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Paraplegia Caused by Infectious Agents; Etiology, Diagnosis and Management

Farhad Abbasi and Soolmaz Korooni Fardkhani

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1. Introduction

Paraplegia or paralysis of lower extremities is caused mainly by disorders of the spinal cord and the cauda equina. They are classified as traumatic and non traumatic. Traumatic paraplegia occurs mostly as a result of traffic accidents and falls caused by lateral bending, dislocation, rotation, axial loading, and hyperflexion or hyperextension of the cord. Non-traumatic paraplegia has multiple causes such as cancer, infection, intervertebral disc disease, vertebral injury and spinal cord vascular disease [1, 2]. Although the incidence of spinal cord injury is low, the consequences of this disabling condition are extremely significant for the individual, family and community [3]. A spinal cord injury not only causes paralysis, but also has long-term impact on physical, psychosocial, sexual and mental health. The consequences of spinal cord injury require that health care professionals begin thinking about primary prevention. Efforts are often focused on care and cure, but evidence-based prevention should have a greater role. Primary prevention efforts can offer significant cost benefits, and efforts to change behavior and improve safety can and should be emphasized. Primary prevention can be applied to various etiologies of injury, including motor vehicle crashes, sports injuries, and prevention of sequelae of infectious diseases and prompt and correct diagnosis and treatment of infections involving spinal cord and vertebrae [4]. Infections are important causes of paraplegia. Several infections with different mechanisms can lead to paraplegia.

2. Infectious diseases and paraplegia

Several infections may cause paraplegia. They are classified into two categories: those that involve the spinal cord directly and those that involve vertebral column and cause pressure

effect on the spinal cord that eventually leads to paraplegia. In fact paraplegia can arise from a lesion either within or outside the spinal cord or cauda equina. These are classified as compressive and non compressive. Compression is caused either by bone or other masses. The main compressive causes are Pott's disease (tuberculosis of spine). The main non-compressive causes are transverse myelitis secondary to viral infections, HIV, TB and very occasionally syphilis [1]. Several bacterial, viral, mycobacterial, fungal and parasitic infections can cause paraplegia. Infectious myelitis is usually caused by neurotropic viruses or mycoplasma in conjunction with concomitant meningitis or encephalitis; these in turn either induces transverse myelitis accompanied by severe sensorimotor deficits or chiefly affect the gray matter [5].

2.1. Bacterial infection

One of the most important causes of paraplegia among infectious causes is bacterial infection. These organisms can produce subdural empyema, epidural abscesses, radiculomyelitis or cause spondylitis with bony destruction or pressure effect.

2.1.1. Subdural empyema

Subdural empyema refers to a collection of pus in the space between the dura and arachnoid [6]. Spinal subdural empyema is a rare condition [7] that usually occurs secondary to metastatic infection from a distant site. The clinical presentation of spinal subdural empyema is usually radicular pain and symptoms of spinal cord compression, which may occur at multiple levels. The clinical presentation is difficult to distinguish from that of spinal epidural abscess [6]. Spinal subdural space remains the least common area of localized infection in the central nervous system (CNS). Infectious processes of the subdural spinal space include subdural spinal empyema, subdural spinal abscess, infected spinal subdural cyst, and infectious spinal subdural cyst [8]. Etiologies of spinal subdural empyema include hematogenous spread from skin lesions, sepsis, direct spread from spinal osteomyelitis, complications of discography and rarely iatrogenic after spinal anesthesia, spinal epidural insertion or acupuncture [9-11]. The most affected region is the thoraco-lumbar spine [12] and the most frequent microbial isolate is *Staphylococcus aureus*, followed by streptococci and coagulase-negative staphylococci. Gram-negative bacilli are less frequently isolated cause [6]. *Mycoplasma hominis* has been isolated from subdural empyema although it is very rare [13].

