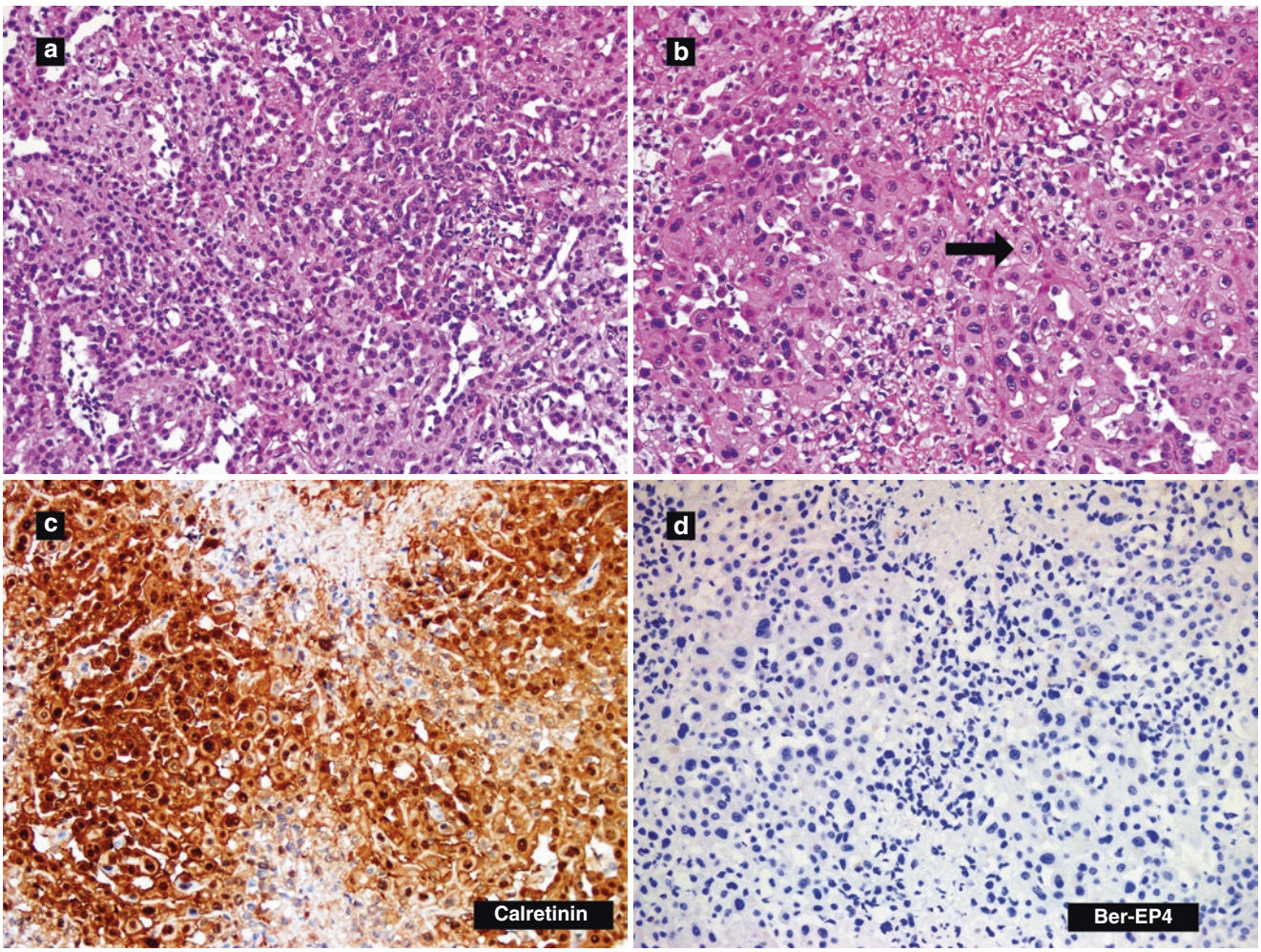

Fig. 15.27 (**a**–**d**) *Malignant mesothelioma:* Malignant mesotheliomas show strong association with asbestos exposure, depending on the type of asbestos fibre. They may be diffuse or localized. Three morphological subtypes have been described including epithelioid, sarcomatoid and biphasic mesotheliomas. Epithelioid type shows a better median survival as compared to other subtypes. On microscopy, an epithelioid mesothelioma shows plump cells with abundant cytoplasm and nuclei with vesicular chromatin and prominent nucleoli (**a**, **b**→). There is positive staining with calretinin (**c**), CK5/CK6, CK7, broad-spectrum keratins and WT1. Ber-EP4 is negative (**d**) which helps in differentiation from a metastatic carcinoma. A newer nuclear marker BAP1 has been described, which shows loss of staining in malignant mesothelioma and helps in differentiation from reactive mesothelial proliferations in difficult cases. These tumours have poor overall prognosis

