Mediastinal Infection and Inflammatory Disease

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30.1 Acute Mediastinitis

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30.1.1 Overview

Mediastinitis refers to focal or diffuse inflammation in the middle of thoracic cavity. Mediastinitis has many infectious and non-infectious causes, and most mediastinitis is caused by infection. Acute mediastinitis refers to an acute attack of severe infection involving connective tissue and/or organs in mediastinum, which is usually caused by bacterial infection.

Primary acute mediastinitis is rare and usually secondary. Common causes include esophageal perforation or rupture, chest trauma or surgery, secondary infection of mediastinal tumor, suppurative inflammation of adjacent tissues of mediastinum spreading to mediastinum, and hematogenous dissemination of infection foci in other parts [1–4]. Esophageal perforation usually occurs in areas of physiological stenosis, such as cricopharyngeal muscles or esophagogastric junction [5]. Most esophageal perforations are iatrogenic, mostly occurring during endoscopic surgery. The incidence of esophageal perforation is low for endoscopic examination alone, and the incidence of esophageal perforation can be increased by endoscopic-guided treatment of pneumatic dilatation. Esophageal perforation can also be secondary to necrosis of esophageal cancer, radiation esophagitis, and ulcer rupture caused by hiatal hernia. Spontaneous perforation (Boerhaave syndrome) is rare, accounting for about 15% of esophageal rupture, which is transmural rupture or full-thickness rupture of esophagus caused by sudden and rapid increase of esophageal pressure, which usually occurs after severe vomiting, after overeating, and heavy drinking. The rupture position is usually located at the esophageal level above the distal cardia, and the left side is often affected more severely [6, 7]. Esophageal rupture caused by esophageal foreign bodies accounts for about 12% of esophageal perforations and is more common at cricopharyngeal muscle. The prognosis of esophageal perforation is closely related to the cause of injury, esophageal diseases, and timely treatment. Anatomically, the mortality rate of cervical esophageal perforation is the lowest (6%), while the mortality rate of thoracic and abdominal esophageal perforation is significantly higher (27% and 21%, respectively). Spontaneous esophageal perforation can cause a higher mortality rate due to being found later, while traumatic esophageal perforation usually has a better prognosis due to being found earlier [6, 7].

Acute mediastinitis can occur after cardiothoracic surgery. Obesity, diabetes, long-term surgery, or internal mammary artery–coronary artery transplantation (especially bilateral), and reoperation all increase the risk of postoperative infection.

There are abundant lymphoid tissue and loose connective tissue in mediastinum. The anterior superior mediastinum is continuous with the anterior tracheal space of neck, and the posterior mediastinum is continuous with the prevertebral space and peripharyngeal space. The peripharyngeal space of the inferior mediastinum connects with the retroperitoneal space of the upper abdomen. Infection in adjacent areas often spreads to mediastinum and causes mediastinal infection. Periodontal infection, tonsil infection, peripharyngeal abscess, and neck postoperative infection can cause acute mediastinitis due to gravity and chest negative pressure spreading rapidly to mediastinum, namely acute descending necrotizing mediastinitis (ADNS) [8]. Mediastinal infection can also be caused by direct spread of chest wall infection. Retroperitoneal inflammation can also spread from retroperitoneal space to lower mediastinum, causing acute mediastinitis.

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The clinical manifestations of acute mediastinitis are related to the etiology, lesion scope, and course of disease. Common clinical symptoms include sudden chills, high fever, retrosternal pain with radiation pain of neck or scapula, and dyspnea. Abscess compression can cause dysphagia and dyspnea. Suffocation may occur in severe cases. Compression of thoracic vessels can cause circulatory disturbance. Clinical physical examination often shows shortness of breath, tachycardia, edema of face and neck, and subcutaneous emphysema of chest and neck. Hamman's sign accompanied by crunching sound can be found during cardiac auscultation.

The mortality of acute mediastinitis is high, and the success of treatment depends on early diagnosis, early anti-infection treatment, and timely surgical drainage. For patients suspected of acute mediastinitis, CT is the preferred imaging examination method [9]. Surgical treatment principles include drainage, primary suture, esophageal exfoliation, esophagostomy and gastrostomy, endoscopic vacuum wound-assisted treatment perforation and related esophageal paramediastinal drainage, and endoscopic stent placement combined with drainage.

