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THE ROLE OF HISTOPATHOLOGICAL EXAMINATION IN THE DEFINITIVE DIAGNOSIS OF ASCENDING AORTIC ANEURYSMS

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ABSTRACT
Ascending aortic aneurysm(AAA) is a potentially life-threatening patology with diverse etiologies, including degenerative, genetic, inflammatory, infectious, and autoimmune diseases. Although modern imaging techniques are essential for diagnosis and surgical planning, they often cannot determine the precise underlying cause of aneurysm formation. Histopathological examination of resected aortic tissue, commonly referred to as biopsy, remains the gold standard for establishing the definitive diagnosis following surgical repair. This review summarizes the role of histopathological assessment in ascending aortic aneurysms, emphasizing its value in differentiating degenerative aortopathy from inherited connective tissue disorders, inflammatory vasculitis, and infectious aortitis. Characteristic microscopic findings, current classification systems, and ancillary molecular techniques are discussed. Histopathological evaluation not only confirms the diagnosis but also provides prognostic information, guides postoperative surveillance, and facilitates genetic counseling in selected patients. Although routine preoperative biopsy is contraindicated because of the risk of aortic rupture, systematic examination of surgically resected specimens remains an integral component of comprehensive patient management.

KEYWORDS: Ascending aortic aneurysm; Histopathology; Aortic biopsy; Aortitis; Medial degeneration; Thoracic aortic aneurysm; Connective tissue disorders; Vasculitis.

INTRODUCTION

Ascending aortic aneurysm is defined as permanent dilation of the ascending aorta exceeding 1.5 times its expected normal diameter. Progressive enlargement predisposes patients to life-threatening complications including aortic dissection and rupture (1). While imaging modalities such as echocardiography, computed tomography (CT), and magnetic resonance imaging (MRI) accurately identify aneurysm morphology and size, they generally cannot determine the exact pathological mechanism responsible for aneurysm development (2).

Consequently, histopathological examination of surgically excised aortic tissue remains the definitive method for establishing the underlying diagnosis. The information obtained from tissue analysis may identify inherited connective tissue disease, inflammatory aortitis, infectious processes, or degenerative medial changes, each of which has different implications for postoperative surveillance, medical therapy, and family screening (3).

Why Histopathology Is Necessary

Radiological imaging provides excellent anatomical information but offers limited insight into the microscopic alterations within the aortic wall. Multiple etiologies may produce similar imaging appearances despite having markedly different biological behavior.

Histopathological evaluation allows differentiation between:

- Degenerative (non-inflammatory) aneurysms
- Genetic connective tissue disorders
- Inflammatory aortitis
- Infectious aortitis
- IgG4-related disease
- Rare metabolic or infiltrative disorders

This distinction is clinically relevant because management extends beyond surgical repair and may require immunosuppressive therapy, antibiotic treatment, or genetic evaluation (4).

Importantly, tissue is obtained almost exclusively during elective or emergency surgical replacement of the ascending aorta. Percutaneous or open diagnostic biopsy of an intact ascending aortic aneurysm is not performed because of the unacceptable risk of hemorrhage and rupture.

Histopathological Features of Degenerative Aneurysms

The majority of ascending aortic aneurysms are associated with degenerative medial changes.

The current international consensus discourages the older term "cystic medial necrosis," since actual cyst formation and necrosis are uncommon. Instead, the preferred terminology is medial degeneration (5).

Characteristic microscopic findings include:

- Fragmentation of elastic fibers
- Loss of vascular smooth muscle cells
- Mucoid extracellular matrix accumulation
- Increased collagen deposition
- Medial fibrosis
- Elastic lamellae disorganization

These abnormalities weaken the structural integrity of the aortic wall and predispose it to progressive dilation and dissection (5).

Special stains including Verhoeff–Van Gieson or Movat pentachrome facilitate assessment of elastic fiber architecture and extracellular matrix organization.

Histopathology in Genetic Aortopathies

Histopathology plays an important supportive role in hereditary thoracic aortic disease.

Marfan Syndrome

Patients with Marfan syndrome typically demonstrate severe medial degeneration characterized by extensive elastic fiber fragmentation and abundant mucoid matrix accumulation (6).

Although histology alone cannot establish the diagnosis, correlation with clinical findings and genetic testing for FBN1mutations confirms the disease.

Loeys-Dietz Syndrome

Loeys-Dietz syndrome often exhibits diffuse medial degeneration accompanied by marked disruption of elastic fibers.

Histological findings may overlap substantially with Marfan syndrome; therefore, molecular genetic testing remains necessary for definitive diagnosis (7).