Mediastinum

Thymomas

Thymomas, despite their name, are malignant tumours of the thymic epithelial cells. These are the most common mediastinal neoplasms of adults. WHO has listed down a number of associated autoimmune and paraneoplastic syndromes, such as myasthenia gravis. There is TNM staging system as well as a Masaoka-Koga staging system, which incorporates the histological features into the TNM classification. Invasion into the adjacent tissue, which is a requirement to call a thymoma an *invasive thymoma,* may be seen in any type of thymomas but is more common in type B3 thymomas when one does not include the thymic carcinomas for this purpose. This feature is of importance for staging, therefore, careful evaluation of the tumour capsule is important.

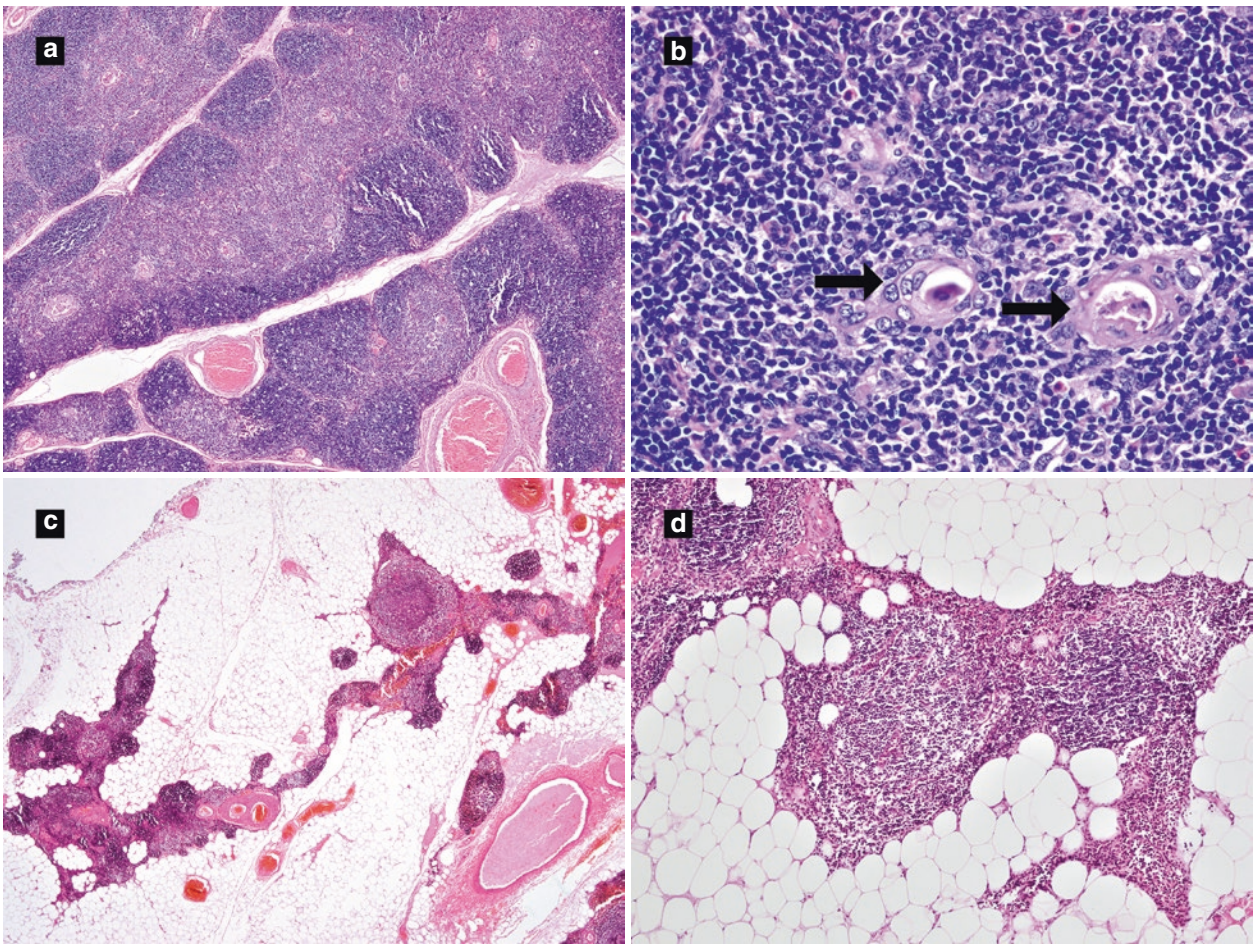

Fig. 15.28 (**a**–**d**) *Thymus and thymic hyperplasia:* Thymus is a lymphoid organ that houses T-lymphocytes. It is active during the early years and starts involuting after puberty. Panel (**a**) shows normal thymic tissue from a toddler. There is a basophilic outer cortex with an