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REVIEW

Benign lesions of the mediastinum

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Benign lesions of the mediastinum

Mediastinal tumours represent a heterogeneous group of entities derived from the manifold structures located in or adjacent to the mediastinum. Due to the occurrence of some of these tumours in characteristic mediastinal compartments, an anatomical subdivision of the mediastinum in the prevascular (anterior), visceral (middle), and paravertebral (posterior) is helpful for the differential diagnosis. Benign anterior mediastinal tumours linked to an enlargement of the thymic gland mainly consist of thymic cysts and several types of thymic hyperplasia: true thymic hyperplasia, rebound hyperplasia, lymphofollicular hyperplasia, and so-called thymic hyperplasia with lymphoepithelial sialadenitis (LESA)-like features. Mature teratomas, ectopic (para)thyroid tissue, and benign thymic tumours such as thymolipoma or thymofibrolipoma represent further typical tumours of the anterior mediastinum. Pericardial, bronchogenic, or oesophageal duplication cysts predominate in the middle mediastinum, whereas neurogenic tumours and myelolipomas are characteristic findings in the posterior compartment. Vascular tumours, lipomas, adenomatoid tumours, Castleman disease, or mediastinitis are further examples of less frequent tumours or tumorous lesions affecting the mediastinum. This review focuses on benign mediastinal lesions with an emphasis on benign tumours of the thymus. Besides histology, characteristic epidemiological and clinical aspects prerequisite for the correct diagnosis and patient management are discussed.

Keywords: rebound hyperplasia of the thymus, thymic cyst; true thymic hyperplasia, thymic follicular hyperplasia, thymic hyperplasia with lymphoepithelial sialadenitis-like features

Introduction

Mediastinal tumours can be categorized according to their biological behaviour and location in one of the mediastinal segments. Based on the radiologic findings, the mediastinum is subdivided into three compartments: the prevascular (anterior) mediastinum situated between the sternum and the anterior contours of the heart and trachea, the paravertebral (posterior) mediastinum in the paravertebral area, and the visceral (middle) mediastinum located in between.[1] Two-thirds of all mediastinal lesions are benign, with half of them found in the anterior mediastinum and the other half located in the posterior and middle mediastinum.[2] The spectrum of entities differs between the compartments, age groups, and genders that altogether help to narrow down the differential diagnosis. For instance, thymic cysts are the most prevalent in the anterior mediastinum, while pericardial cysts, bronchogenic cysts, and oesophageal duplication cysts constitute the most common benign lesions in the middle mediastinum. Neurogenic tumours are typically located in the posterior mediastinum and are usually benign in adults; however, they are more frequently malignant in children.[3]

This work reviews benign mediastinal lesions with a special emphasis on benign tumours of the thymus.

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Anterior Mediastinal Tumours

Benign anterior mediastinal tumours linked to an enlargement of the thymic gland mainly consist of

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thymic cysts and several types of thymic hyperplasia: (a) true thymic hyperplasia, (b) rebound hyperplasia, (c) lymphofollicular hyperplasia, and a recently described entity named "thymic hyperplasia with lymphoepithelial sialadenitis (LESA)-like features".[4] For a comprehensive overview of benign mediastinal lesions, see Table 1. Cysts represent 24% of all solitary lesions in the anterior mediastinum, making them the second most common lesion after thymomas.[5] Mediastinal cysts are classified into unilocular or multilocular, and congenital or acquired. Most congenital cysts are unilocular, while inflammatory and neoplastic cysts tend to be multilocular.[6]

TRUE THYMIC HYPERPLASIA

True thymic hyperplasia (TTH, also termed thymic parenchymal hyperplasia) is characterized by diffuse thymic enlargement with normal histology and an organ weight exceeding the regular age-adjusted maximal weight.[7–9] It is rare in adults and typically found in newborns and children, where the weight of the enlarged organ can be far beyond 100 g.[10] Unlike thymic follicular hyperplasia (TFH), which is frequently linked to autoimmune diseases and exhibits an elevated presence of lymphoid follicles in the medulla and perivascular spaces, TTH can induce localized symptoms.[11] The aetiology is unknown, although secondary cases may occur in association with endocrine diseases such as acromegaly, hypopituitarism, Graves', and Addison's disease. Symptoms derived from a mass lesion, eventually aggravated by an acute haemorrhage, are frequent and can be life-threatening.[12] The diagnosis is usually straightforward when examining whole organ explants; however, the differential diagnosis can be challenging on biopsies: A fibrous capsule and septa with adjacent medullary islands showing no Hassall corpuscles suggest a B1 thymoma. Expansive lymphoblast growth, clonality, and the presence of Notch1 or Lmo2 expression in some cases should raise the suspicion of T-lymphoblastic lymphoma. The differentiation from a rebound hyperplasia of the thymus, which also shows regular organ architecture, does not pose a problem if information on the patient's history is available (e.g. a preceding immunosuppression or infection, see below). Moreover, TTH affects rather younger children, whereas rebound hyperplasia affects adolescents and adults. The possibility of an accidentally sampled normal thymic tissue unrelated to the actual tumorous process or as a part of a thymolipoma, thymolipofibroma, or lipofibroadenoma should also be considered; however, the three latter entities show rather an atrophic thymic parenchyma.

REBOUND HYPERPLASIA OF THE THYMUS

Rebound hyperplasia of the thymus shows a normal organ architecture with surprisingly mild (or no) age-typical signs of atrophy (Figure 1A). The organ weights usually do not exceed 100 g. It is mostly an incidental finding in children and young adults suffering from endocrine disorders, after recovery from infectious diseases or after cessation of radiotherapy, chemotherapy, or immunosuppression.[10,13] The information on the patient's history is a prerequisite for the correct diagnosis. The differential diagnoses overlap with the TTH (see above).

