Pathophysiology of Spinal Infection

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Abstract

Although rare, spondylodiscitis is the main manifestation of hematogeneous osteomyelitis in patients aged more than 50 years. In this chapter, we discuss the pathophysiology of spinal infections. We review the vascular supply of the spine and its development with age, which is important in understanding the typical patterns of infection in adults and children. Routes of pathogen spread are detailed, with a review of the literature. We identify specificities of pathophysiology in the most common causes of spinal infection, namely, pyogenic and tuberculous spondylodiscitis.

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1 Introduction

Spinal infection is defined as an infectious disease that affects the vertebral body, intervertebral disk, or the adjacent paravertebral tissue. There are two main infection routes that can contribute to the development of spinal infection. Infectious spread may be hematogeneous or non-hematogeneous; the latter can be either the result of direct external inoculation or extension from a contiguous infection site (Gouliouris et al. 2010; Mavrogenis et al. 2017).

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2 Routes of Pathogenic Spread

2.1 Hematogeneous Route

Two hematogenous routes have been described, namely, arterial and venous routes. Recent studies have concluded that hematogeneous arterial spread is the most common route, allowing bacteria from distant sites to contaminate the spine in the setting of bacteremia. The origin of infection in these patients may be the oral cavity, skin, any infected implanted device and the respiratory, urinary, or gastrointestinal tracts (Gouliouris et al. 2010; Sundaram and Doshi 2016; Mavrogenis et al. 2017). Rarely, the propagation of organisms can occur via the venous circulation (Moraru 2012). An understanding of the vascular supply of the spine and its development with age is important in understanding the typical patterns of infection within the spinal column in adults and children (Gouliouris et al. 2010; Sundaram and Doshi 2016).

The arterial supply to each vertebral body consists of paired segmental arteries that arise, depending on the location, from the vertebral arteries, aorta, or iliac arteries (Fig. 1). The segmental arteries run in the equatorial plane around their respective vertebral body, toward the transverse processes, and give off multiple extraosseous anastomotic channels (Sundaram and Doshi 2016). Ratcliffe (1980) demonstrated that on the anterolateral surface of the spine, there is a longitudinal ladder-like anastomosis of arteries in the periosteum. The horizontal components consist of the segmental arteries in the equatorial plane of the vertebra and two horizontal metaphyseal anastomoses, one at each metaphysis. The vertical components of the anastomosis consist of primary periosteal arteries, which join the segmental arteries to the metaphyseal anastomoses and transdiscal arteries, that travel in the adventitia of the disk and connect the metaphyseal anastomosis of one vertebral body to the metaphyseal anastomosis of the adjacent vertebral body (Ratcliffe 1980) (Fig. 2).

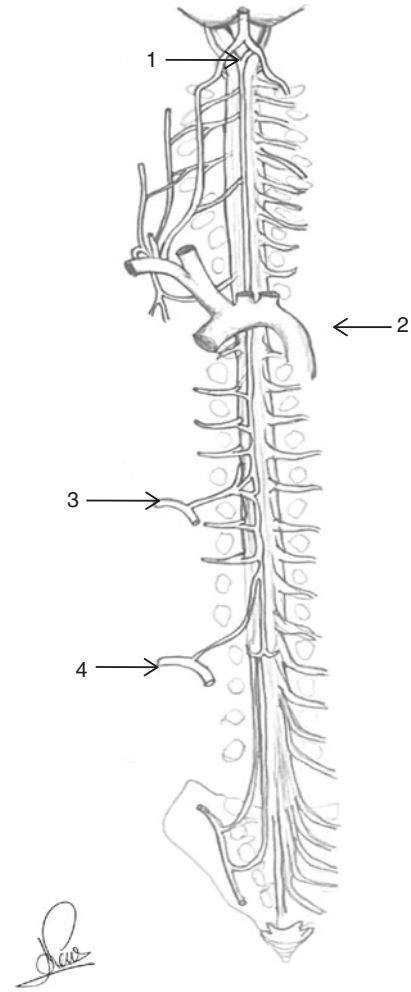

Fig. 1 Diagram shows arterial supply of the spine. Key: *1* vertebral artery, *2* aorta, *3* intercostal artery, *4* lumbar artery. [Adapted from: Kamina P (2008). Anatomie clinique; Tome 5 Neuroanatomie. 2008.197]