eosinophilic medullary region, which contains Hassall's corpuscles (**b**→). These are groups of keratinized thymic epithelial cells with central debris. With advancing age, there is fatty infiltration of the thymic tissue, paired with depletion of the lymphocytes, resulting in adipose tissue with scattered islands of thymic tissue. This thymic tissue may show hyperplasia for various reasons. Thymic hyperplasia is measured using the weight of the gland and may show normal histological features on microscopy (**c**, **d**). *Thymic follicular hyperplasia* is the term used when there is a prominence of lymphoid follicles having germinal centres, which are positive for Pan B (CD20). This condition is commonly associated with Myasthenia gravis

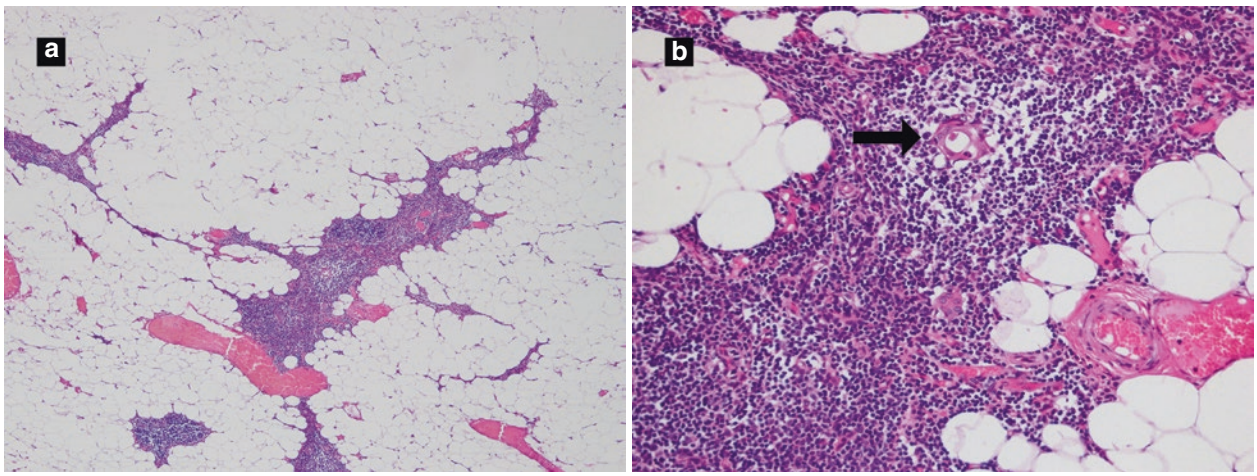

Fig. 15.29 (**a**, **b**) *Thymolipoma:* Thymolipoma is a benign adipocytic neoplasm with normal thymic tissue showing Hassall's corpuscles (**a**, **b**→) on microscopy. Clinically there is enlargement of the gland. The adipose tissue shows a lobulated appearance. Areas of dense fibrosis may also be seen