2.1.2. Epidural abscess

Epidural abscess refers to a localized collection of pus between the dura mater and vertebral column. Epidural abscess of the spinal column is a rare condition that can be fatal if left untreated. It promptly progresses and can cause neurologic paralysis, urinary retention or cauda equina syndrome [14]. It usually occurs secondary to hematogenous dissemination from foci elsewhere in the body to the epidural space or by local extension from vertebral osteomyelitis. Compromised immune system that occurs in patients with diabetes mellitus, AIDS, chronic renal failure, alcoholism, or cancer is a predisposing factor [6, 15]. Paraplegia and paralysis in spinal epidural abscess may be the result of spinal cord compression, spinal cord arterial or venous ischemia and thrombophlebitis or a combination of these. The most common

Etiology/ disease	Diagnosis	Medical treatment	Surgical intervention	Comment
Subdural empyema	MRI, CT Scan	Antibiotic	Yes	Combination antibiotic therapy is necessary
Epidural abscess	MRI, CT Scan	Antibiotic	Yes	Combination antibiotic therapy is necessary
Tuberculosis	MRI, CT-guided biopsy	Anti TB drugs	Yes	Four drugs combination is necessary
Syphilis	MRI, CSF analysis, VDRL, FTA-ABS	Penicillin, Doxycycline, amoxicillin, ceftriaxone	May be needed	-
Lyme	ELISA, PCR, CSF analysis	Doxycycline, amoxicillin, cefuroxime, ceftriaxone, cefotaxime	Usually not necessary	-
Brucellosis	MRI, Wright, 2ME, IFA, ELISA	Doxycycline, rifampin, trimethoprim-sulfamethoxazole, streptomycin, gentamicin, ciprofloxacin, ceftriaxone	Yes	Combination antibiotic therapy is necessary (usually 3 antibiotics)
HIV	ELISA, Western blot, P24 antigen, IFA, RIPA	ART	Usually not necessary	ART is used if HIV treatment is indicated
HTLV-I	Serology, antigen detection, PCR	Zidovudine and lamivudine may be used	Usually not necessary	-
Herpes zoster	Serology, PCR, IHC	Aciclovir	Usually not necessary	-
CMV	PP65 antigen, PCR	Ganciclovir, foscarnet, cidofovir	Usually not necessary	Combination therapy may be considered
Aspergillus	Histopathology, serology, antigen detection and PCR, culture	Amphotericin B, voriconazole, itraconazole	Yes	Voriconazole is treatment of choice
Candida	Histopathology, culture	Amphotericin B, fluconazole, echinocandins	Yes	-
Zygomycosis	Histopathology, culture	Amphotericin B, posaconazole, caspofungin	Yes	Posaconazole is treatment of choice
Schistosomiasis	Stool exam, IFA, ELISA	Praziquantel	May be needed	Steroid is usually used for treatment

Table 1. Summary of ethologic agents, diagnosis and treatment of paraplegia

organisms are *Staphylococcus aureus*, aerobic and anaerobic *Streptococcus*, *Escherichia coli* and *Pseudomonas aeruginosa*. Other organisms like *Klebsiella pneumoniae*, *Bacteroides fragilis*, *Enterococcus faecalis*, *Salmonella*, *Nocardia*, etc. can cause spinal epidural abscess [6]. Paralysis in spinal epidural abscess may be the result of spinal cord compression, spinal cord arterial or venous ischemia and thrombophlebitis or a combination of these [16].