The most common microorganism is colonized bacteria in the upper digestive tract, and the pathogenic bacteria of mediastinal infection caused by different causes are different. Mixed infection of aerobic and anaerobic bacteria is common in esophageal rupture and descending mediastinal infection of oropharynx. Pathogenic bacteria of mediastinal infection after cardiothoracic surgery include *Staphylococcus epidermidis* and *Staphylococcus aureus*, Gram-negative bacteria, fungi, and mycobacteria. As the disease progresses, mediastinal abscess or severe sepsis may occur.

30.1.2 Imaging Manifestations

1. X-ray: It often shows widened mediastinum and blurred upper mediastinum edge. Acute mediastinitis is often caused by esophageal perforation. The indirect signs of esophageal perforation on X-ray radiographs include mediastinal emphysema, left pneumothorax, and pleural effusion. Mediastinal emphysema is characterized by linear lucency shadows in soft tissue on both sides of the mediastinum and neck. External penetration of oral contrast agent into mediastinum or thorax is a reliable sign of esophageal perforation. During acute descending necrotizing mediastinitis, X-ray examination of neck soft tissue can show widened soft tissue in front of neck and throat or pneumatosis in neck.
2. CT: It is the best examination method to show mediastinal inflammation and mediastinal emphysema (Fig. 30.1). CT findings included localized mediastinal effusion, mediastinal pneumatosis, increased mediastinal fat density, mediastinal widening, pleural effusion, pericardial effusion, and mediastinal lymphadenectasis. In addition, oral contrast media can show the degree of esophageal perforation, which is very important for the choice of subsequent treatment methods.

Acute descending necrotizing mediastinitis is an acute, rapidly progressive mediastinal infection, the spread of which is attributed to gravity drainage from the neck to the mediastinum, intrathoracic negative pressure, and synergistic effects of bacterial growth. CT findings show the disappearance of normal fat space caused by single or multiple effusion/fasciitis, cellulitis, or myositis in adjacent tissues of neck. Other related signs include pleural effusion, pericardial effusion, jugular vein thrombosis, or lymphadenovarix.

30.1.3 Diagnostic Key Points

1. Diagnosis of mediastinal infection: At least one of the following criteria must be met: ① microorganisms can be cultured in mediastinal tissue in vitro or exudate; ② evidence of mediastinal infection can be found during operation; and ③ one of the following conditions: chest pain, sternal instability, or fever (body temperature higher than 38 °C) accompanied by mediastinal purulent secretion or positive microbial blood culture or microorganisms cultured in mediastinal drainage fluid.
2. The typical CT manifestations of acute mediastinitis: ① localized mediastinal effusion and pneumatosis; and ② other auxiliary signs: increased fat density in mediastinum, widened mediastinum, pleural effusion, pericardial effusion, and mediastinal lymphadenectasis.

30.1.4 Differential Diagnosis

1. Postoperative edema or effusion of mediastinum: Nonspecific changes such as edema or effusion may occur in local tissues 2–3 weeks after cardiothoracic surgery, which causes difficulty in distinguishing from postoperative acute mediastinitis. Therefore, it is necessary to combine with clinical manifestations to determine the diagnosis of mediastinal infection, and if necessary, puncture biopsy can be performed to make a definite diagnosis.
2. Mediastinal hematoma or hemorrhage: Trauma can cause local mediastinal hemorrhage, showing high density on plain CT, which is helpful for differential diagnosis.
3. Fibrosing mediastinitis: It has a subacute or chronic course. CT shows high density of mediastinal soft tissue, or local soft tissue mass or calcification, generally without mediastinal effusion or pneumatosis.