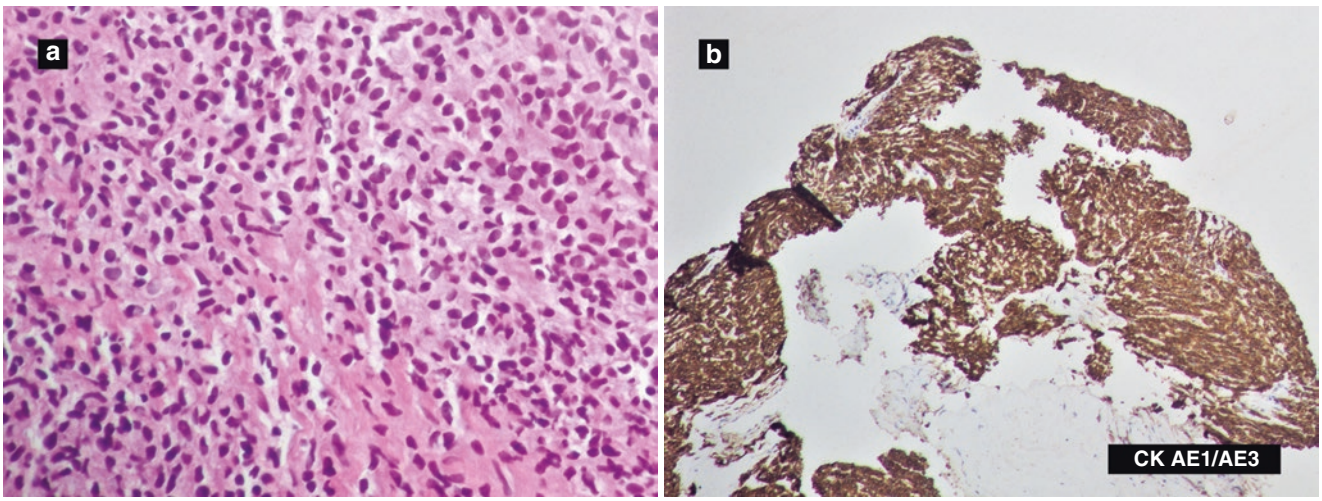

Fig. 15.30 (**a**, **b**) *Thymoma type A:* It is a thymic epithelial neoplasm, composed of spindle shaped to oval cells with either little or no admixed lymphoid cells (**a**). It is also known as 'spindle cell thymoma'. A number of growth patterns may be observed, including lobules, rosettes, microcystic areas, glandular and glomeruloid structures, whorls and fascicles, etc. The cells have bland morphology with fine powdery chromatin. The number of T-lymphocytes is none to scanty. If there are any lymphocyte-rich areas, then type AB thymoma should be considered. There is strong diffuse positivity for pan-cytokeratins CK AE1/AE3 (**b**). Tumours with some degree of atypia including the presence of focal necrosis, increased mitotic figures, or hypercellularity are classified as *atypical type A thymomas*, although their clinical significance remains to be ascertained

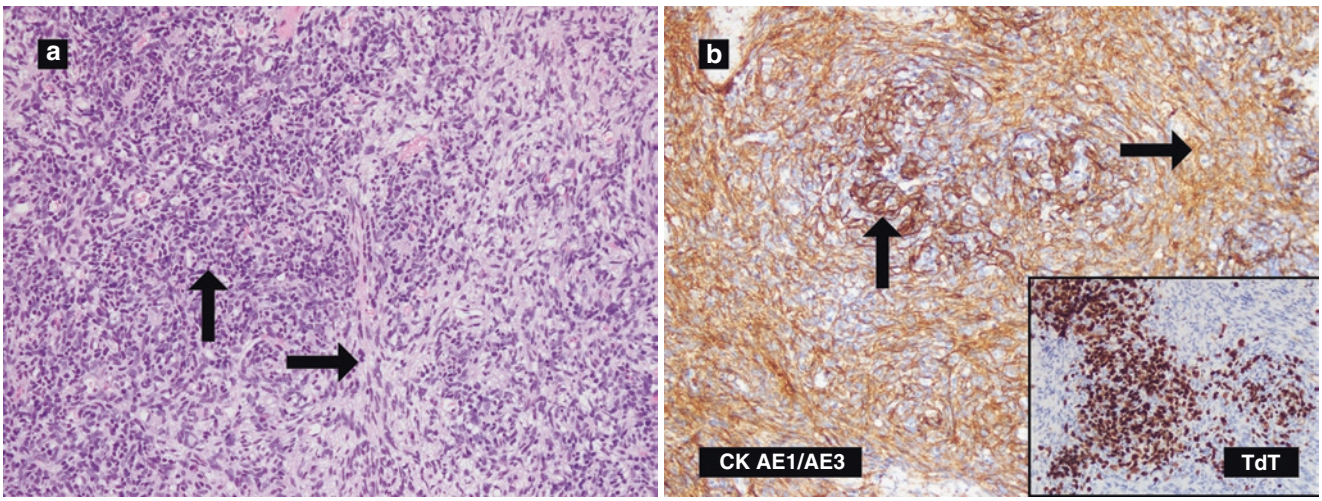

Fig. 15.31 (**a**, **b**) *Thymoma type AB:* Thymoma type AB shows a mixture of areas with typical type A morphology and areas having a significant population of TdT-positive T-lymphocytes. These two areas can be seen admixed together or in distinct lobules within the same tumour. The epithelial cells in areas with lymphocytes may be spindly, oval, or polygonal in shape. The presence of lymphocyte population is the most significant one to make a diagnosis of type AB thymoma. Panel (**a**) shows an admixture of spindly (→) cells with polygonal (↑) cells on H&E stained sections. Pan-cytokeratin CK AE1/AE3 shows spindle cell component (**b**→) and shows epithelial component (**b**↑), the latter having numerous TdT-positive T-lymphocytes (**b**, inset)