THYMIC FOLLICULAR HYPERPLASIA

The hallmark of TFH is the occurrence of lymphoid follicles in the medulla and perivascular spaces in more than one-third of thymic lobes (Figure 1B–E). Isolated follicles can also be found in healthy persons and may not necessarily indicate a disease. TFH is commonly observed in patients with early-onset myasthenia gravis who test positive for anti-acetylcholine receptor autoantibodies. However, it is not exclusively linked to this condition and can be detected in individuals with other autoimmune diseases or in those who are asymptomatic.[14–16] TFH *per se* typically does not cause any symptoms. In cases where immunosuppressive therapy is administered prior to surgery, as often seen in myasthenia gravis, it can lead to organ atrophy, particularly affecting the cortical region. Immunohistochemistry for CD23 (or CD21) can be helpful in visualizing the lymphoid follicles.

The differential diagnosis can be problematic on biopsies, as the presence of lymphoid follicles can be nonspecific and unrelated to a tumorous process eventually missed by the biopsy. In case of myasthenia gravis, exact information on serology might be helpful, as antibodies against titin, ryanodine receptor, or striated muscle are rare in TFH and should raise a possibility of thymoma-associated (or late onset) myasthenia gravis.[14] When numerous follicles are present alongside pronounced lymphoepithelial lesions, epithelial hyperplasia, cysts, and either substantial or complete cortical atrophy, it is important to consider the diagnosis of the so-called Thymic hyperplasia with lymphoepithelial sialadenitis (LESA)-like features (LESA-like TH) (see below). The micronodular thymoma (or carcinoma) with lymphoid stroma, which also show prominent lymphoid follicles, can be easily recognized due to their dense trabecular epithelial component, lack of Hassall corpuscles, and paucity (or absence, in case of carcinoma) of immature TdT-expressing

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Table 1. Benign lesions of the mediastinum

Entity	Epidemiology	clinical features	Pathology	Ancillary techniques	Prognosis	Ref.
Tumours occurring predominantly in the prevascular (anterior) mediastinum						
Ectopic tissue	Any age and sex, mostly in the fifth to eighth decades	Cough, dyspnea, hemoptysis, hyperparathyroidism	Parathyroid or thyroid tissue presenting as mediastinal mass	Serum PTH	Surgical excision is curative	[23,24]
Fibrosing mediastinitis	Complication of granulomatous infections; mostly between 20 and 40 years	Chest pain, dyspnea, dysphagia, cough, superior vena cava obstruction	Extensive, mass-forming, paucicellular fibrous tissue	Exclude IgG4-associated disease	Variable	[46–49]
Lipofibroadenoma	Young adults	Cough	Tubular epithelial cells in a fibromyxoid tissue with fat tissue, resembling fibroadenoma of the breast		Surgical excision is curative	[24,28]
Rebound hyperplasia of the thymus	Children and young adults	Following recovery from infections, radio/chemotherapy, immunosuppression or in endocrinopathies	Normal organ architecture with surprisingly mild (or no) age-typical atrophy and organ weights <100 g		Surgical excision to differentiate from other diseases	[10,13]
Teratoma	Childhood	Dyspnea, cough, chest pain	Multiple tissues foreign to the mediastinum		Surgical excision is curative	[22,50,51]
Thymic cyst	Any age and sex	Chest pain, dyspnea, hoarseness, cough	Cystic spaces lined with fibrous squamous epithelium with variable inflammatory changes and, most notably, Hassall's corpuscles	Exclusion of differential diagnoses	Symptomatic cysts are excised	[6,19]
Thymic follicular hyperplasia	Younger adults, typical in patients with anti-acetylcholine receptor autoantibody positive early-onset myasthenia gravis	As such asymptomatic	Lymphoid follicles in the medulla and perivascular spaces in more than one third of thymic lobes	CK19, CD20, CD23, TdT	Surgical excision eventually in combination with immunosuppression	[14–16]
Thymic hyperplasia with LESA-like features	Adults, slight male predominance	As such asymptomatic. Increased incidence of lymphomas and autoimmune diseases	Expanded epithelial cells meshworks, lymphoepithelial lesions, cysts, subtotal cortical atrophy and lymphofollicular hyperplasia with a lymph node-like appearance	CK19, CD20, CD23, TdT, exclude lymphoma	Surgical excision	[17,18]

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Table 1. (*Continued*)

Entity	Epidemiology	clinical features	Pathology	Ancillary techniques	Prognosis	Ref.
Thymolipoma	Any age and sex; commonly young	Dyspnea, chest pain, weight loss, chronic heart failure	Large, encapsulated mass composed of mature adipose and thymic tissue	CD1a, CD99, TdT	Surgical excision is curative	[2,26]
True thymic hyperplasia	Newborns and children	Mass lesion, eventually aggravated by haemorrhage, life threatening	Normal histology and an organ weight > 100 g		Surgical excision is curative	[10,12]
Tumours occurring predominantly in the visceral (middle) mediastinum						
Bronchogenic cyst	Congenital	Cough, dyspnea, pain, pneumonia, fever	Primarily manifest in the mediastinum, with the tracheal carina and paratracheal regions being the most common locations, and rarely in the lung parenchyma. These cysts are characterized by a wall comprising cartilage, smooth muscle, and respiratory epithelium		Sometimes associated with other congenital pulmonary malformations	[19,30]
Oesophageal duplication cyst	Congenital	Often asymptomatic; dysphagia, pain	Contact with the oesophagus (middle mediastinum). Mucosal, submucosal, and muscular layer of the gastrointestinal tract. Mucosa with squamous, gastric, primitive, or ciliated columnar epithelium			[19]
Pericardial cyst	Congenital	Most patients are asymptomatic; chest pain, cough, fever, arrhythmias	Unilocular cysts, primarily found in the middle mediastinum. They are characterized by a single layer of mesothelium lining and a fibrocollagenous stroma		May become infected	[19]
Tumours occurring predominantly in the paravertebral (posterior) mediastinum						
Myelolipoma	Adults of any age and sex	Mostly asymptomatic	Mature adipose tissue with islands of extramedullary haematopoiesis and variable degenerative changes, such as haemorrhage		Surgical excision is curative	[37]