The intraosseous arteries arise from the periosteal arteries of this longitudinal anastomosis and its branches in the spinal canal. From each metaphyseal anastomosis, there arise 15–30 metaphyseal arteries which have long straight stems and terminate in a leash of centrifugal branches (Fig. 3). The stems of all these arteries lie more or less in a horizontal metaphyseal plane parallel to the disk surface (Ratcliffe 1980). In the equatorial zone, one or two anterolateral

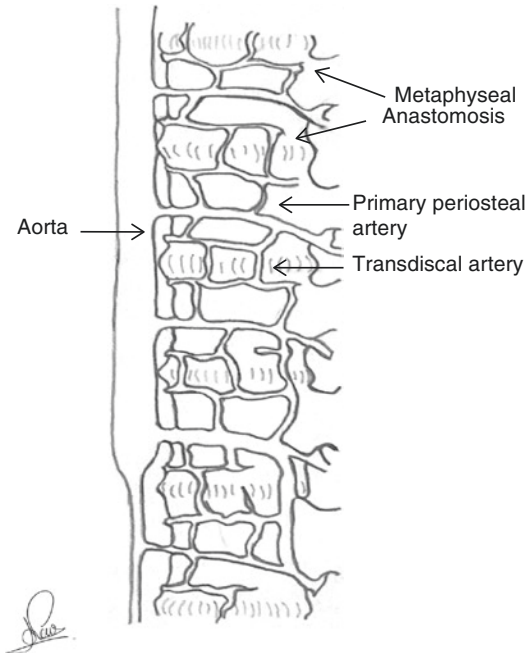

Fig. 2 Diagram shows the longitudinal anastomosis with horizontal and vertical components. [Adapted from: Ratcliffe JF (1985) Anatomic basis for the pathogenesis and radiologic features of vertebral osteomyelitis and its differentiation from childhood discitis. A microarteriographic investigation. Acta Radiologica Diagnosis 26: Fasc 2]

equatorial arteries on each side arise directly from the segmental artery; and on the posterior surface, the nutrient artery also lies in the equatorial plane and arises from the spinal branch of the segmental artery (Ratcliffe 1980) (Fig. 3).

In childhood, there is widespread intraosseous arterial anastomoses; this arterial network extends to the level of the intervertebral disk and provides a rich capillary network that is considered to be end vessels and are typically the final location for septic emboli. In adults, however, the rich capillary network regresses, and the arterial end vessels terminate at the superior and inferior end plates of the vertebral bodies, resulting in a different typical initial location for spinal infection compared to pediatric patients (Ratcliffe 1982; Sundaram and Doshi 2016). In adolescents and adults, the metaphyseal arteries are end arteries, and septic embolism forms a septic infarct of the subdiscal area of bone. The thrombus extends proximally in the metaphyseal artery to its origin from the metaphyseal anastomosis. The thrombus then extends circumferentially around the metaphyseal anastomosis and obstructs the origins of the other metaphyseal arteries sequentially (Ratcliffe 1980) (Fig. 4).

The area of vertebral metaphysis supplied by each artery will undergo sequential septic infarction. The thrombotic process can thus spread around the metaphysis of the same vertebral body. The spreading septic thrombosis in small arteries may cross the disk space in the adventitial arteries to involve the metaphyseal anastomosis of the adjacent vertebral body. Transdiscal metaphyseal spread is characteristic of vertebral osteomyelitis in adults. The equatorial region is supplied by arteries which arise from the main segmental artery in which there is a sufficiently fast flow of blood to wash away septic thrombus. The equatorial region of the vertebral body is thus relatively protected (Ratcliffe 1980) (Fig. 5).

