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The Role of Anaerobic Bacteria in Mediastinitis

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Contents

Abstract

The management of mediastinitis involves directing appropriate antibacterial therapy against the potential bacterial pathogens. The increased recovery of anaerobic bacteria from mediastinal infections has led to a greater appreciation of their role in this condition and to re-evaluation of the proper treatment of this condition. Mediastinitis caused by anaerobic bacteria generally emerges following perforation of the oesophagus, extension of retropharyngeal abscess, suppurative parotitis, cervical cellulitis or abscess of dental origin. The bacteria recovered from these infections are often of oral origin and involve mixed aerobic-anaerobic oral flora. The predominant anaerobic isolates include *Bacteroides* spp., *Peptostreptococcus* spp., pigmented *Prevotella* and *Porphyromonas* spp. and *Fusobacterium* spp. Treatment includes surgical intervention, antibacterial therapy and supportive measures. Appropriate management of mediastinal infections due to aerobic and anaerobic infections requires the administration of antibacterials that are effective against both the aerobic and anaerobic components of the infection. Selection of antibacterials for the treatment of mediastinitis is determined by bacteriological studies.

Mediastinitis is a rare but life-threatening condition with extremely high mortality if recognised late or treated improperly.[1] The mediastinum contains essential, vital structures and organs. These include the thymus, trachea, bronchi, oesophagus, aorta and aortic arch, pericardium, heart lymph nodes and nerve tissue. Acute and chronic forms of mediastinitis are recognised.[2]

The management of mediastinitis involves directing appropriate antibacterial therapy against the potential bacterial pathogens.[2] The increased recovery of anaerobic bacteria from mediastinal infections[2] has led to a greater appreciation of their role in this condition and to re-evaluation of the proper treatment of this condition. This review describes the microbiology, diagnosis and management of me-

diastinal infections, highlighting the role of anaerobic bacteria.

1. Pathogenesis

Infection of the mediastinum is always a secondary event, and this determines its aetiology. In most patients, mediastinitis occurs following cardiovascular surgery.[1,2] Risk factors for the development of mediastinitis following cardiovascular surgery include bilateral internal mammary artery grafts; diabetes mellitus; emergency surgery; external cardiac compression; obesity; postoperative shock, especially when multiple blood transfusions are required; prolonged bypass and operating room time; re-exploration following initial surgery; sternal wound dehiscence; and surgical technical factors.[3]

Oesophageal perforation is the second most common cause of mediastinitis.[4] The causes of esophageal perforation include erosion of esophageal wall by malignancy; foreign bodies; instrumentation from endoscopes during diagnostic or therapeutic procedures; placement of nasogastric tubes or feeding tubes; spontaneous oesophageal rupture; and trauma, mostly blunt trauma, to the chest or abdomen.

Other causes of mediastinitis are tracheobronchial perforation, resulting from either penetrating or blunt trauma or instrumentation during bronchoscopy; descending infection following surgery of the head and neck, great vessels or vertebrae; progressive odontogenic infection (i.e. Ludwig angina, extension of an abcess of dental origin); mediastinal extension of lung infection, extension from paravertebral abscess or osteomyelitis of the sternum or ribs, and extension from mediastinal or cervical lymph nodes; chronic fibrosing mediastinitis due to granulomatous infections; and blood-borne infection.[1-3]

The origin of bacterial pathogens causing the infection following open-heart surgery is unknown in most patients.[1,2] Possible sources are areas of sternal osteomyelitis or sternal instability leading eventually to sternal separation and migration of bacteria into deeper tissues. Inadequate mediastinal drainage in the operating room may also contribute to the development of a deeper chest infection. The patient's own skin or oropharyngeal flora, as well as external bacteria in the local surgical environment, can be a source of infection.

Mediastinitis that follows cardiac surgery, blood-borne infection, extension from paravertebral abscess or osteomyelitis of the sternum or ribs and extension from mediastinal or cervical lymph nodes is not likely to be caused by anaerobic bacteria.[5,6] Anaerobes are extremely rare in postcardiac surgery. However, mediastinitis that follows perforation of the oesophagus, extension of retropharyngeal abscess, suppurative parotitis[7] or cervical cellulitis,[8] or abscess of dental origin,[9,10] all of which are usually caused by anaerobes of oral origin, is very likely to involve mixed aerobic-anaerobic oral flora. Since anaerobic bacteria are part of the normal oral flora, their presence in mediastinitis that is associated with exposure to oropharyngeal bacterial flora is not surprising. Similar anaerobic bacteria are also found in mediastinitis as a result of extension of pulmonary, pleural and pericardial infections or secondary to deep and postsurgical neck infections.[11]