2.1.3. Tuberculosis

Tuberculosis is one of the most common infections worldwide [17]. Extrapulmonary sites most commonly involved by tuberculosis are lymph nodes, pleura, genitourinary tract, bones and joints, meninges, peritoneum and pericardium. However all organ systems may be involved [18]. There are reports about disseminated tuberculosis involving CNS and spine [19]. Tuberculosis may involve any part of CNS. Meningitis, CNS tuberculoma [20] and spinal cord involvement are neurologic presentation of tuberculosis. In some cases one, several or all presentation may be present [21]. In developing countries, a recognized etiology of paraplegia can be tuberculous radiculomyelitis or tuberculomas, especially in patients with evidence of either active or latent tuberculosis. Spinal deformity arises from tuberculosis is the leading cause of paraplegia [22]. It arises from hematogenous spread of the tubercle bacillus from pulmonary infection. The paraplegia occurs either at the time of the primary infection or more commonly 3-5 years later by reactivation [1]. Spinal tuberculosis can present with wide spectrum of symptoms, with back pain being the most common symptom. It is the leading cause of non-traumatic paraplegia in developing countries [23]. Spine is affected in 50% of skeletal tuberculosis patients. Tuberculous infection of the spine causes a bony destruction and collapse of the vertebra, with a gibbus deformity, skip lesion, intervertebral disc involvement, epidural abscess, paravertebral abscess and edema in the soft tissue planes [17]. Characteristically, there is destruction of the intervertebral disk space and the adjacent vertebral bodies, collapse of the spinal elements, and anterior wedging leading to kyphosis and gibbus formation. The thoracic region of vertebral column is most frequently affected. Formation of a 'cold' abscess around the lesion is another characteristic feature. The incidence of multi-level noncontiguous vertebral tuberculosis occurs more frequently than previously recognized. Common clinical manifestations include constitutional symptoms, back pain, spinal tenderness, paraplegia and spinal deformities [24]. In Abbasi's study on tuberculosis spondylitis in Iran, back pain was detected in 100%, anorexia in 100%, fever in 90%, cough in 50% and limb paralysis in 2.5% of patients [25]. These entities should also be considered in high-risk patients or in patients who have emigrated from regions with a high prevalence of tuberculosis [22]. Neurological complications in spinal tuberculosis occur in active stage of disease by mechanical compression, instability and inflammation changes, while in healed disease, these occur due to intrinsic changes in spinal cord secondary to internal salient in long standing kyphotic deformity [26]. Tuberculomas are rare tumorlike growth of tuberculous tissue in the central nervous system, characterized by symptoms of expanding these lesions. They result from enlargement of a caseated tubercle. Intramedullary tuberculomas can cause paraplegia although it is a rare event [27].

2.1.4. Syphilis

Syphilis is a sexually transmitted disease caused by the spirochete *Treponema pallidum*. The involvement of the CNS by *Treponema pallidum* has increased in the past 20 years, particularly as a result of HIV pandemic. However, tertiary forms, and especially syphilitic gumma, are rare as a result of the widespread use of penicillin. Spinal cord compression due to syphilitic gumma is an exceptional event that may cause paraplegia [28]. Syphilitic myelitis is a very rare manifestation of neurosyphilis that may lead to paraplegia [29]. There are several reports in literature about syphilitic aortic aneurysm with destructive spinal erosion that cause paraplegia [30, 31].

2.1.5. Lyme

Lyme disease is a tick-borne infection caused by *Borrelia burgdorferi* [32]. It is one of the most important arthropod-borne zoonosis-pathogen [33] and is transmitted from infected Ixodes ticks to a mammalian host following a tick bite [34]. Lyme borreliosis causes a multisystemic disease which may result in dermatologic, musculoskeletal, cardiovascular, and neurologic manifestations [35]. Lyme borreliosis is a multisystem disease and when involve neurologic system is named neuroborreliosis. Each part of neurologic system may be involved. A broad range of neurologic disorders have been described in Lyme disease, of which peripheral facial nerve palsy and aseptic meningitis are more prevalent [36]. The most common clinical picture of neuroborreliosis is meningitis with cranial or peripheral neuropathies connected with radiculalgia. Encephalitis, myelitis, neuropathies, polyneuropathies, encephalopathies and cerebellar involvement are less common presentation [36, 37]. Acute transverse myelitis is a rare *Borrelia burgdorferi*-related neurologic complication [36]. Encephalomyelitis is the most serious form of neuroborreliosis. Encephalopathy is due to neuroimmunomodulators, like lymphokines and by toxico-metabolic effect could be connected with each form of systemic borreliosis [37]. Neuroborreliosis can cause paraplegia. In Salonen's study paraplegia caused by lyme was complete, flaccid and upper motor neurone type [38].

2.1.6. Brucellosis

Brucellosis is a systemic infectious disease caused by *Brucella* and is a common zoonosis that still remains a major health problem in certain parts of the world such as the Mediterranean region, the Middle East, and Latin America. It may involve multiple organs and tissues. Osteoarticular involvement is the most frequent complication of brucellosis, in which the diagnosis of brucella spondylitis is often difficult since the clinical presentation may be obscured by many other conditions [39]. Brucellosis can cause multisystemic involvement [40]. One of the most common complications is bone and joint involvement, particularly sacroilitis and spondylitis [41]. *Brucella* spondylitis may be complicated with paravertebral or epidural abscess, radiculitis and psoas abscess [42]. Rarely CNS involvement causes serious manifestations. Neurobrucellosis occurs less than 5% of patients and presents with meningitis, encephalitis, myelitis, myelopathy, stroke, paraplegia, radiculoneuritis, intracerebral abscess, epidural abscess, demyelination and cranial nerve involvement or any combination of these manifestations [40, 43]. Spinal epidural abscess may be caused due to brucellosis [44]. It is a