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Table 1. (*Continued*)

Entity	Epidemiology	clinical features	Pathology	Ancillary techniques	Prognosis	Ref.
Neurofibroma	Children or young adults; M = F	Posterior mediastinal lesion with possible extension into vertebral canal, forming a so-called "dumbbell tumour"	Expansion of multiple nerve fascicles with disorganized arrays of thin, bland spindle cells in a loose myxoid stroma mixed with fibroblasts and fibrous tissue	S100, SOX10, CD34	Surgical excision is curative. In patients with Neurofibromatosis type 1 high lifetime risk of malignant peripheral nerve sheath tumour	[32–35]
Schwannoma	Fourth to sixth decades; M / F	Posterior mediastinal lesion with possible extension into vertebral canal, forming a so-called "dumbbell tumour"	Antoni A: dense spindle cells with nuclear palisading; Antoni B: loose arrangement of stellate cells with degeneration	S100, SOX10	Surgical excision is curative; association with Neurofibromatosis type 2	[32,33,52]
Other benign tumorous conditions						
Acute mediastinitis	40% after cardiac surgery; 33% with oesophageal perforation	Acute inflammation, arrosion of organs	Acute to necrotizing inflammation		High morbidity and mortality	[47,53]
Adenomatoid tumour	Mostly in the fifth to eight decades	Cough	Epithelioid cells arranged in cords and tubular structures in a fibrous or fibromyxoid stroma	CK7, D2-40, WT-1	Surgical excision is curative	[45,54]
Castleman disease	Any age, slight female predominance	Lymphadenopathy	Lymphatic follicles composed of small, regressed germinal centers and expanded mantle zones with an "onion skin" appearance and hyaline-sclerosed vascular "lollipop" lesions	HHV8	Surgical excision is curative; recurrence is rare	[42–44,55]
Granulomatous mediastinitis	Complication of granulomatous infections	Chest pain, dyspnea, dysphagia, cough	Granulomatous inflammation	Consider infections, autoimmune disorders, neoplasia, pneumoconiosis	Depending on aetiology	[47,49]
Hemangioma/ vascular malformation	Any age and sex	Chest pain, cough, dyspnea	Well-formed, blood-filled vessels lined by bland endothelium	CD31, CD34	Surgical excision is curative	[24,56–58]

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Table 1. (*Continued*)

Entity	Epidemiology	clinical features	Pathology	Ancillary techniques	Prognosis	Ref.
Hemolymphangioma	Any age; female predominance	Chest pain, cough, haemorrhage	Composed of both lymphatic and blood vessels	CD31, CD34, D2-40	Recurrence and invasion have been reported	[38,59,60]
Lipoma	Any age and sex	Cough, Dyspnea	Benign neoplasm of mature adipose tissue		Surgical excision is curative	[24,25]
Lymphangioma	Children and young adults	Pleural effusion, vocal cord paralysis, venous compression, stridor	Thin-walled dilated lymphatic vessels lined by bland endothelium	CD31, ERG, D2-40	Surgical excision is curative	[24,61]

AFP, Alpha-fetoprotein; F, Female; M, Male; PTH, Parathyroid hormone.

T-lymphocytes. Follicles with an aberrant architecture should raise the suspicion of a lymphoma, in particular the mucosa-associated lymphoid tissue (MALT) lymphoma, and warrant a further haematopathologic workup. Castleman's disease should be considered if atypically small, onion-skin-shaped follicles, and hyalinised blood vessels are found (see below).

THYMIC HYPERPLASIA WITH LYMPHOEPITHELIAL SIALADENITIS (LESA)-LIKE FEATURES

LESA-like TH is a tumorous proliferation of thymic epithelial cells and lymphoid follicles.[17,18] The lesion is characterized by expansion of epithelial cell meshworks with prominent lymphoepithelial lesions, numerous Hassall corpuscles undergoing cystic changes, a substantial or even complete cortical atrophy, and lymphofollicular hyperplasia, potentially resulting in an organ appearance reminiscent of a lymph node (Figure 2). The largest cohort published so far showed a slight male predominance and a mean age of 52 years (range 32–80 years).[17] Moreover, it revealed that 14% of the patients had an associated lymphoma, in most cases a thymic MALT lymphoma, and 33% of the patients suffered from nonmyasthenic autoimmune diseases such as systemic lupus erythematosus, rheumatoid arthritis, scleroderma, Sjögren syndrome, pure red cell aplasia, or Graves' disease (Figures 3 and 4). These findings indicate that LESA-like TH is not merely an aggravated form of a TFH, but rather an entity of its own standing and that a haematologic and rheumatologic work-up should be warranted in patients diagnosed with LESA-like TH.[17] The differential diagnosis overlaps with entities listed in the paragraph dealing with TFH. Moreover, because the cystic change can be prominent, some of these lesions may primarily present as cysts.