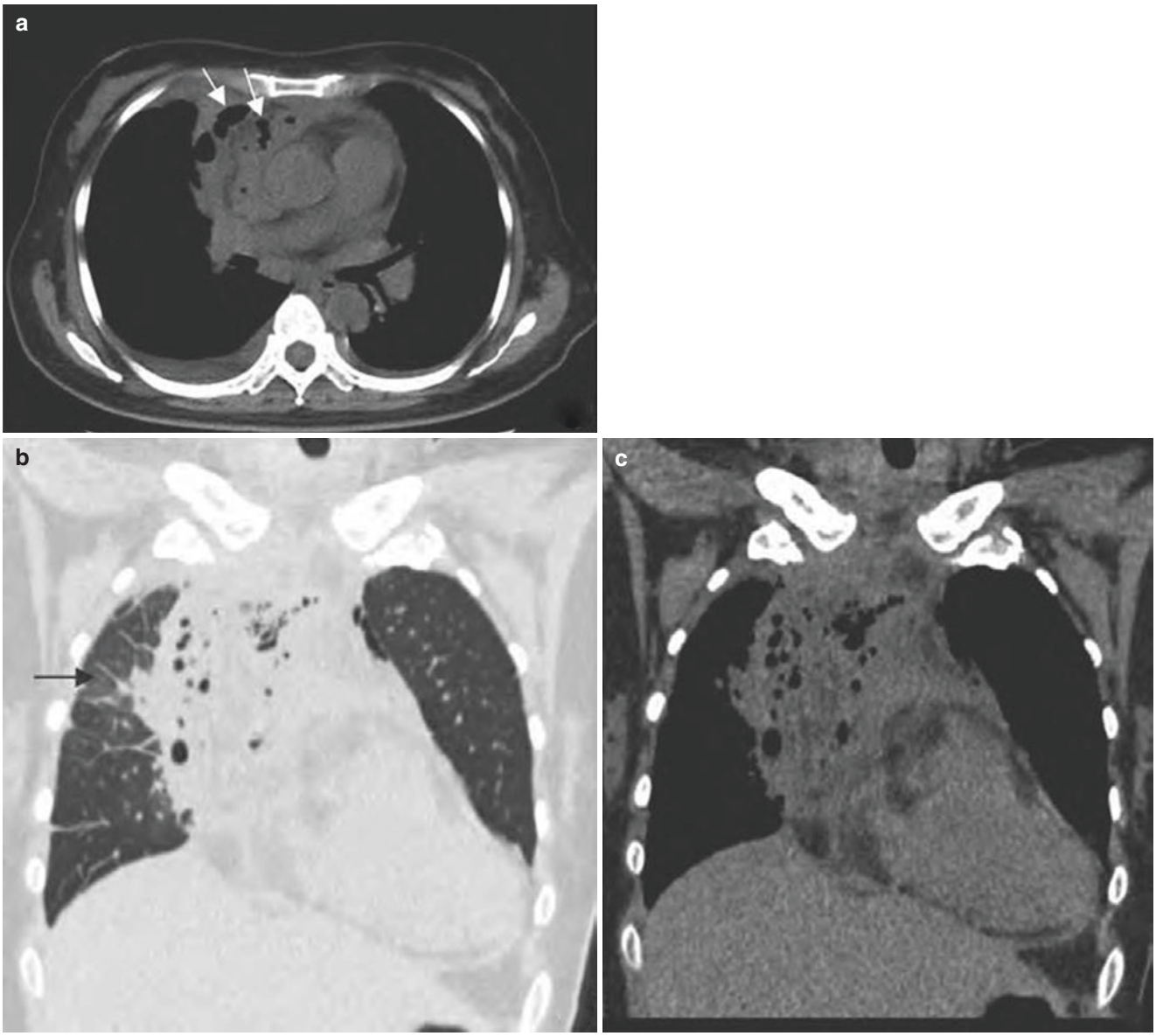

Fig. 30.1 Acute mediastinitis. (**a**) CT mediastinal window showed multiple free gases (arrows) in anterior mediastinum, increased local fat density, and bilateral pleural effusion; and (**b** and **c**) coronary reconstruction showed a wide scope of mediastinal lesions. Acute mediastinal edema compressed pulmonary veins and caused thickening of right pulmonary interlobular septum (arrow)

30.1.5 Research Status and Progress

MRI shows T_1WI hypodensity and T_2WI hyperdensity in mediastinal inflammation, with significant comparison with normal mediastinal fat. Therefore, MRI can well show the scope of mediastinal inflammation and the situation of blood vessels and lymph nodes in mediastinum. With no X-ray radiation, MRI provides an alternative for children and can be used in cases where there are still uncertainties after CT examination. However, due to the larger slice thickness of MRI scan and lower sensitivity to esophageal perforation and mediastinal gas than those of CT, MRI is only used as a supplementary examination choice for CT examination at present.