Extensive vascular bone infarcts and spread of infection to adjacent structures lead to the classic appearance of spondylodiscitis on imaging, namely, destruction of vertebral end plates, osteolytic lesions, and compression fractures, which can lead to spine instability, deformity, and risk of spinal cord compression (Cheung and Luk 2012; Duarte and Vaccaro 2013). Neurological deficit during pyogenic osteomyelitis may have several mechanisms which can be isolated or associated: epidural abscess with narrowing of the spinal canal, septic embolization of the vertebral artery with spinal cord ischemia, and septic vertebral fracture with mechanical compression (Lemaignen et al. 2017). On the other hand, tuberculous osteomyelitis may cause a vasculitis that leads to ischemia in the spinal cord and that even with decompression, neurological recovery may not be as significant as expected (Finger et al. 2019). In childhood, a septic embolus in a metaphyseal artery will cause the death of cells in only a very small area of bone because the

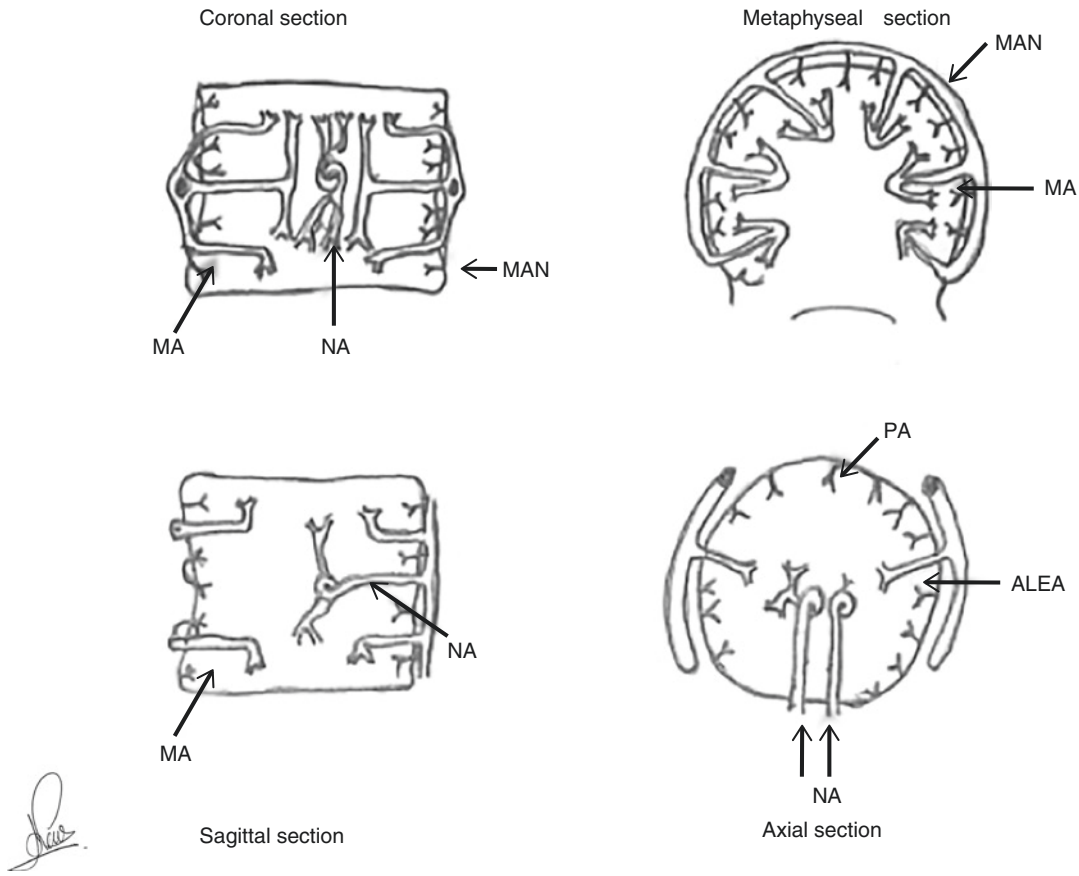

Fig. 3 Diagram shows the intra-osseous arteries of the adult lumbar vertebral body. Key: *ALEA* anterolateral equatorial artery, *LA* lumbar artery, *MA* metaphyseal artery, *MAN* metaphyseal anastomosis, *NA* nutrient artery, *PA* periosteal artery, *PPA* primary periosteal artery. [Adapted from: Ratcliffe JF (1980) The arterial anatomy of the adult human lumbar vertebral body: a microarteriographic study. J Anat 131:57–79]

Fig. 4 Schematic diagram shows the mode of spread of septic thrombosis. The thrombus (brown dot) extends circumferentially around the metaphyseal anastomosis (arrows) and obstructs the origins of the other metaphyseal arteries (crosses)

intraosseous anastomoses prevent infarction and the infection is located essentially within the disk. The clinical disease is mild and radiographic changes are often minimal in juveniles (including infants and small children) compared with adults (Ratcliffe 1980).