THYMIC CYST

Thymic cysts are most common in the anterior mediastinum, accounting for 1%–3% of all mediastinal masses.[19] Congenital cysts are rather unilocular, whereas inflammatory cysts that are thought to be derived from a dilatation of Hassall corpuscles tend to be multilocular.[6] Most patients are asymptomatic. Microscopically, thymic tissue with Hassall corpuscles is the key finding. Most cysts display a fibrous wall lined by squamous epithelium (Figure 5A), although it is worth noting that cuboidal to columnar epithelium, sometimes even resembling respiratory epithelium, can also be observed.

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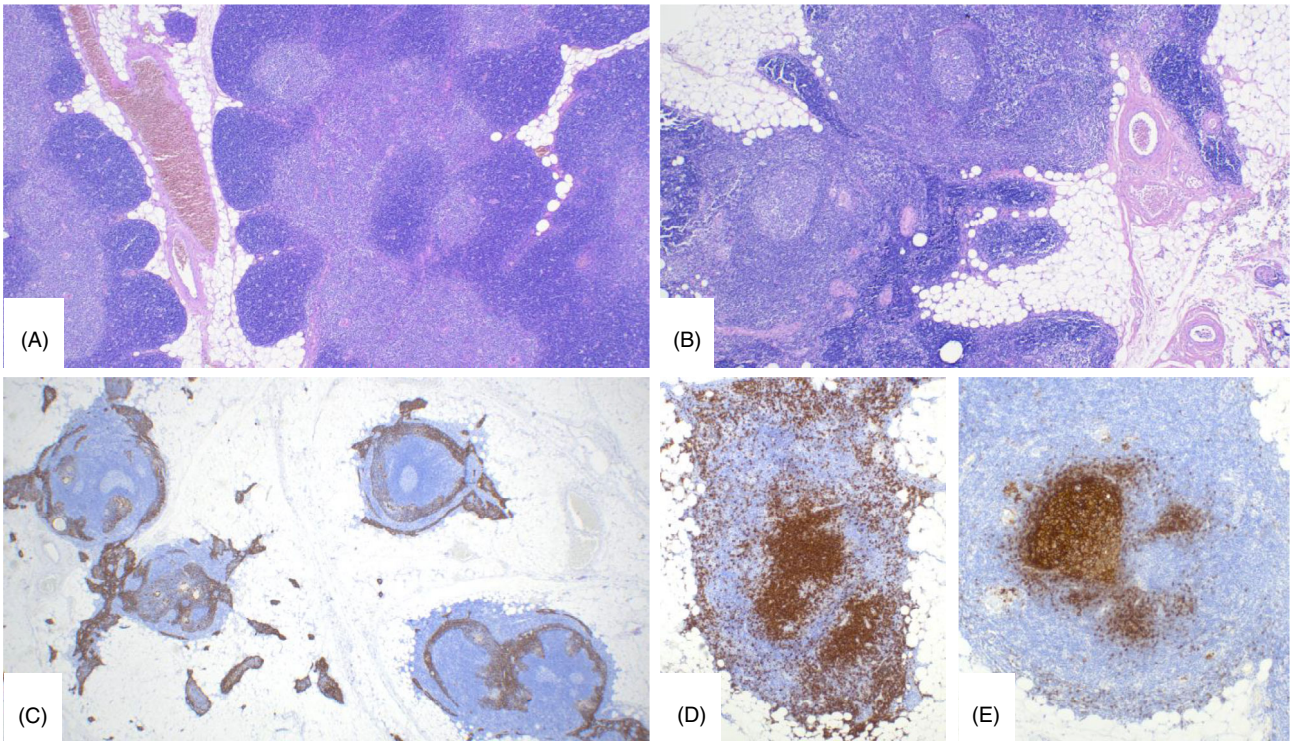

Figure 1. Rebound and thymic follicular hyperplasia. **A:** Rebound hyperplasia with unremarkable morphology showing well-developed cortical and medullary structures. This resection specimen comes from a 30-year-old male with a tumorous mediastinal lesion following a viral infection and lacks age-typical signs of atrophy or lymphoid follicles. **B–E:** Thymic follicular hyperplasia characterized by expansively growing lymphoid follicles in the medulla (**B**) and repelling the epithelial meshwork visualized by immunohistochemistry for cytokeratin 19 (**C**). The follicle-forming B-lymphocytes and follicular dendritic cells can be demonstrated by stains for CD20 (**D**) and CD23 (**E**), respectively.

Importantly, regardless of the type of epithelium, the presence of varying amounts of thymic tissue strongly suggests a diagnosis of a thymic cyst.[4,20] Necrosis, cholesterol granulomas, germinal centres, calcifications, and haemorrhage may be present. In the differential diagnosis, other lesions with cystic transformation must be considered: germ cell tumours, thymomas, lymphoepithelial sialadenitis-like thymic hyperplasia, or adenocarcinomas.

MATURE TERATOMA

Mediastinal germ cell tumours are typically localized in the anterior mediastinum and their histological classification is identical to that of the gonads.[21] Mature teratomas that are composed exclusively of mature somatic tissues (bronchial or gastrointestinal mucosa, pancreatic, and mature neural tissue) are benign.[22] These tumours are often asymptomatic. Symptoms of a mediastinal mass lesion, erosion of the adjacent structures, or hyperinsulinism due to the endocrine activity of the pancreatic tissue can occasionally occur.