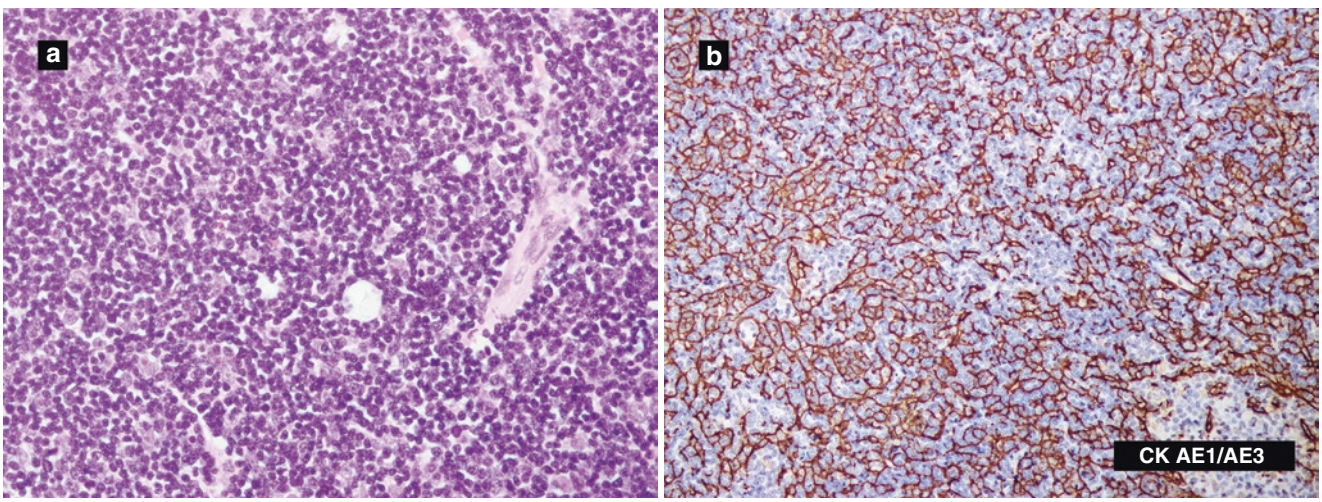

Fig. 15.32 (**a**, **b**) *Thymoma type B1:* Thymoma type B1 is a neoplasm of thymic epithelial cells that resembles the normal uninvoluted thymic tissue morphologically. The distinction is made when there is increased population of epithelial cells within the dense lymphoid thymic tissue (**a**). Foci of medullary differentiation, characterized by vaguely nodular pale areas, are always seen in B1 thymomas and help in distinguishing these tumours from other types of thymomas. The epithelial cells are reactive with pan-cytokeratins CK AE1/AE3 on immunohistochemistry (**b**)

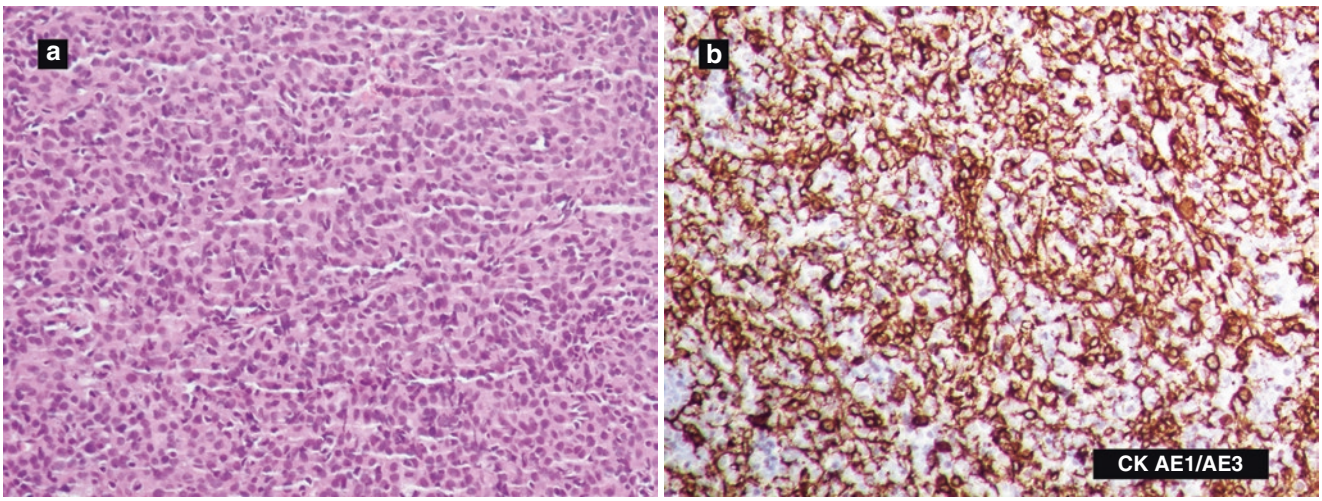

Fig. 15.33 (**a**, **b**) *Thymoma type B2:* Thymoma type B2 comprises clusters of neoplastic epithelial cells with admixed immature T-lymphocytes (**a**). The epithelial cells are polygonal and have rounded nuclei with small but prominent nucleoli. Characteristic perivascular spaces may also be seen, which are composed of a central venule surrounded by clear area containing either proteinaceous material or lymphocytes. Pan-cytokeratins CK AE1/AE3 are again useful to highlight the increased population of neoplastic epithelial cells (**b**)