2. Microbiology

Staphylococcus aureus, *S. epidermidis*, Enterobacteriaceae, *Enterobacter cloacae, Enterococcus* spp., *Pseudomonas* spp., *Proteus* spp., *Haemophilus* spp., *Corynebacterium xerosis, Mycoplasma* spp., nontuberculous mycobacterium, *Nocardia* spp., *Aspergillus* spp. and *Candida* spp. are the predominant aerobic and facultative bacteria and fungal species (i.e. *Aspergillus* and *Candida*) seen after cardiovascular surgery.[12,13] These organisms can also be recovered mixed with anaerobic bacteria whenever polymicrobial infection is present. Histoplasmosis and tuberculosis are the most common identifiable causes of chronic mediastinitis (table I).[13]

The major bacteria recovered from infections originating from the oral flora are group A streptococci and oral anaerobic bacteria. The latter includes pigmented *Prevotella* and *Porphyromonas* spp., *Fusobacterium* spp. and *Peptostreptococcus* spp.[14] There are also a few reports of involvement of *Bacteroides fragilis* group.[15]

Table I. Predominant organisms recovered from mediastinitis[12-21]

Aerobic bacteria
Staphylococcus aureus
S. epidermidis
Streptococcus pyogenes
Microaerophilic streptococcus
Enterococcus spp.
Haemophilus spp.
Enterobacteriaceae
Enterobacter cloacae
Klebsiella pneumoniae
Pseudomonas spp.
Proteus spp.
Corynebacterium xerosis
Nocardia spp.
Anaerobic bacteria
Peptostreptococcus spp.
Clostridium spp.
Bacteroides spp.
Pigmented *Prevotella and Porphyromonas* spp.
Fusobacterium spp.
Other organisms
Mycoplasma spp.
Nontuberculous mycobacterium
Fungi
Aspergillus spp.
Candida spp.
Histoplasma spp.

The role of anaerobic bacteria in mediastinitis was not established by prospective studies and most of the data in the literature are based mostly on several case reports.

Ferzli et al.[16] reported a 17-year-old female who developed anaerobic mediastinitis that complicated infectious mononucleosis. They recovered *S. aureus*, *Streptococcus constellatus*, *S. milleri* and *Prevotella melaninogenica*. Several reports described the concomitant recovery of *Clostridium* spp. including *Clostridium perfringens* in mediastinitis secondary to oesophageal perforation.[17] Guardia et al.[7] reported a case of fatal necrotising mediastinitis secondary to acute suppurative parotitis. The infection was the result of synergistic necrotising cellulitis caused by mixed aerobic and anaerobic bacteria. The causative isolates were *E. coli*, *Enterococcus* spp., *B. fragilis*, *C. perfringens*, *P. melaninogenica* and *Candida albicans*. Isaacs et al.[18] reported a case of a 34-year-old woman with an upper respiratory infection who developed parapharyngeal, retropharyngeal and mediastinal abscesses. *Peptostreptococcus* and *Bacteroides* spp. were isolated from the infected sites.

Murray and Finegold[14] reported two cases of anaerobic mediastinitis and summarised the literature that included an additional 18 cases reported between 1930 and 1981. The predominant origin of the infection in these patients was odontogenic in seven, oral abscess in three, pleural fluid in two and trauma in two. Polymicrobial flora was found in all but one patient and the predominant anaerobic bacteria isolated from these patients were *Bacteroides* spp., *Peptostreptococcus* spp., pigmented *Prevotella* spp. and *Fusobacterium* spp. Moncada et al.[19] recently reported five cases of mediastinitis caused by anaerobes, originating from odontogenic and deep cervical infections; two of these were in children.

Wheatley et al.[20] reported two cases of descending necrotising mediastinitis due to anaerobic bacteria, in which infection arising from the oropharynx spread to the mediastinum. They also reviewed the English language literature on this disease from 1960 to 1990 summarising 43 additional cases. Polymicrobial aerobic-anaerobic flora was present in 30 of 36 (83%) cases where the microbiology was given, anaerobes only in one (3%) and aerobes alone in five (14%).

A recent study highlights the polymicrobial aerobic-anaerobic nature of mediastinitis, providing the microbiological and clinical characteristics of 17 adults with mediastinitis.[21] Aerobic or facultative bacteria were only present in three patients (18%), anaerobic bacteria only in seven (41%), and mixed aerobic-anaerobic flora in seven (41%). There were a total of 42 isolates, 13 aerobic or facultative and 29 anaerobic bacteria, an average of 2.5 isolates per specimen. Anaerobic bacteria predominated in infections that originated from oesophageal perforation, and orofacial, odontogenic and gunshot sources. The predominant aerobes were α-haemolytic streptococci (three isolates), *S. aureus* (two isolates), and *Klebsiella pneumoniae* (two iso-

lates). The predominant anaerobes were *Prevotella* and *Porphyromonas* spp. (eight isolates), *Peptostreptococcus* spp. (seven isolates) and *B. fragilis* group (three isolates).

3. Diagnosis

Oesophageal perforation can be associated with acute or delayed symptoms. Perforation can also occur following mechanical obstruction by foreign bodies that induce necrosis. Perforation may occur following oesophageal surgery. Abrupt onset of neck and chest pain, dyspneoa, tachycardia, hypotension, chills, fever and leukocytosis are generally observed. Subcutaneous emphysema is seen when the perforation site is at the level of the cricopharyngeal muscle.