ECTOPIC TISSUE

Ectopic thyroid tissue accounts for about 1% of all mediastinal tumours and typically occurs in the anterior mediastinum, although rare cases have been reported in the posterior mediastinum or intracardially.[23] Most patients are asymptomatic. Occasionally, symptoms related to a mass lesion or diseases affecting the thyroid gland (including malignancy) occur. Ectopic parathyroid lesions are also typically located in the anterior mediastinum, the majority of them being functional and leading to symptoms of hyperparathyroidism.[24]

MESENCHYMAL TUMOURS

Benign mesenchymal tumours of the mediastinum are rare, accounting for only 2% of all mediastinal neoplasms.[25] Symptoms may result from the compression of adjacent structures; however, most patients are asymptomatic, and the tumours are diagnosed incidentally. Notably, in older individuals, an association with myasthenia gravis may be observed.

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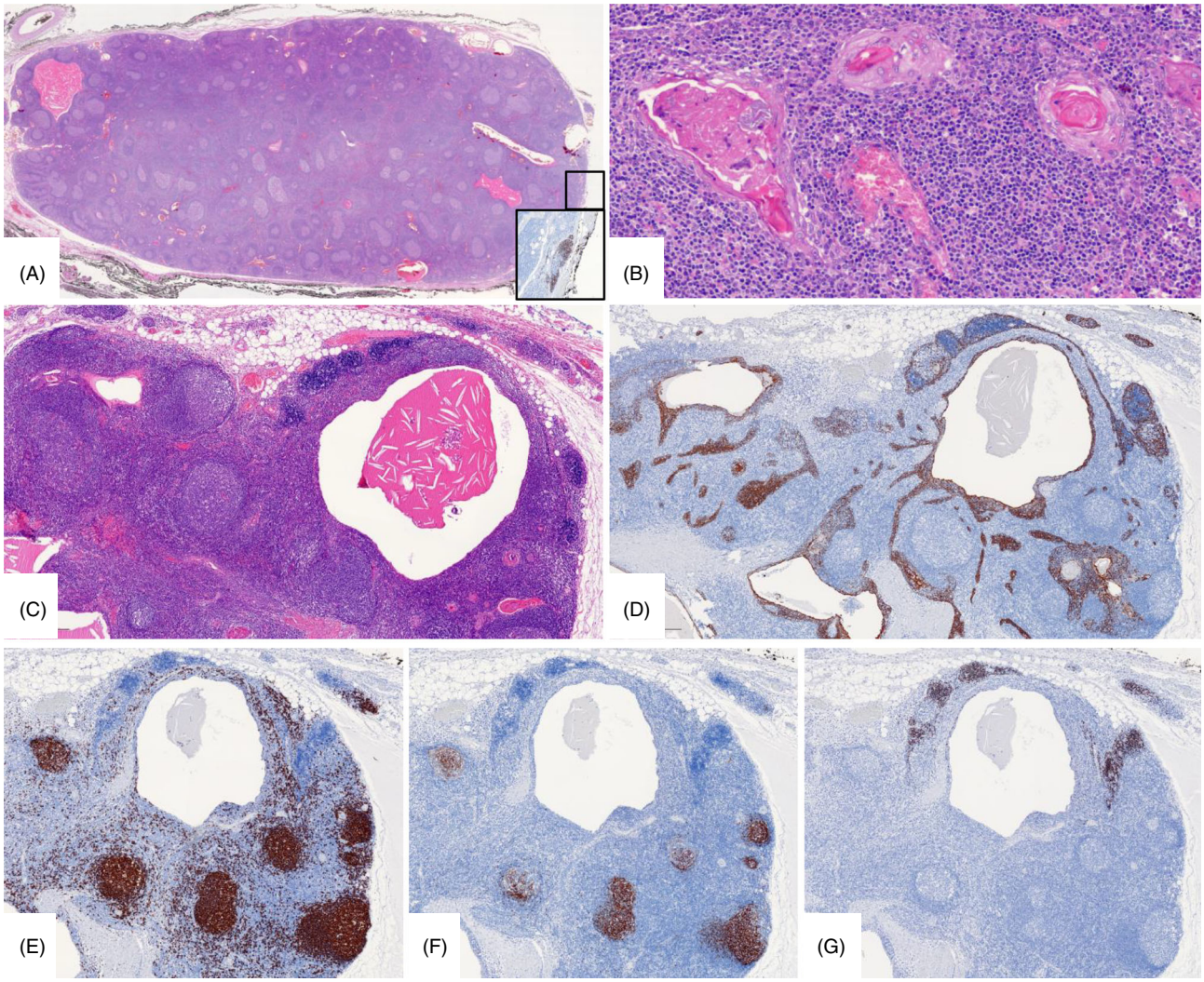

Figure 2. Thymic hyperplasia with lymphoepithelial sialadenitis (LESA)-like features. **A:** A low-power view showing a severe lymphofollicular hyperplasia leading to a lymph node-like appearance. In severe cases, immunohistochemistry for TdT (inlay) can be helpful in identifying the cortical structures that are atrophic; abutted to the periphery are barely discernible in haematoxylin and eosin (HE) stains. Note also cysts containing cholesterol clefts. **B:** Hyperplasia of the medullary epithelium and Hassall corpuscles with cysts in *statu nascendi*. **C–G:** Serial sections demonstrating hyperplasia of the medullary epithelium with lymphoepithelial lesions and transition into cystic structures as visualized by immunohistochemistry for cytokeratin 19 (**D**). Between the epithelial trabeculae, a dense follicle-forming B-cell infiltrate can be seen in stains for CD20 (**E**) and CD23 (**F**). Cortical structures with a delicate epithelial meshwork and immature TdT-expressing T-cells are atrophic and located in the noninflamed area (G).