The venous route in the pathogenesis of spondylodiscitis has often been considered a common route, with retrograde spread of infection from abdominal and pelvic organs, such as in urinary tract infection. Batson (1940) discovered that the vertebral veins are a large-capacity longitudinal valveless venous plexus that lies outside the thoracoabdominal cavity and anastomoses with the pelvic venous plexus caudally, and postulated its role in the spread of metastases. He concluded that, when intra-abdominal pressure rises as a

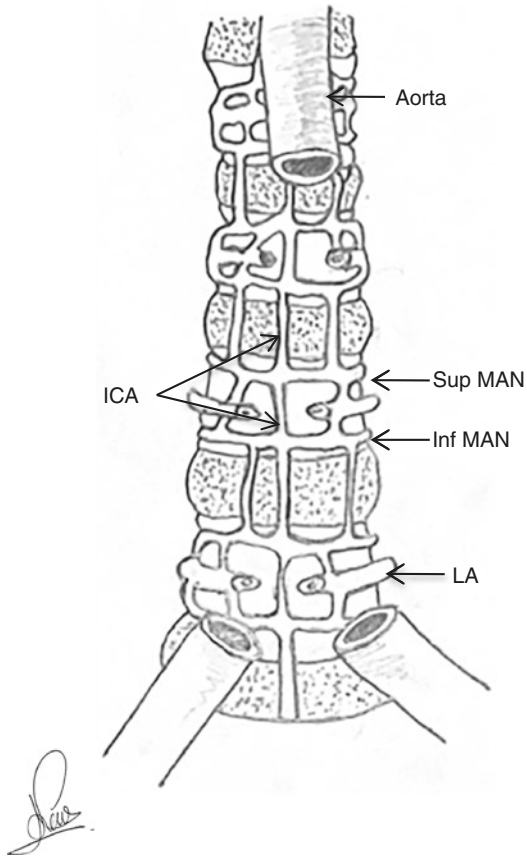

Fig. 5 Diagram shows the spread of septic thrombosis from one metaphysis to the other in a single vertebral body and in the adjacent vertebral metaphysis via intermetaphyseal communicating arteries without destruction of the equator of the vertebral body. Key: *ICA* intermetaphyseal communicating artery, *inf* inferior, *LA* lumbar artery, *MAN* metaphyseal anastomosis, *sup* superior. [Adapted from: Ratcliffe JF (1985) Anatomic basis for the pathogenesis and radiologic features of vertebral osteomyelitis and its differentiation from childhood discitis. A microarteriographic investigation. Acta Radiologica Diagnosis 26: Fasc 2]

result of coughing or straining, pelvic infection could spread via the vertebral collateral venous system to cause spinal lesions (Gouliouris et al. 2011; Sundaram and Doshi 2016).

However, since 1959, Wiley and Trueta, using anatomical contrast studies to demonstrate that the veins of the vertebral bodies could only be filled retrogradely utilizing high pressures, postulated that the vertebral veins form predominantly a drainage system. Furthermore, the radiological findings in cases of spondylodiscitis displayed the characteristic anterior metaphyseal vertebral lesions, which are rich in arterial but not venous supply (Wiley and Trueta 1959; Gouliouris et al. 2011). The involvement of adjacent vertebrae is also suggestive of arterial spread, in view of the bifurcation of the feeding arteries. Finally, in clinical cases of spondylodiscitis arising from a pelvic source, preceding symptoms of bacteremia such as fever and rigors are commonly documented, suggesting systemic spread (Gouliouris et al. 2011).

2.2 Non-hematogeneous Route

Direct bacterial inoculation is mainly iatrogenic, following spinal surgery, lumbar puncture, or epidural procedures. This infectious route accounts for 14–26% of spinal infections (Mavrogenis et al. 2017). Multiple factors increase the rates of infection following spinal surgery. These include the staging of surgery (multiple sequential operations), long operative time (>5 h), blood transfusions, use of allograft, and a greater number of operated levels. A higher infection rate is also related to the introduction of posterior spinal instrumentation and is mainly attributed to increased wound exposure to air and greater posterior soft tissue dissection (Kasliwal et al. 2013).