30.2 Fibrosing Mediastinitis

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30.2.1 Overview

Fibrosing mediastinitis (FM), also known as mediastinal fibrosis or sclerosing mediastinitis, is a rare disease characterized by hyperplasia of fibrous tissue in mediastinum. At present, it is considered as a chronic mediastinal inflammation. Even as a benign disease, FM is usually progressive and leads to compression and occlusion of tracheobronchial tree, esophagus, superior vena cava, and pulmonary vessels in mediastinum, thus causing related clinical symptoms.

FM may be manifested as a clinicopathological syndrome rather than a single disease, and its exact etiology and pathogenesis are still unclear. It may be idiopathic and secondary according to the etiology. Idiopathic FM may be related to IgG4 disease. Secondary FM may be related to infection, connective tissue diseases, sarcoidosis, mediastinal radiotherapy, and drugs. At present, most FM is considered to be caused by host immune overreaction in previous granulomatous infection. *Histoplasma capsulatum* and *Mycobacterium tuberculosis* are the most common pathogens of infection. Other infections, such as aspergillosis, bacillus disease, and cryptococcosis, can also cause FM. In addition, some scholars have confirmed that some FM may be related to autoimmune diseases, such as Behcet's disease, retroperitoneal fibrosis, orbital pseudotumor, and Riedel (fibrous) thyroiditis [10]. The relationship between human leukocyte antigen A2 (HLA-A2) and mediastinal fibrosis has been reported, suggesting that abnormal immune response is related to the pathogenesis of FM [11]. CD20 positive B lymphocytes may be involved in the pathogenesis of the disease.

At present, there is no accurate epidemiological data of fibrosing mediastinitis. Some studies in the United States show that FM mostly occurs in young females (20–40 years old), and the average diagnosis age is 33 years. Although histoplasmosis is the main cause of FM, less than 1% of patients with histoplasmosis can have fibrosing mediastinitis [12]. Histoplasmosis is rare in China, but tuberculosis has high occurrence. The research report of 12 FM patients in China [13] has shown that most of the patients are middle-aged and elderly females, and 50% of the patients has tuberculosis, so the relationship between *Mycobacterium tuberculosis* infection and FM may be closer in China.

The clinical manifestations of FM depend on the degree of damage and compression in mediastinal structure. The most common clinical manifestations are dyspnea, cough, and hemoptysis caused by central airway involvement. Calcified lymph nodes invade bronchus, leading to bronchial stones. These complications are most common in the upper lobe of the right lung. Esophageal compression can lead to dysphagia and/or odynphagia and may also cause tracheoesophageal fistula. Unilateral or bilateral phrenic nerve involvement can be manifested as diaphragmatic paralysis. Unilateral or bilateral main pulmonary artery obstruction can cause pulmonary hypertension, cor pulmonale, and right heart failure. Superior vena cava syndrome may occur if superior vena cava is compressed, which is manifested as neck swelling, upper limb swelling, dyspnea, and chest wall venous plexus dilatation. Chylothorax and chylous pericardial effusion may occur if thoracic duct is involved.

30.2.2 Pathological Manifestations

Fibrosing mediastinitis is mainly manifested as granulomatous mediastinitis. At present, most cases are caused by infection of histoplasmosis or *Mycobacterium tuberculosis*. Currently, the source of infection is not completely clear. It is speculated that the infection may originate from lung, then spread to mediastinal lymph nodes, and lead to mediastinal lymphadenitis. In a few patients, mediastinal lymph node granuloma expands and ruptures, releasing antigen into mediastinum, thereby stimulating mediastinal fibroinflammatory reaction and forming localized or invasive mass, causing mediastinal fibrosis. Histologically, fibrosing mediastinitis can be divided into three stages: Stage I shows that edematous fibromucous tissue contains many fusiform cells, eosinophils, mast cells, lymphocytes, plasma cells, and thin-walled blood vessels. Stage II shows thick hyalinized randomly arranged collagen with focal interstitial spindle cells, lymphocytes, and plasma cells. Stage III shows dense scattered lymphoid follicles with collagen and occasional dystrophic calcification.