Thymolipomas are circumscribed encapsulated tumours composed of adipose tissue intermingled with thymic tissue, which can be atrophic or normal, often containing Hassall corpuscles (Figure 5B). Probably due to their slow and non-infiltrative growth, thymolipomas can reach a large size (up to 30 cm). Variants like thymofibrolipoma or thymoangiolipoma exhibit extensive collagen fibres and varying amounts of blood vessels, respectively (Figure 5C). Thymolipomas lack amplification of mouse double minute 2 homologue (*MDM2*) and do not demonstrate cytological atypia.[26]

Lipofibroadenoma is a very rare benign tumour of the thymus. Macroscopically, this tumour presents as a large circumscribed intrathoracic fatty mass. Histologically, the tumour is composed of mature adipose tissue with fibrous stroma containing trabeculae or collaptic tubular epithelial structures, making the tumour resembling a fibroadenoma of the breast (Figure 5D). Remnants of thymic parenchyma with

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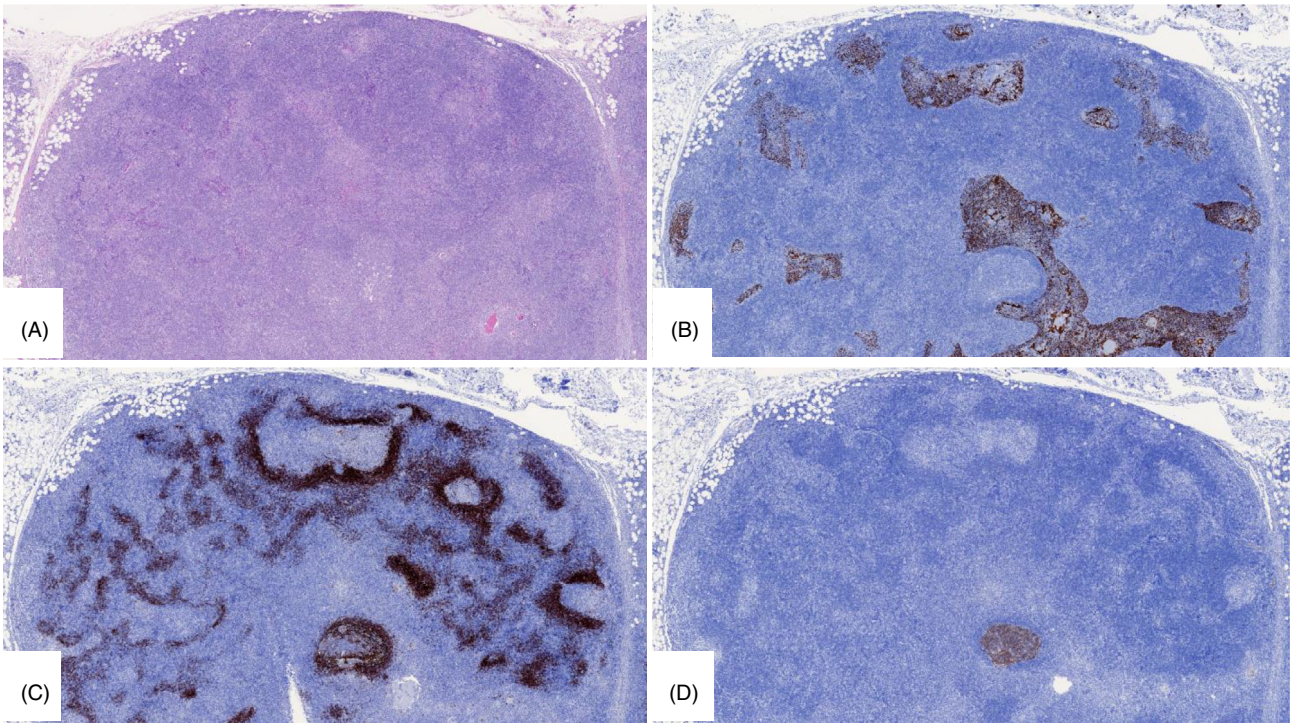

Figure 3. Thymic hyperplasia with lymphoepithelial sialadenitis (LESA)-like features in transition to a marginal zone lymphoma. Transition to a marginal zone lymphoma is visible as a loss of the typical follicular architecture (**A**) and prominent lymphoepithelial lesions discernible in the immunohistochemistry for cytokeratin 19 (**B**). The stains for CD23 (**C**) and CD10 (**D**) help to identify the atypically enlarged and irregular follicles colonized by CD10-negative cells. In the lower part, a normal follicle populated by CD10+ follicular cells can still be seen.