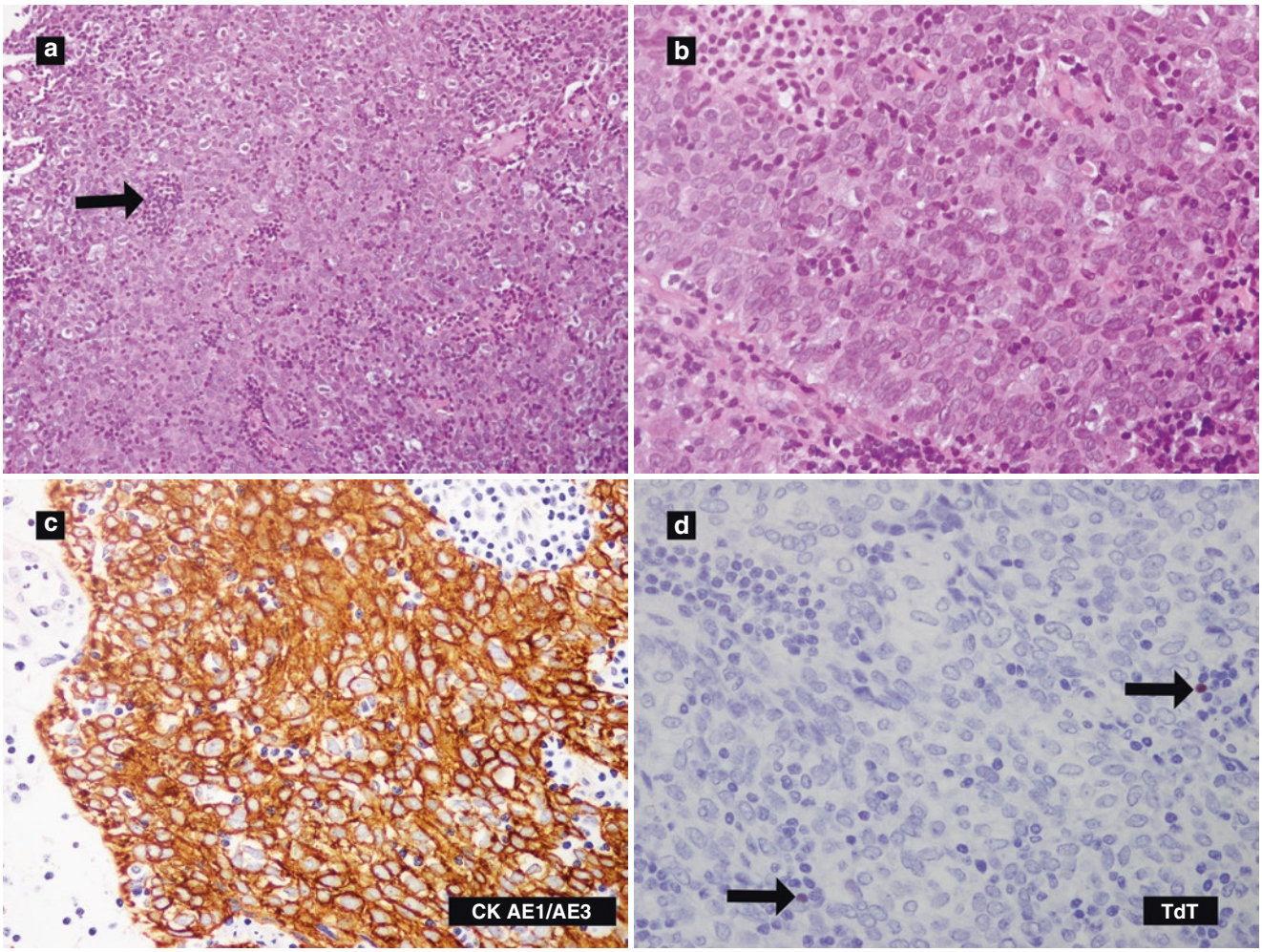

Fig. 15.34 (**a**–**d**) *Thymoma type B3:* Thymoma type B3 shows sheetlike or solid growth of neoplastic atypical epithelial cells with intermingled T-lymphocytes (**a**→). These tumours frequently show invasion/extension into the adjacent adipose tissue. The tumour cells are polygonal, lack intercellular bridges and contain moderately atypical elongated to grooved or resinoid nuclei (**b**). Immunohistochemistry for cytokeratins shows sheetlike growth of epithelial cells (**c**) and a paucity of TdT-positive T-lymphocytes (**d**→)