The risk of infection varies with the type of implant, due to an increased susceptibility to the development of biofilm which is a microbial agglomeration characterized by cells that are embedded in a matrix of extracellular polymeric substances, which they produce (Kasliwal et al. 2013). Within biofilm, bacterial cells become irreversibly attached to the implant. Implants vary in their susceptibility to the development of biofilm. Soultanis et al. (2008) found that titanium had a lower infection rate than stainless steel. Contiguous spread is extremely rare. Infection in these cases may spread from adjacent infected tissues such as a ruptured esophagus or an infected aortic graft (Gouliouris et al. 2010; Mavrogenis et al. 2017).

3 Pyogenic Spondylodiscitis

Based on the typical adult arterial anatomy, hematogeneous pyogenic spondylodiscitis often first affects the subchondral region of the vertebral body end plates and spreads in an anterior to posterior direction. Over time, bacteria with more virulent and proteolytic properties, such as *Staphylococcus aureus*, cause cortical destruction and invade beyond the end plates and into the intervertebral disks. They can also spread along the arterial anastomotic networks to multiple, sometimes noncontiguous, vertebral bodies, or into the epidural space (Sundaram and Doshi 2016). Pyogenic facet involvement also exists as an independent entity but is extremely rare (Hadjipavlou 2000). The pathogenesis of this posterior involvement can be explained either as a primary hematogeneous osteomyelitis with extension into the facet joint or as a primary paravertebral soft tissue infection with direct spread into the facet joint and subsequent osteomyelitis (Ehara et al. 1989).

4 Tuberculous Spondylodiscitis

The pathophysiology of tuberculous spondylodiscitis still remains a subject of controversy. Tuberculous osteomyelitis and arthritis are generally believed to arise from foci of bacilli lodged in the bone during the original mycobacteremia of primary infection (Agrawal et al. 2010). The primary focus may be active or quiescent, apparent or latent, either in the lungs or in the lymph glands of the mediastinum, mesentery, kidney, or other viscera (Agrawal et al. 2010). Tuberculous bacilli may travel from the lung to the spine by Batson paravertebral venous plexus or by lymphatic drainage to the para-aortic lymph nodes (Agrawal et al. 2010). However, according to Trecarichi et al. (2012), tuberculous spondylodiscitis can result from arterial hematogeneous seeding of *Mycobacterium tuberculosis* starting from a quiescent or active pulmonary focus or can be due to contiguous or lymphatic spread from pleural disease (Trecarichi et al. 2012). The predominant localization of tuberculosis in the thoracic segment would be related to the frequent involvement of mediastinal lymph nodes and the pleura in pulmonary tuberculosis, from where microorganisms can reach the vertebral bone through the lymphatic route (Trecarichi et al. 2012).

Since the intervertebral disk does not have a direct blood supply in adults, most hematogeneous infections of the disk space are the result of the dissemination from the adjacent bone. The natural evolution of the infection is the formation of a granuloma, whose center tends to caseate and become necrotic. The infection can then progress to destroy the bone, causing pain and leading to the collapse of the vertebral body (Trecarichi et al. 2012). The bacilli may then spread beneath the anterior spinal ligament and involve the anterosuperior aspect of the adjacent inferior vertebra, giving rise to the typical "wedge-shaped" deformity. Further spread may result in adjacent abscesses. The infection may spread cranially and caudally, stripping the anterior and posterior longitudinal ligaments and the periosteum from the front and the sides of the vertebral bodies (Agrawal et al. 2010). Disk space narrowing occurs secondarily and usually is limited relative to the degree of bone destruction. A lack of proteolytic enzymes in the mycobacterium as compared with pyogenic infection has been proposed as the cause of relative preservation of the intervertebral disk (Smith et al. 1989).

5 Conclusion

Hematogeneous arterial spread is the most common route of spinal infection. In childhood, discitis is common due to the intra-osseous arterial anastomoses extending to the level of the intervertebral disk. In adults, as the disk is avascular, the infection is located initially at the superior or the inferior end plate of the vertebral body, and then extensive vascular bone infarcts and spread of infection to adjacent structures leads to the classic spondylodiscitis. Iatrogenic direct bacterial inoculation has increased in frequency

because spinal instrumentation became an integral component in the treatment of multiple spinal pathologies. The understanding of the pathogenesis of this pathology has evolved with the improved knowledge of the role of biofilm and the development of newer spinal implants.

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