very rare disease which is usually a consequence of spondylodiscitis. The spinal column can be affected at any joint; however, the lumbar spine is the most common region, especially at the level of the L4-5 and L5-S1. Spinal involvement may be seen at the lumbar, thoracic and cervical spine [45]. There are several reports about paraplegia caused by brucellosis [46, 47].

2.2. Viral infection

Several viral infections can cause paraplegia. Paraplegia is a major neurological disorder in HIV infection. It can occur during the asymptomatic stage of HIV infection when CD4 counts are $>200/\text{cm}^3$ and more commonly during the symptomatic stage when CD4 counts are low ($<100/\text{cm}^3$). The main causes are opportunistic processes and direct HIV involvement of the spinal cord. Opportunistic infections include tuberculosis, herpes zoster, herpes simplex, cytomegalovirus (CMV), syphilis and co-infection with human T-lymphotropic virus-1 (HTLV-I) in endemic areas [1]. In developed countries, the most prominent reported spinal cord disease in HIV/AIDS patients is vacuolar myelopathy. Other causes of myelopathy in HIV/AIDS patients include opportunistic infections, neoplasms, vascular lesions and metabolic disease. In developing regions, opportunistic infections are more common [48]. In patients with HIV infection, chronic inflammation can lead to a lesion that compresses the spinal cord and should be considered in differential diagnosis [49]. HTLV-I is a retrovirus which is endemic in some areas of western, southern and central Africa with just a few clusters reported in eastern Africa. It is endemic in areas of Japan, the Caribbean and South America. It is transmitted perinatally, sexually and by blood transfusion. Chronic infection for up to 20-30 years can result in a slow progressive form of tropical spastic paraplegia known as HTLV-I associated myelopathy [1]. This diagnosis should be considered in every patient with progressive spastic paraplegia [50]. Herpes zoster myelitis may cause paraplegia especially in HIV positive patients. Subacute onset paraplegia with a sensory level, which developed 10 days after herpes zoster dermatomal rash, is typical presentation of disease [51]. Extensive necrotic and hemorrhagic changes with marked necrotizing vasculitis involved the entire spinal cord and spinal roots, may be seen [52]. Neurological syndromes attributed to CMV include encephalitis, myelitis, and peripheral neuropathy [53]. Acute lumbosacral polyradiculopathy caused by the CMV infection is a rare neurological complication usually is seen in immunocompromised patients especially in AIDS. Progressive flaccid paraplegia with sensory disturbance, radicular pain, or bladder dysfunction are characteristic symptoms [54]. CMV may cause a severe motor polyradiculopathy by selective destruction of the motor neurons of ventral spinal roots and motor cranial nerves [55]. Several other viruses like Poliovirus, Enterovirus 71, Echovirus, Cocksackie B, Cocksackie A, etc can cause myelitis and paralysis.

2.3. Fungal infection

Aspergillosis of the spine has been reported infrequently. It has usually been attributed to hematogenous infection or spread from an adjacent pulmonary infection. Acute paraplegia may develop after aspergillus infection. Direct extension of aspergillus infection can cause spondylitis, vertebral destruction, spinal cord compression and paraplegia [56, 57]. Vertebral osteomyelitis caused by Aspergillus is rare and usually affects immunocompromised patients.

Aspergillus may lead to epidural abscesses [58, 59], kyphosis, discharging sinus in the back, vertebral destruction and paraplegia [60]. Spondylodiscitis has been reported due to candida [61]. Zygomycosis may be the cause of epidural abscess and paraplegia usually in immunocompromised patients [62]. Spinal cord histoplasmosis with flaccid paralysis has been reported [63].