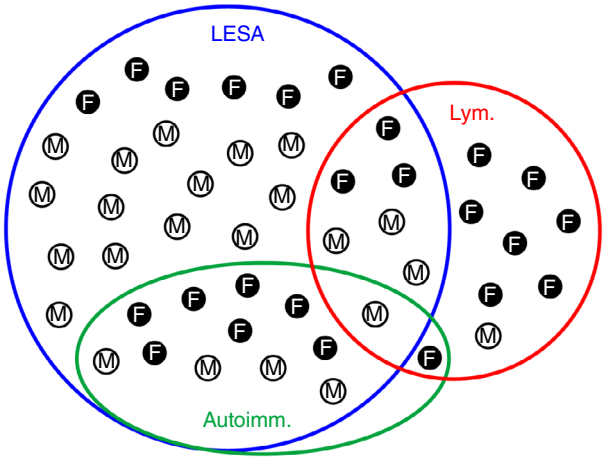

Figure 4. Overlaps between LESA-like TH, lymphomas, and autoimmune diseases. Venn diagram demonstrating the overlaps between the diagnoses of LESA-like TH (LESA), lymphoma (Lym.), and autoimmune disorders (Autoimm.). M, male; F, female. Diagram reprinted from Thymic Hyperplasia with Lymphoepithelial Sialadenitis (LESA)-Like Features: Strong Association with Lymphomas and Non-Myasthenic Autoimmune Diseases. Author S Porubsky *et al.*, *Cancers* (*Basel*). 2021 Jan 16;13(2):315(17). Copyright 2021 by the Authors. Licensee MDPI, Basel, Switzerland (CC BY licence). Reprinted from the Authors with permission.

Hassall corpuscles and calcifications can be identified focally.[27] In a few cases, they have been observed in proximity to a type B1 thymoma.[28]

Middle Mediastinal Tumours

PERICARDIAL CYST

Cysts are the most common lesion in the middle mediastinum.[5] In this region, most cysts are congenital. Pericardial cysts, found at the right cardiophrenic angle, are lined by a single layer of mesothelial cells, and have a fibrocollagenous connective tissue stroma. These cysts usually contain serous fluid.[29]

BRONCHOGENIC CYST

Bronchogenic cysts and oesophageal duplication cysts are both developmental malformations arising from the foregut.[6,19] Bronchogenic cysts predominantly occur in the mediastinum, with common locations being carinal, paratracheal, and paraesophageal, although they may also be found intrapulmonary or hilar. Typically presenting as unilocular structures, these cysts are

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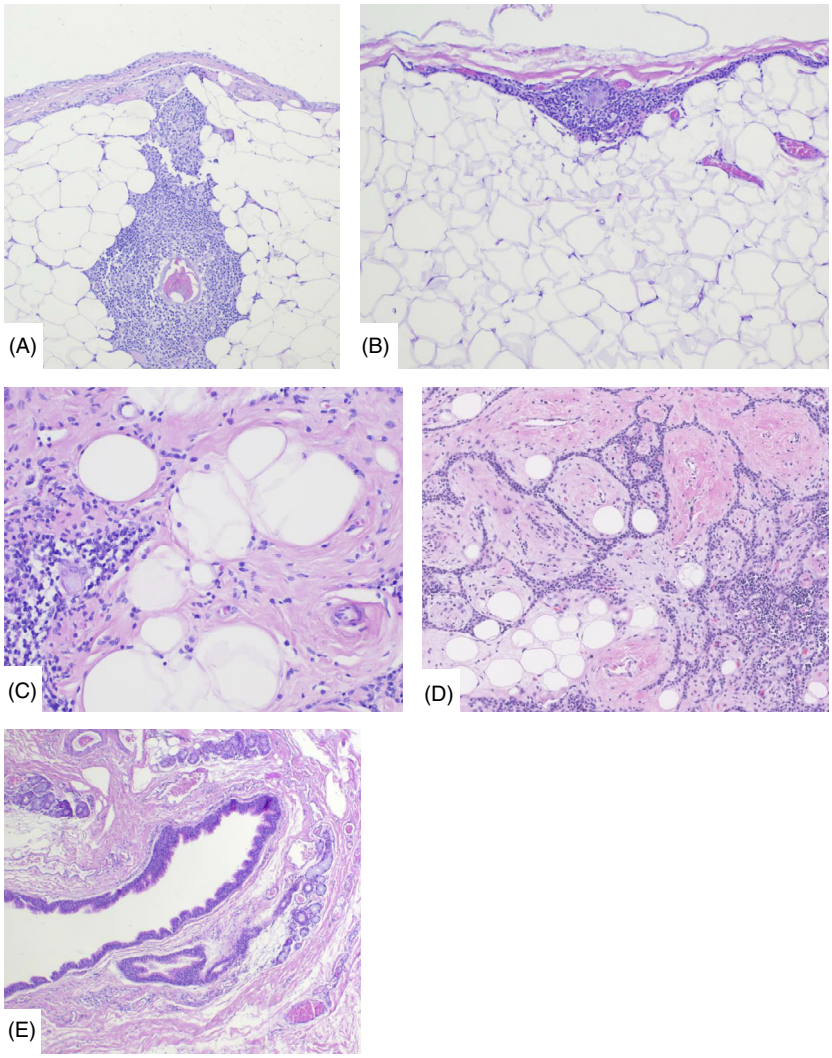

Figure 5. Other lesions. **A:** Thymic cyst lined by cuboid to squamous epithelium surrounded by a thin fibrous capsule and thymic tissue with Hassall corpuscles. **B:** Thymolipoma composed of mature adipose tissue and atrophic thymus rimmed by a thin fibrous capsule. **C:** Thymofibrolipoma with thymic remnants (left) and mature adipose tissue with coalescing fibrous septs. **D:** Lipofibroadenoma composed of mature adipose tissue, fibrous septs, and a network of narrow epithelial strands. Image kindly provided by Prof. Dr. Michael den Bakker, Erasmus MC, Rotterdam, The Netherlands. **E:** Bronchogenic cyst lined by ciliated epithelium, sparse smooth muscle fibres, and peribronchial-like glands.

filled with clear fluid, haemorrhagic secretions, or air. Histologically, bronchogenic cysts are characterized by a lining of columnar ciliated (respiratory) epithelium, while their walls may contain cartilage, smooth muscle, and small peribronchial glands (Figure 5E). Complications arise in 45% of cases, including pneumonia, hemoptysis, and pneumothorax.[30]