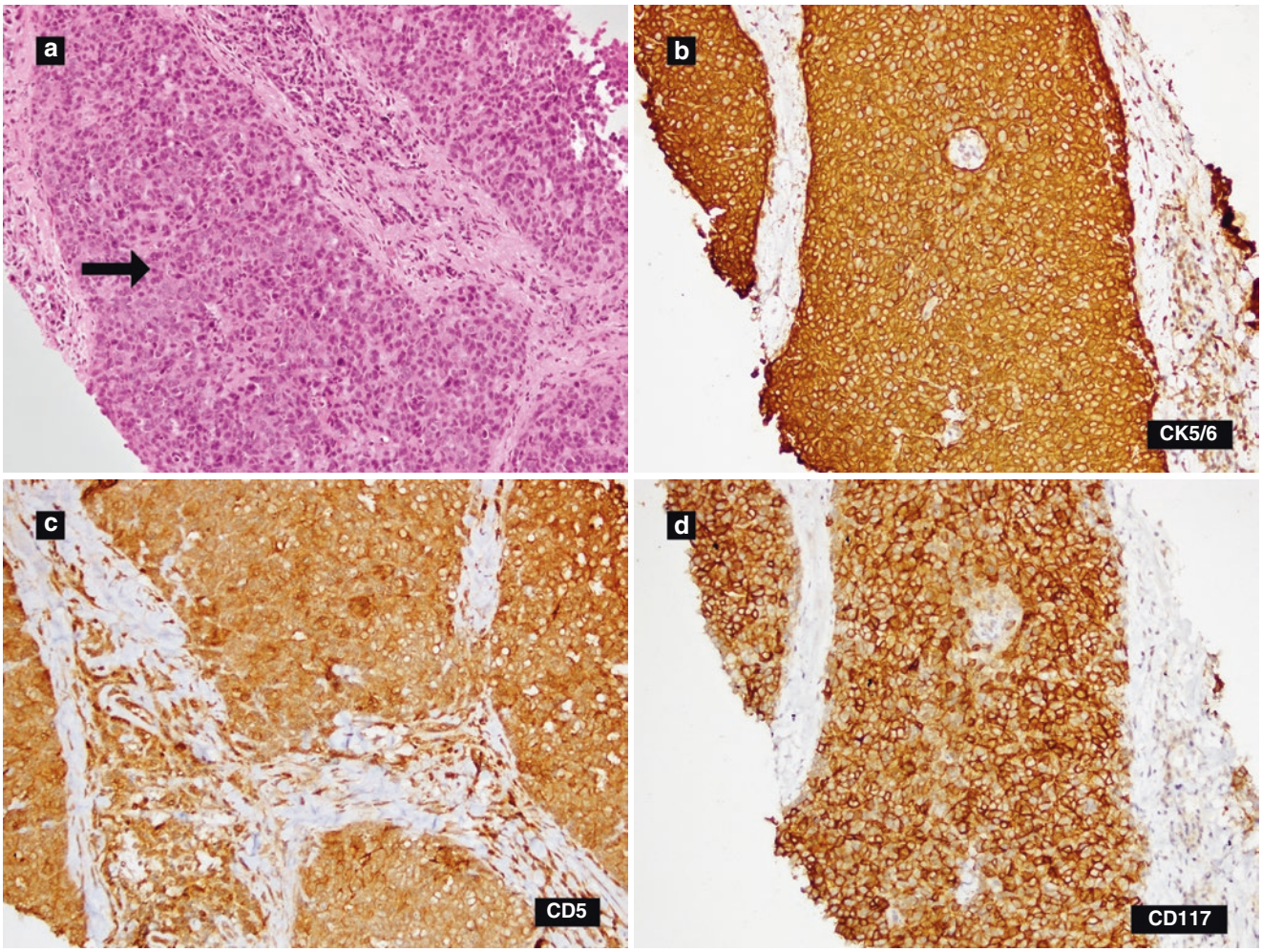

Fig. 15.35 (**a**–**d**) *Thymic carcinoma:* Thymic carcinomas, as per recent WHO classification of thymic neoplasms, encompass a large number of tumours under the umbrella of thymic carcinomas, with squamous cell carcinoma being the most common type. These tumours in general are distinguished from thymomas by the lack of resemblance to normal thymus, lack of lobulation and an absence of TdT-positive T-lymphocytes. Panel (**a**) shows one such example, which is composed of aggregates and sheets of pleomorphic cells (→) which are positive for immunohistochemical stains CK5/CK6 (**b**), CD5 (**c**) and CD117 (**d**), which are the characteristic markers for diagnosing thymic carcinomas