2.4. Schistosomiasis

Schistosomiasis is a parasitic disease caused by blood flukes of the genus *Schistosoma*. Currently more than 200 million people worldwide are affected. Neuroschistosomiasis constitutes a severe presentation of the disease. Neurological symptoms result from the inflammatory response of the host to egg deposition in the brain and spinal cord. Neurological complications of cerebral schistosomiasis include delirium, loss of consciousness, seizures, dysphasia, visual field impairment, focal motor deficits and ataxia [64]. Transverse myelitis and myeloradiculopathy affecting the conus medullaris and cauda equina are the most common spinal cord syndromes. Transverse myelitis can present as flaccid areflexic paraplegia with sensory level and sphincter dysfunction [65]. Schistosomal myelopathy tends to occur early after infection and is more likely to be symptomatic than cerebral schistosomiasis [64]. Involvement of the spinal cord is considered to be uncommon, although 1-5% of all cases of non traumatic paraplegia in endemic parts of Africa are reported to be caused by schistosomiasis. Paraplegia occurs mostly with *S. mansoni* and occasionally with *S. haematobium* [1].

2.5. Other microorganism

Rarely some other organisms like non-tuberculosis mycobacteria [66, 67], *Nocardia* [68], *pasteurella* [69], etc may involve spinal column, cause spondylitis, epidural or subdural abscess that may lead to paraplegia.

3. Diagnosis

3.1. Subdural empyema

Spinal subdural empyema is an unpredictable disease, with an unfavorable outcome if left untreated. If there is suspicion of a spinal subdural abscess, urgent radiological examination followed by immediate surgical drainage and appropriate antibiotic therapy is warranted [70]. Morbidity and mortality in intracranial and spinal subdural empyema directly relate to the delay in diagnosis and therapy [71]. The diagnostic procedure of choice for spinal subdural empyema is magnetic resonance imaging (MRI) with gadolinium enhancement. Occasionally spinal subdural empyemas may be detected by computed tomography (CT) myelography where MRI is negative [72]. The timing of performing MRI is very important in these patients. Early diagnosis and emergent treatment is necessary to prevent neurologic deficits [12].

3.2. Epidural abscess

A high level of clinical suspicion is necessary for rapid diagnosis and treatment initiation [73]. MRI with gadolinium enhancement is the diagnostic procedure of choice for diagnosis. MRI is recommended over CT scan because it can better visualize the spinal cord and epidural space in both sagittal and transverse sections and can also identify accompanying osteomyelitis, intramedullary spinal cord lesions, and discitis [6].

3.3. Tuberculosis

The diagnosis of Pott's disease is usually made by clinical suspicion, in combination with an elevated ESR and typical radiologic findings. Biopsy may be necessary for confirmation [1]. The awareness and suspicion of an atypical presentation of spinal tuberculosis should be high in order to obtain a good outcome [74]. MRI is the most valuable investigation in the patients with spinal tuberculosis. It is highly sensitive in detection of various pathological processes of Pott's disease [17]. For the diagnosis of spinal tuberculosis MRI is more sensitive imaging technique than x-ray and more specific than CT scan [24]. MRI allows the diagnosis of a tuberculous lesion, with a sensitivity of about 100% and specificity of 88%, well before deformity develops [74]. MRI frequently demonstrates involvement of the vertebral bodies on either side of the disk, disk destruction, cold abscess, vertebral collapse and presence of vertebral column deformities [24]. Marrow edema, preservation of disc space, subligamentous extension of abscess, paravertebral abscess, epidural extension, endplate erosions and discitis were consistently observed in 83% cases of spine tuberculosis on MRI [75]. If pus exists, the diagnosis may be confirmed by histopathological demonstration of Mycobacterium tuberculosis in drained pus [76]. CT-guided needle biopsy from the affected site in the center of the vertebral body is the gold standard technique for early histopathological diagnosis [24].

