Pathology of vaccine-preventable infectious disease and the central nervous system

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Abstract

Infections of the central nervous system are important sources of morbidity and mortality worldwide. The risk for infections with specific bacterial, viral, fungal and parasitic agents varies greatly with the patient's age, immune status, prior vaccination history, seasonality and geographic exposures. While vaccines are available for many viral and bacterial pathogens, there has been a resurgence of vaccine-preventable diseases in recent years due to under-vaccination of eligible children and adults. This review will discuss key pathognomonic features of vaccine-preventable infectious diseases of the central nervous system that may be encountered in general surgical and autopsy practice.

Keywords autopsy pathology; central nervous system; histopathology; infectious disease; microbiology; neuropathology; public health; vaccines

Introduction

Central nervous system (CNS) infections are caused by a wide array of bacterial, viral, fungal and parasitic agents.[1–4] While the blood brain barrier and other specialized immunologic mechanisms provide a high resistance to infection, vulnerability arises with structural and immune compromise, extremes of age, and exposure to neurotropic pathogens.[2,3,5] Infections of the CNS are particularly notable for their diversity, ranging from common to rare, acute to chronic, self-limited to progressive, and benign to fatal.[1–4]

Fortunately, many viral and bacterial CNS infections are preventable using vaccination (Tables 1 and 2). Although global efforts have led to tremendous reductions in vaccine-preventable diseases over the past century, challenges remain for achieving complete vaccination of all susceptible individuals. In some regions of the world, vaccination efforts are hampered by insufficient public health resources, war, and civil unrest. In other regions, religious beliefs or fear of vaccine-associated adverse advents have caused parents to refuse or delay vaccination of their children.[4,6–10] Studies have linked focal outbreaks of vaccine-preventable diseases in the United States to regions where high rates of vaccination refusal exist.[9,10]

Given the opportunities for re-emergence of vaccine-preventable diseases, it is important for pathologists to be familiar with their associated gross and histopathologic features. This review discusses the important clinical, radiological, pathological and microbiological features of vaccine-preventable CNS infections.

Bacterial infections

A nearly limitless number of bacteria may involve the CNS. The most common form of bacterial CNS infection is meningitis; other manifestations include encephalitis, brain abscess and subdural empyema.[3] Bacteria enter the CNS hematogenously, through direct spread, or rarely via axonal transport.[2,3] Infection location varies with route of entry and causative organism, thus identifying a primary source of infection may be clinically relevant. Important considerations include a recent history of upper respiratory infection, otitis media, head trauma, or neurosurgical procedure and presence of dental carries or ventricular shunt.[2,3] Hematogenous spread is commonly associated with cerebral convexity-predominant meningitis and involvement of the grey-white matter junctions. Direct extension favours skull base-predominant meningitis or, in the example of sinusitis, frontal lobe abscesses.

Bacterial infections are potentially life-threatening and require rapid diagnosis and treatment to prevent death and/or permanent neurological sequelae.[2,3] Diagnosis is commonly made on clinical grounds in conjunction with radiologic findings and analysis of the cerebral spinal fluid (CSF); pathology specimens are not commonly obtained except in cases of undiagnosed or fatal infections. Common clinical findings of bacterial meningitis include fever, nuchal rigidity, headache, vomiting, photophobia, and neurologic deficits.[3] Radiologic findings are non-specific with bacterial meningitis but neuroimaging importantly excludes herniation prior to lumbar puncture and detects complications such as venous thrombosis and hydrocephalus.[11] Characteristic CSF findings include increased opening pressure, high cell counts with neutrophil predominance, elevated protein, and low glucose.[3] Culture is considered the diagnostic standard, but PCR commonly offers high sensitivity and specificity for detection of specific organisms and may provide a more rapid result. Given the high associated morbidity and mortality, antibiotics should be started immediately when bacterial meningitis is suspected.[3]

Abscesses may present acutely or have an insidious onset; symptoms include headache, fever, ataxia, and seizures. Magnetic resonance imaging offers increased sensitivity over computed tomography and is considered the modality of choice for differentiating abscess from necrotic tumour.[3,11] Treatment relies on antibiotics and, in some instances, surgical abscess drainage.