30.2.3 Imaging Manifestations

1. X-ray: Chest radiograph is nonspecific and usually underestimates the lesion scope. The usual manifestations include mediastinal widening, hilar, or mediastinal lymphadenectasis, often secondary to histoplasmosis or pulmonary tuberculosis, showing localized calcification. Chest radiographs can also show stenosis of trachea or main bronchus due to compression, obstruction of superior vena cava, or esophageal stenosis.
2. CT: Fibrosing mediastinitis is divided into focal type and diffuse type [14]. The typical manifestations of focal type include localized soft tissue mass, and calcification occurs in 60–90% of the lesions, which is often located in the paratracheal, subcarina, or hilar areas, causing stenosis of adjacent blood vessels or airway. The typical manifestations of diffuse type include diffuse non-calcified soft tissue invasive mass involving multiple mediastinal areas, with blurred adipose tissue enclosing and invading adjacent structures. Enhanced CT scan shows different degrees of enhancement of mediastinal fibrotic tissue (Fig. 30.2). MSCT multiplanar reconstruction is helpful

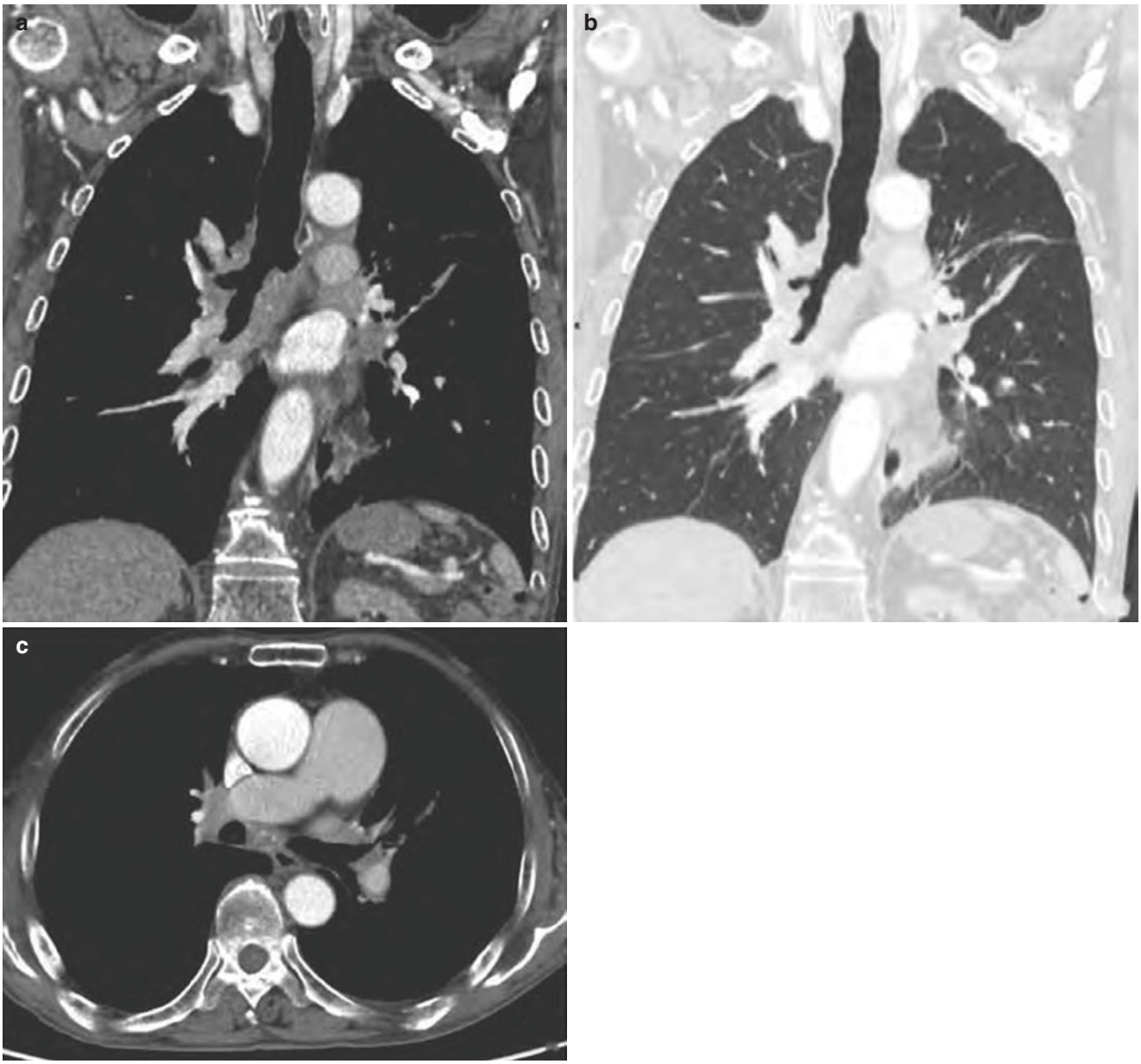

Fig. 30.2 Fibrosing mediastinitis. (**a**) CT-enhanced scan mediastinal window showed thickening and calcification of mediastinum and bilateral hilar soft tissue; (**b**) the lung window showed the bronchial compression and stenosis and local atelectasis in the left lung; and (**c**) pulmonary artery widening suggested pulmonary hypertension, which may be related to bilateral pulmonary artery branch compression

to show airway stenosis. The most common site is right main bronchus, followed by left main bronchus, middle bronchus, right upper lobe bronchus, etc. Bronchial obstruction is often accompanied by obstructive pneumonia and pulmonary atelectasis. CTA can evaluate the degree of mediastinal vascular occlusion and show the collateral vessels around the occluded vessels. Pulmonary artery stenosis or obstruction can cause blurred markings, reduced volume, or thrombosis in the corresponding area. Pulmonary vein obstruction usually shows pulmonary edema, interlobular septal thickening, and bronchial cuff sign.

3. MRI: It can show masses with uneven signal intensity. Decreased signal intensity on T_2WI suggests fibrosis. Compared with CT, MRI can better show the scope of lesions, especially the degree of vascular involvement, but it has less effect on finding calcification in lesions. MRI and CT are consistent in differentiating mediastinal lymph node lesions from hilar lymph node lesions. MR angiography can provide the information of vascular