3.4. Syphilis

The diagnosis of neurosyphilis depends on the serological detection of antibodies in both blood and cerebrospinal fluid (CSF). The Venereal Disease Research Laboratory (VDRL) is the screening test most commonly used. More sensitive and specific diagnostic antibody tests include the fluorescent treponemal antibody absorption (FTA) and the treponemal antibody immobilization test (TPI) [1]. CSF study confirms the diagnosis of neurosyphilis [77]. CSF pleocytosis with positive CSF VDRL often is obvious [78]. MRI appearance of syphilitic myelitis is not well documented and only a few cases have been reported. MRI of the spine shows diffuse high signal intensity in the whole spinal cord on T2-weighted images. Focal enhancement may be observed in the dorsal aspect cord on T1-weighted gadolinium-enhanced images [29]. MRI imaging provides documentation of spinal cord involvement and is useful in monitoring recovery [77]. Marked sclerosis and osteophytes restricted to lumbo-dorsal spine, absence of ligamentous calcification and lack of long standing spinal symptoms may be seen in patients with syphilitic paraplegia [79].

3.5. Lyme

Serological tests, including enzyme linked immunosorbent assay (ELISA) and Western blot analysis can be used for diagnosis. *B. burgdorferi* polymerase chain reaction (PCR) may be used to confirm the diagnosis. Different techniques have been developed to aid in laboratory diagnosis of Lyme disease. Detection of serum antibodies is currently the most practical means of confirming *B. burgdorferi* infections. Although most assays may not detect low amounts of IgM antibody during the initial weeks of infection, application of a capture ELISA method has been reported to improve test sensitivity [80]. Detection of large amounts of IgM and IgG borrelia antibodies in the acute phase and complete disappearance of IgM antibody during the review period confirms the diagnosis [38]. Diagnosis of neuroborreliosis is based on culturing of *B. burgdorferi* from CSF, detection of specific antispirochaetal antibodies produced in subarachnoid space, detection of activated lymphocytes and antigens or borrelial DNA detection in CSF [37].

3.6. Brucellosis

In endemic regions brucella spondylitis should always be considered in the differential diagnosis especially in older patients with back pain and constitutional symptoms. An early diagnosis will help to prevent the development of more severe complications such as spinal cord compression [47]. Rose Bengal, standard agglutination, indirect immunofluorescent assay (IFA) and ELISA tests usually used for diagnosis [41, 46]. Serologic tests provide valuable information but always point to a generic and not a specific diagnosis [81]. ESR and CRP are usually highly positive [82]. Imaging studies, including radiography, computed tomography, magnetic resonance imaging and bone scintigraphy have been used for diagnosis. Radiography is limited to evaluating the focal form of spinal brucellosis. CT and bone scintigraphy have limited value because of their inadequate soft tissue resolution. MRI is the method of choice to assess the extent of disease and follow up the treatment response. However, MRI has a low specificity to predict the exact cause spondylodiscitis, the index of suspicion should be high in regions where the disease is endemic [83]. Serological test for Brucella is usually positive and MRI may reveal epidural abscess or spondylodiscitis [44]. Early diagnosis and specific treatment are important to prevent later complications [41].

3.7. Viral infection

HIV is diagnosed by serological tests, including ELISA and Western blot. Several other tests such as P24 antigen, IFA, radioimmunoprecipitation assay (RIPA) and PCR may be used. Serologic assays, antigen detection and viral Isolation are used to diagnosis of HTLV infection. Serologic tests, PCR and Immunocytochemistry method are used for diagnosis of Varicella zoster virus (VZV) [52]. CMV infection should be included in the differential diagnosis of transverse myelitis of uncertain etiology [84]. CMV-DNA amplification in PCR method or immunohistochemical approach from CSF is a useful procedure for diagnosis of CMV infection [54]. If viremia exists PP65 antigen detection enables early and rapid diagnosis of CMV [85].

3.8. Fungal infection

In the era of transplantation and increase in use of immunosuppressive medications, spinal fungal infection should be considered in differential diagnosis of spinal infectious involvement [60]. The best method for diagnosis of fungal infection is biopsy and visualization of hyphae. Histopathologic findings confirm the diagnosis. Several serologic tests, antigen detection and PCR method for different fungal infection exist. *Aspergillus* can be identified by fungal culture and PCR [58]. *Rhizopus* may be identified by smear or culture from tissue biopsy [86].

3.9. Schistosomiasis

The diagnosis is difficult because the paraplegia mainly occurs during the early invasive phase of the adult worms, when there is little clinical or laboratory evidence of underlying schistosome infection. Stool examination for eggs and rectal snips are used for diagnosis [1]. Although laboratory investigations, including serological tests are of limited diagnostic value [87] Immunofluorescence assay and ELISA has been used for diagnosis [88].