Bicuspid Aortic Valve Aortopathy

Ascending aneurysms associated with bicuspid aortic valve generally demonstrate moderate medial degeneration with altered extracellular matrix remodeling, increased matrix metalloproteinase activity, and smooth muscle cell apoptosis (8).

These findings support the concept that bicuspid valve disease involves intrinsic abnormalities of the aortic wall rather than being solely a consequence of altered blood flow.

Role in Diagnosing Inflammatory Aortitis

Histopathological examination is particularly valuable for identifying inflammatory diseases that may not have been clinically suspected before surgery.

Giant Cell Arteritis

Microscopy demonstrates granulomatous inflammation with multinucleated giant cells, disruption of the elastic lamina, and chronic inflammatory infiltrates.

Recognition of these findings has immediate therapeutic implications because corticosteroid treatment is required to prevent progression in other arterial territories (9).

Takayasu Arteritis

Histology typically reveals granulomatous inflammation involving all layers of the vessel wall with fibrosis and destruction of elastic tissue.

Diagnosis may prompt long-term immunosuppressive therapy and surveillance for additional vascular involvement (10).

Isolated Non-Infectious Aortitis

Some patients exhibit localized inflammatory changes confined to the ascending aorta without evidence of systemic vasculitis.

These cases are increasingly recognized after routine pathological examination of surgical specimens and may require postoperative rheumatological evaluation (11).

Diagnosis of Infectious Aortitis

Although uncommon, infectious aortitis represents a surgical emergency.

Histological examination may demonstrate:

- Neutrophilic infiltration
- Tissue necrosis
- Microabscess formation
- Destruction of the media
- Microorganisms identified using special stains

Gram stain, Ziehl-Neelsen stain, fungal stains, culture, polymerase chain reaction (PCR), and next-generation sequencing may aid identification of causative pathogens (12).

Early diagnosis allows prolonged targeted antimicrobial therapy following surgery.

IgG4-Related Aortitis

IgG4-related disease has emerged as an increasingly recognized cause of thoracic aortic aneurysms.

Histopathological criteria include:

- Dense lymphoplasmacytic infiltrate

- Storiform fibrosis
- Obliterative phlebitis
- Increased IgG4-positive plasma cells on immunohistochemistry

Identification of this entity is important because corticosteroid therapy may prevent disease progression in other organs (13).

Ancillary Diagnostic Techniques

Modern pathology extends beyond routine hematoxylin-eosin staining.

Additional techniques include:

- Elastic tissue stains
- Masson's trichrome stain
- Immunohistochemistry
- Immunofluorescence
- Electron microscopy (selected cases)
- Molecular genetic analysis
- Whole-exome sequencing
- PCR for infectious agents

These complementary investigations improve diagnostic accuracy and facilitate personalized management (14).

Clinical Impact of Histopathological Diagnosis

Histopathological findings influence patient management in several ways.

First, inflammatory or infectious etiologies require disease-specific medical therapy beyond surgical repair.

Second, recognition of hereditary connective tissue disorders leads to referral for genetic counseling and family screening.

Third, identification of aggressive aortopathies may justify more intensive imaging surveillance because residual segments of the thoracic aorta remain at risk of future aneurysm formation (15).

Routine pathological evaluation also contributes to research by improving understanding of the biological mechanisms responsible for aneurysm development.

Limitations

Despite its importance, histopathology has several limitations.

Some microscopic abnormalities overlap considerably among different diseases, reducing diagnostic specificity. Tissue sampling may also fail to capture focal inflammatory lesions. Furthermore, histological changes should always be interpreted alongside clinical presentation, imaging findings, laboratory investigations, and genetic testing.

Histopathology therefore represents one component of a multidisciplinary diagnostic approach rather than a standalone diagnostic test.

Future Perspectives

Digital pathology, artificial intelligence, spatial transcriptomics, and single-cell RNA sequencing are transforming the evaluation of thoracic aortic disease.

These technologies may identify molecular signatures predictive of aneurysm growth or dissection risk, enabling more individualized patient management.

Integration of histopathology with genomic and proteomic profiling is likely to redefine classification of ascending aortic aneurysms in the coming years.

CONCLUSION

Histopathological examination of surgically resected ascending aortic tissue remains the gold standard for establishing the definitive etiology of ascending aortic aneurysms. Although imaging accurately identifies aneurysm size and morphology, only microscopic evaluation can reliably distinguish degenerative medial disease from inherited connective tissue disorders, inflammatory vasculitis or infectious aortitis. Routine pathological assessment provides valuable diagnostic and prognostic information, guides postoperative treatment, informs genetic counseling, and supports long-term surveillance. Future integration of molecular pathology and genomic techniques is expected to further improve the understanding and management of ascending aortic aneurysms.

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