OESOPHAGEAL DUPLICATION CYST

Oesophageal duplication cysts are found in proximity to the oesophagus. They exhibit a layered structure resembling the oesophageal wall, with smooth muscle layers lined by squamous, rarely respiratory, or primitive epithelium. One-third of cases may contain heterotopic gastric mucosa, while occurrences of pancreatic heterotopia or Peyer's patches have also been reported.[19,31]

Posterior Mediastinal Tumours

NEUROGENIC TUMOURS

Neurogenic tumours can arise from any tissue derived from the neural crest and are classified based on differentiation and cells of origin. In mediastinum, they are typically found in the costovertebral sulcus

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of the posterior compartment.[32,33] Among neurogenic tumours, nerve sheath tumours are the most prevalent, with schwannomas and neurofibromas accounting for 75% and 20%, respectively, of these tumours. Importantly, they can exhibit atypical changes, posing challenges in distinguishing them from malignant peripheral nerve sheath tumours (MPNST).[34,35] For a comprehensive review on neurogenic tumours of the posterior mediastinum, we refer to the parallel publication.[36]

MYELOLIPOMA

Myelolipoma is a benign tumour composed of haematopoietic cells and mature adipose tissue.[37] It is typically localized in adrenals, but occasionally found also in the mediastinum, especially the posterior part.

Other Mediastinal Tumours and Mass-Forming Lesions

VASCULAR TUMOURS AND ABNORMALITIES

In the mediastinum, the most benign vascular tumours are hemangiomas, vascular malformations, lymphangiomas, and hemolymphangiomas. These lesions are often at least partially cystic.[38] Lymphangiomas are typically composed of dilated lymphatic vessels. They can be in any part of the body but are often found in the anterior mediastinum in young patients and infants. In older patients, they are found in the posterior and middle mediastinum.[39] Hemolymphangiomas are rare tumours composed of a mixture of cystically dilated lymphatic and blood vessels. They can be located at any site of the body.[40] About two-thirds of hemolymphangiomas are diagnosed in female patients.[38] Hemangiomas are composed of ectatic vessels lined by endothelial cells and filled with red blood cells. Well-differentiated angiosarcoma can mimic hemangiomas. Angiosarcoma, in contrast, is typically distinguished by infiltration, cellular atypia, and necrosis. It is important to note that especially anastomosing hemangiomas can sometimes resemble well-differentiated angiosarcomas. However, anastomosing hemangiomas often exhibit distinctive features such as intralesional mature adipose tissue, small thrombi, extramedullary haematopoiesis, and the presence of *GNAQ* mutations.[41]

CASTLEMAN'S DISEASE

Castleman's disease is a rare lymphoproliferative disorder typically involving lymph nodes. Depending on histological findings, three subtypes are differentiated: hyaline-vascular, plasmacytic, and mixed subtypes. It can occur in a unicentric or multicentric fashion. Castleman's disease can occur in all compartments of the mediastinum, with 90% of cases encountered here being of the unicentric hyaline-vascular subtype.[42–44]

ADENOMATOID TUMOUR

Adenomatoid tumours are well-circumscribed benign neoplasms of mesothelial origin that typically occur in the abdominal region. However, they can rarely be found in all compartments of the mediastinum.[45] These tumours are composed of epithelioid cells forming pseudoglands and pseudovascular spaces. They must be distinguished from vascular tumours and mesotheliomas, which typically diffusely involve pleura, and show invasive growth and cytological atypia.[24]

MEDIASTINAL LIPOMA

Mediastinal lipomas can occur in any compartment of the mediastinum and are very rare. They are composed of mature adipocyte tissue. The presence of thymic tissue speaks in favour of a thymolipoma. Exclusion of *MDM2* amplification may be helpful in the distinction of well-differentiated liposarcoma.[24,25]

MEDIASTINITIS

Inflammation of the mediastinal tissue can be subdivided into three types: acute, chronic, and granulomatous. Acute mediastinitis is rare and typically of an infectious origin, often following surgery, but can also be caused by oesophageal perforations and oropharyngeal or odontogenic infections. Chronic fibrosing mediastinitis is an inflammation that is often incited by granulomatous infections. Dense lymphoplasmacytic infiltration with increased IgG4-positive plasma cells and storiform fibrosis are clues for IgG4-associated fibrosing mediastinitis.[46] Mediastinal granulomas can show a self-limiting course; however, the finding of a granulomatous inflammation should elicit a differential diagnostic work-up with regard to possible infections, autoimmune disorders, neoplasia, and pneumoconiosis.[47]

Conclusion

Mediastinal tumours are a heterogeneous group of entities derived from the manifold structures located

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in or adjacent to the mediastinum. The exact tumour localization (i.e. anterior, middle, or posterior compartment), patient age, sex, and symptoms (e.g. autoimmune disorders) represent important clues for the differential diagnosis. Benign thymic tumours mainly consist of thymic cysts and several types of thymic hyperplasias that have a characteristic histology and patients' history. Mature teratomas, ectopic tissue, and thymolipomas represent further benign tumours typical for the anterior mediastinum. Pericardial, bronchogenic, or oesophageal duplication cysts predominate in the middle mediastinum, whereas neurogenic tumours and myelolipomas are characteristic findings in the posterior compartment.

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Conflict of interest

All authors declare that they do not have any conflicts of interest.

Data availability statement

Data sharing is not applicable to this article, as no new data were created or analysed.

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