4. Treatment

4.1. Subdural empyema

Treatment in virtually all cases of spinal subdural empyema requires prompt surgical drainage and antibiotic therapy [72] although a more expectant approach consisting of antibiotics and observation has also been proposed [8]. Provisional antibiotic therapy of spinal subdural empyemas should be directed against *S. aureus* and streptococci, and should include nafcillin, oxacillin, or vancomycin [72]. In some cases treatment with intravenous antibiotics and drainage is not enough and complete surgical excision of the lesion may be necessary [89].

4.2. Epidural abscess

The principles of therapy for spinal epidural abscess are prompt surgical decompression, drainage of the abscess, and long-term antimicrobial therapy. Empirical antimicrobial therapy for spinal epidural abscess must include antistaphylococcal agent plus coverage for aerobic gram-negative bacilli [6]. Recent reports have advocated for conservative, non-operative management of this devastating disorder with appropriate risk stratification. Crucial to a successful management strategy are definitive diagnosis, prompt intervention, and consistent follow-up care [90]. Although there are some case reports that present spinal epidural abscess treated with antibiotics alone [91] result of several studies strongly support immediate surgical decompression combined with appropriately tailored antibiotic therapy for the treatment of symptomatic spinal epidural abscess presenting with focal neurological deficit [90]. Recent evidence indicates the following areas of investigation and management can improve outcome in spinal epidural abscess: minimally invasive surgery early versus medical management when there are no significant neurological deficits, neuroradiologic arterial evaluation with therapies directed at vascular ischemia and thrombosis and aggressive rehabilitation [16].

4.3. Tuberculosis

Four anti tuberculosis drugs plus surgical intervention when indicated are cornerstones of treatment. In patients with multi drug resistant tuberculosis anti biogram and more prolong course of treatment is necessary. Anti tuberculosis therapy should be considered for at least 12 months [17]. A combination of conservative therapy and operative decompression when needed should form a comprehensive integrated course of treatment for spinal tuberculosis with neurological complications. The patients showing relatively preserved cord with evidence of edema or myelitis with predominantly fluid collection in extradural space on MRI may be managed by non-operative treatment, while the patients with extradural compression of mixed or granulomatous nature showing entrapment of spinal cord should be candidate for early surgical decompression. The disease focus should be debrided with removal of pus and sequestra. The viable bone should only be removed to decompress the spinal cord and resultant gap should be bridged by bone graft. The preserved volume of spinal cord with edema or myelitis and wet lesion on MRI usually would show good neural recovery. The spinal cord showing myelomalacia with reduced cord volume and dry lesion likely to show a poor neural recovery. The internal kyphectomy is indicated for paraplegia with healed disease. The best form of treatment of late onset paraplegia is the prevention of development of severe kyphosis in initial active stage of disease [26]. Surgery may be required in selected cases, e.g. large abscess formation, severe kyphosis, neurological deficit or lack of response to medical treatment [24].

4.4. Syphilis

Recognition of unusual complication of neurosyphilis is important, because it is a treatable cause of paraplegia with good recovery [77]. Greater alertness to diagnosis may result in earlier therapy and thus possibly lead to improved prognosis [78]. Aqueous crystalline penicillin G 3-4 million units intravenous every 4 hours for 10-14 days is treatment of choice. For patients with penicillin allergy other regimens may be used. Docycycline, amoxicillin and ceftriaxone are alternative treatments [92].

4.5. Lyme

The tick-borne spirochete responsible for Lyme disease is highly antibiotic-sensitive. Treatment is highly effective in the vast majority of patients, including those with nervous system disease. Nervous system infection, most typically meningitis, cranial neuritis, radiculoneuritis, and other forms of mononeuropathy multiplex, is highly antibiotic responsive. In patients with infection not involving the CNS, oral treatment with amoxicillin, cefuroxime axetil, or doxycycline for 2-4 weeks is almost always curative. Despite historic preferences for parenteral treatment with ceftriaxone, cefotaxime, or meningeal dose penicillin, patients with the forms of nervous system involvement listed above are highly responsive to oral doxycycline. Parenteral regimens can be reserved for those very rare patients with parenchymal CNS involvement, other severe forms of infection or the approximately 5% of patients who fail to respond to oral regimens [93].