lesions in addition to the results provided by CT. Granulomatous fibrosing mediastinitis is characterized by moderate intensity signal on T_1WI and uneven intensity signal on T_2WI. The degree of enhancement by contrast enhancement is variable. Lesions show relatively low signal intensity on T_1WI and T_2WI, which may be caused by calcification or fibrous scar.

30.2.4 Diagnostic Key Points

1. The characteristic features of CT and MRI are localized masses/invasive soft tissue lesions in mediastinum or hilum, accompanied by airway and vascular stenosis.
2. If mediastinal soft tissue masses are accompanied by calcification, it suggests lesions secondary to infection by histoplasmosis or *Mycobacterium tuberculosis*, which is helpful for diagnosis.
3. The diagnosis of fibrosing mediastinitis should exclude primary lung cancer, mediastinal, or hilar lymph node metastasis and lymphoma.

30.2.5 Differential Diagnosis

1. Lymphoma: It is manifested as multiple enlarged lymph nodes. Multiple nodules often fuse to form large soft tissue masses. Untreated lymphoma usually shows no calcification.
2. Other mediastinal tumors: Different types of mediastinal tumors are manifested as local soft tissue masses in mediastinum, which needs to be differentiated from focal fibrosing mediastinitis. Clinical background and calcification in tissues are helpful to differential diagnosis.
3. Acute mediastinitis: The disease generally has acute course, and patients often have a clear history of esophageal perforation or cardiothoracic surgery. CT of acute mediastinitis can show mediastinal pneumatosis or effusion, while fibrosing mediastinitis generally has no pneumatosis or effusion.

30.2.6 Research Status and Progress

Mediastinal fibrosis is a disease with complex etiology, in which the hyperplasia of fibrous tissue in mediastinum leads to compression and stenosis of pulmonary vessels, bronchus, and other organs, resulting in pulmonary hypertension and obstructive ventilation dysfunction. Its clinical manifestations mostly include chronic onset, dyspnea, cough, and expectoration. The diagnosis mainly depends on the typical imaging manifestations of enhanced CT and MRI. However, CT or MRI can only show the compression of mediastinal structure but cannot show the location, scope, and degree of pulmonary ventilation and blood perfusion injury. Ventilation/perfusion (V/Q) imaging can reflect the pulmonary perfusion and ventilation function by showing the radiation distribution in the lung and evaluate the pulmonary function noninvasively [15].

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