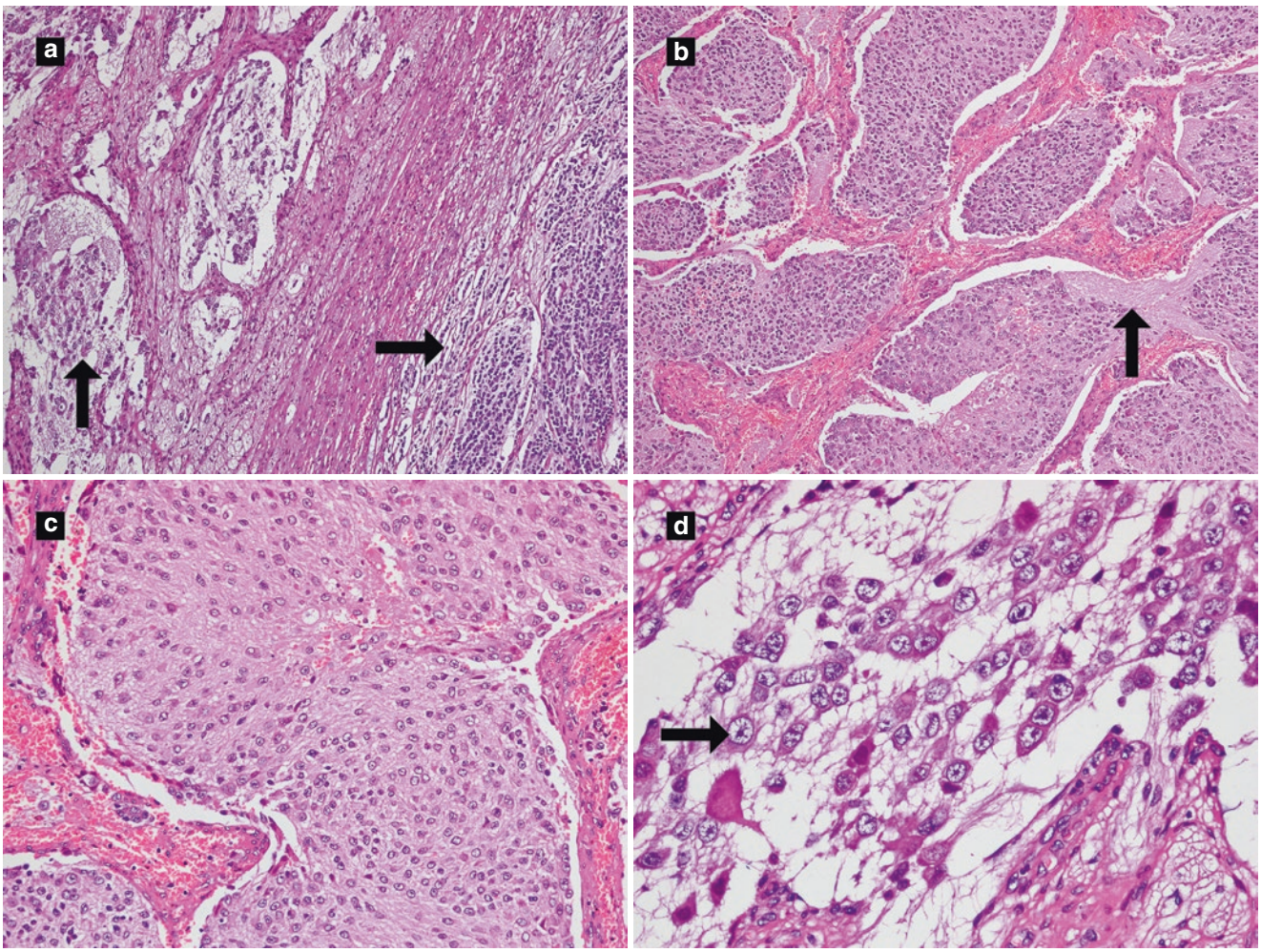

Fig. 15.36 (**a**–**d**) *Ganglioneuroblastoma:* Ganglioneuroblastomas are tumours of the sympathetic nervous system that are more common in the retroperitoneum as compared to the mediastinum. However, in mediastinum, they tend to be better differentiated. Therefore, a neuroblastoma may rarely be seen in this location. Ganglioneuroblastoma is the commonest of these tumours in this region. It is mostly seen in children and shows intermediate differentiation. It is of two types, intermixed and nodular. The nodular type shows areas with schwannian stroma-poor nodules (**a**→) which are grossly visible and areas with schwannian stroma-rich appearance (**a**↑), while the intermixed type shows intermingled foci of neuroblastic elements with naked neuropil (**b**↑, **c**) in an expanding schwannian stroma, comprising more than 50% of the tumour. The neuroblastic elements show various degrees of differentiation from primitive-appearing neuroblasts to mature ganglion-like cells with amphophilic cytoplasm and vesicular nuclei having prominent nucleoli (**d**→)