Gross features of bacterial meningitis include cerebral edema and ventricular compression.[3] Subarachnoid purulence is initially focal and may be absent in rapidly progressive fatal

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Vaccine-preventable bacterial infections of the central nervous system[2,3]

Organism (Disease)	Disease characteristics	Pathology	Epidemiology and vaccine indications
Bacillus anthracis (Anthrax)	Cutaneous, gastrointestinal and inhalation forms; meningitis; highest risk with inhalational exposure	Purulent meningeal exudate with hemorrhage; large Gram-positive bacilli in neutrophilic exudate	*Occurrence*: worldwide; animal exposure (cutaneous, GI), bioterrorism or lab accident (inhalational) *Vaccination*: high risk adults (laboratory and animal workers)
Corynebacterium diphtheria (Diphtheria)	Usually mild respiratory illness; toxin-mediated croup, myocarditis, neuropathy (oculomotor cranial nerve dysfunction, laryngeal, pharyngeal, and limb innervation dysfunction); case fatality rate 5—10%	Bacteria not seen; macrophages and mononuclear cells in spinal ganglia and nerve roots; demyelination	*Occurrence*: worldwide; major cause of childhood death in pre-vaccine era; rare in regions with high vaccine coverage *Risk factors for severe disease*: age <5 years and >40 years (up to 20% case fatality rate) *Vaccination*: routine paediatric and adult, post exposure toxoid booster.
Haemophilus influenza type B (meningitis)[a]	URI; invasive disease with meningitis (most common), otitis media, epiglottitis, gastroenteritis, arthritis, pneumonia, cellulitis; 3—6% case fatality rate despite appropriate antibiotic therapy, neurologic sequelae in 15—30%	Purulent meningeal exudate, involving cerebral sulci, basilar cistern; Gram negative pleomorphic coccobacilli within neutrophils and extracellularly	*Occurrence*: worldwide; most invasive disease in children <1 year old; caused 50—65% of meningitis in the US in the pre-vaccine era; rare in regions with high vaccine coverage. *Risk factors for severe disease*: defects in humoural immunity, asplenia, population crowding, chronic disease, low SES, male sex *Vaccination*: routine paediatric
Mycobacterium tuberculosis (tuberculosis)	Primary pulmonary infection; usually latent disease; primary and reactive disease may involve any organ; slowly progressive; meningitis, tuberculoma, abscess formation. Miliary TB has high association CNS spread	Immunocompetent: basilar caseating granulomatous meningitis, tuberculoma: rare acid fast bacilli; Immunosuppressed: non-granulomatous inflammation, abscess, many acid fast bacilli	*Occurrence*: worldwide; major infectious cause of death world-wide, predominantly developing countries; 1/3 of the global population has latent TB *Risk factors for severe disease*: immune compromise (e.g. AIDS), malnourishment, alcoholism, extremes of age *Vaccination*: routine for infants/ children in high incidence countries
Neisseria meningitidis[a] (Meningococcal meningitis)	Asymptomatic carriage; meningitis most common form of invasive disease; rash, pneumonia, arthritis, adrenal hemorrhage, multi-organ failure; Up to 40% fatality rate; 20% survivors have permanent deficits.	Purulent meningeal exudate, focal hemorrhage; Gram negative encapsulated diplococci within neutrophils and extracellularly	*Occurrence*: worldwide; epidemics in crowded living environments, endemic in sub-Saharan Africa ("meningitis belt") *Risk factors for severe disease*: defects in humoural immunity, asplenia *Vaccination*: at-risk individuals (microbiologists, military recruits, travellers to endemic areas) and for outbreak control
Streptococcus pneumoniae[a] (Pneumococcal meningitis)	*General*: preceding URI or otitis media, pneumonia (most common), bacteraemia *CNS*: meningitis with cranial nerve	Purulent meningeal exudate, predominantly involving cerebral hemisphere convexities; Gram positive lancet-shaped diplococci	*Occurrence*: worldwide; most common cause of bacterial meningitis in the US; especially children <5 years old. Winter/early

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