4.6. Brucellosis

Neurobrucellosis, if not treated early, can result in severe neurological morbidity and sequelae, which may be irreversible. Hence it is important to consider the possibility of neurobrucellosis in endemic region and treat aggressively (94). Treatment with streptomycin, rifampicin and doxycycline significantly improve the symptoms [44]. Doxycycline, rifampin, trimethoprim-sulfamethoxazole, streptomycin, gentamicin, ciprofloxacin and ceftriaxone are used for treatment of neurobrucellosis [95]. The mean duration of antimicrobial therapy is 18 weeks with range of 12-56 weeks. Prolonged duration of treatment especially in complicated cases in order to avoid possible sequelae is necessary [42]. In Gul's study duration of antibiotic therapy was ranged from 2 to 15 months (median 5 months) [96]. Neurobrucellosis and brucella spondylitis usually are treated with 3 drugs combination [46, 97]. The standard treatment of brucella spondylitis with a combination of two antibiotics for 6-12 weeks is associated with high rates of treatment failure and relapse. Prolonged administration of a triple combination of suitable antibiotics appears to be an effective treatment for brucella spondylitis [98]. The most commonly-used antibiotics are combinations of rifampin, doxycycline and trimethoprim-sulfamethoxazole [99].

4.7. Viral infection

For treatment of HIV usually 2 nucleoside analogue plus one protease inhibitor or one non-nucleoside reverse transcriptase inhibitor are used. Although nucleoside analogues, such as zidovudine and lamivudine, have long been recognized to have activity against HTLV reverse transcription in vitro, there is little clinical evidence of their efficacy in vivo, so treatment of asymptomatic HTLV carriers is not indicated. A combination of zidovudine and lamivudine has been used for treatment, but no clinical improvement was seen, and there was no effect on HTLV-I proviral load or immunologic markers [100]. The most commonly antiviral agents used for treatment of CMV are: ganciclovir, foscarnet, cidofovir, valganciclovir and valganciclovir [101]. Ganciclovir has been used in patients with CMV polyradiculopathy successfully [53].

4.8. Fungal infection

Depending on fungal infection, antifungal regimen such as amphotericin B, posaconazole, voriconazole, etc may be used with surgical intervention. Voriconazole has been used to treat aspergillosis [58]. The gold standard of systemic antifungal treatment is voriconazole, which has been proved to be significantly superior to conventional amphotericin B. Liposomal amphotericin B appears to be a suitable alternative for primary treatment, while caspofungin, amphotericin B lipid complex or posaconazole have shown partial or complete response in patients who had been refractory to or intolerant of primary antifungal therapy [101]. Itracozazole is more frequently used in immunosuppressed patients who are able to take oral therapy and for use as sequential oral therapy [102]. Options for initial therapy for invasive Candida infections include fluconazole, echinocandin compounds or liposomal amphotericin B. Voriconazole is the secondary alternative treatment [101]. Amphotericin B, caspofungin or posaconazole are used for treatment of Zygomycosis [103, 104].

4.9. Schistosomiasis

Praziquantel and corticoids have been successfully used to treat neuroschistosomiasis [65]. Surgery has been tried for acute cases of failed medical treatment [1].

5. Conclusion

Infectious diseases are important causes of non-traumatic paraplegia. High index of suspicion, precise history taking, exact physical examination and proper use of laboratory tests and radiologic studies are necessary for making accurate diagnosis. Sometimes the diagnosis is dependent to invasive procedure such as CT guided biopsy and subsequent histopathologic study, without them appropriate diagnosis may be impossible. Sometimes for accurate diagnosis using several laboratory and radiologic modalities, simultaneously, may be needed. Paying attention to specific treatment and its duration is very important. Sometimes combination antibiotic therapy is needed. If treatment or its duration is not appropriate, relapse may occur. Although paraplegia due to infectious diseases can be with high mortality rate, early diagnosed and successful treatment can prevent neurological sequelae.

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Author details

Farhad Abbasi¹ and Soolmaz Korooni Fardkhani²

1 Bushehr University of Medical Sciences, Iran

2 Shiraz University of Medical Sciences, Iran

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