Postoperative patients generally present with fever, high pulse and complaints suggestive of a sternal wound infection. Most patients present with mediastinitis within 2 weeks of surgery. However, a delay of months is occasionally seen. Patients usually describe increasing sternal pain, draining wound site and progressive redness. Infants may present with irregular breathing characterised by an inspiratory halt with resumption of inspiration after a brief rest.[22]

Subcutaneous emphysema can be found in proximal perforation. Chest radiography may show widened mediastinum, subcutaneous and mediastinal emphysema, and pleural effusions.[15] Basilar or retrocardiac infiltrates may be observed. Foreign bodies may be detected by plain films, CT, magnetic resonance imaging or fluoroscopy. Mediastinal emphysema is suggestive of an oesophageal perforation as well as other conditions, such as perforations of tracheobronchial tree, or penetration of air following surgical procedures in the upper respiratory tract. Oesophageal dye studies are the most useful study in patients with suspected oesophageal perforation. If no extravasation is observed, barium is given to provide better definition of the oesophageal wall. Fiberoptic bronchoscopy is performed when a perforated airway is suspected as the cause of the mediastinitis.

Purulent drainage, erythema, tenderness, fever and leukocytosis, and occasionally sternal instability can be present in mediastinitis secondary to sternotomy wound infection. No symptoms may accompany chronic mediastinitis and the lesion may be only detected by chest radiographs.

Systemic signs of sepsis strongly suggest mediastinal involvement. Compression of adjacent structures (oesophagus, tracheobronchial tree or superior vena cava) may be present. Other features are low-grade fever, weight loss and anaemia. Diagnostic and therapeutic surgical exploration may be warranted. Appropriate cultures for aerobic and anaerobic bacteria of blood, pleural fluid, wound site or surgical specimen, including mediastinal pacing wires, should be taken. Any sternal drainage should be sent for Gram stain and culture for aerobic and anaerobic bacteria, as well as fungi. This helps to establish a diagnosis and to tailor antimicrobial therapy. In addition, diagnosis can be established by tuberculin skin test and histoplasma serology, and proper cultures for tuberculosis and histoplasma should be performed.

Bacteraemia is found in almost 60% of patients with postoperative mediastinitis.[23] The mortality rate is high, especially if diagnosis and therapy are delayed.

4. Management

Treatment includes surgical intervention, antimicrobial therapy and supportive measures. Maintaining the airway, monitoring vital signs and administration of parenteral fluids are essential.[24] Surgical correction of perforations, debridement of wound infection, mediastinal irrigation and excision of chronic lesions are an integral part of management. In severe infection, it may be necessary to leave the wound open until subsequent secondary closure.[24,25] Topical use of granular sugar was suggested as a means to treat refractory severe infection.[26]

Prophylactic antibacterials should be administered prior to surgical sternotomy, usually with a first generation cephalosporin. Coverage for anaerobic bacteria is not indicated. Selection of an-

tibacterials for the treatment of mediastinitis is determined by bacteriological studies. Often, no pathogen is recovered and antibacterial therapy is empirical. Such treatment should be effective against the oral aerobic and anaerobic flora as well as *S. aureus*. Treatment effective against anaerobic bacteria should be administered to those where exposure to oral flora might have occurred (i.e. after perforation of the oesophagus, extension of retropharyngeal abscess, suppurative parotitis or cervical cellulitis, or abscess of dental origin). There is generally no need for empirical anti-anaerobic antibacterial agents in postsurgical mediastinitis, unless exposure to oral flora has occurred. Antibacterials also effective against enteric bacteria are important in mediastinitis secondary to a sternal wound.

Clindamycin or the combination of metronidazole plus a β-lactamase resistant penicillin, vancomycin or linezolid are effective against Gram-positive anaerobes and *S. aureus*. Carbapenems (i.e. imipenem cilastatin, meropenem) or the combination of a penicillin (amoxicillin, ticarcillin or piperacillin) and a β-lactamase inhibitor (clavulanic acid, sulbactam, or tazobactam) are adequate for anaerobes, Enterobacteriaceae and *S. aureus*. Aminoglycosides, fluoroquinolones or a fourth-generation cephalosporin (i.e. cefepime) are effective additives against aerobic Gram-negative rods. Systemic antibacterial therapy should be given for at least 4–6 weeks.[14,15,21]

5. Conclusion

Mediastinitis is a life-threatening infection with a high mortality when it is recognised late or treated improperly. Mediastinitis caused by anaerobic bacteria often occurs after perforation of the oesophagus, or extension of retropharyngeal abscess, suppurative parotitis, cervical cellulitis or abscess of dental origin. The bacteria recovered from these infections are often of oral origin and involve mixed aerobic-anaerobic oral flora. The management of mediastinitis evolves directing appropriate antibacterial therapy against the potential bacterial pathogens. Future research should be directed at rapid identification of the potential pathogens and development of newer antibacterials against the potential aerobic-anaerobic pathogens.

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