Cytomegalovirus Infection

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Risk

- Seroprevalence increases with age and low socioeconomic status in USA: From 58.9% in those aged ≥6 y to 90.8% in those ≥80 y. Also higher in non-Hispanic blacks, Mexican Americans, and women.
- Severe disease from CMV is rare in immunocompetent individuals.
- Risk for CMV disease in transplant recipients: 10–40% with preventive measures.
- Risk for CMV disease in HIV-positive pts: 20–30% (increased risk with low CD4 count).
- Approximately 1:150 children is born with congenital CMV.

Perioperative Risks

- CMV transmission from tissue or blood products from a CMV-seropositive donor to a seronegative recipient
- Related to severity of CMV-induced organ dysfunction (if present): Pulmonary, CNS, hepatic, GI, cardiac, bone marrow, adrenal

Worry About

- Giving CMV-seropositive blood products to a CMV-seronegative immunocompromised host; filters that remove leukocytes from the blood can be used to prevent transmission of CMV if CMV-seropositive blood donors are used.
- Abnormal hepatic metabolism if CMV hepatitis is present may alter drug clearance.
- Elevated ICP if CMV encephalitis/meningitis.
- Abnormal oxygenation if CMV pneumonitis.
- Myocardial dysfunction or arrhythmias if CMV myocarditis.
- Perforated viscus secondary to colonic/gastric CMV.
- Bone marrow suppression resulting in abnormal bleeding from thrombocytopenia, anemia, and neutropenia.
- Adrenal insufficiency due to CMV adrenalitis.

Overview

- Double-stranded DNA betaherpesvirus; member of the *Herpesviridae* family—largest virus to infect humans.
- Vast majority of North American adults have had prior exposures and are CMV seropositive.
- Establishes latency after primary infection. Secondary infection occurs after reactivation of a latent virus in an immunocompromised host.
- Transmission through close contact, blood and blood products, organ transplantation, and sexually and perinatally.

Manifestations

- Immunocompetent host: Asymptomatic, heterophile antibody–negative mononucleosis-like syndrome
- Immunocompromised host: Symptomatic or asymptomatic viremia with or without organ involvement—retinitis, encephalitis, meningitis, myelitis, polyneuropathy, pneumonitis, esophagitis, gastritis, colitis, hepatitis, cholangitis, myocarditis, adrenalitis, vasculitis, and bone marrow suppression
- Neonates: Petechial rash, jaundice with hepatosplenomegaly; neurologic abnormalities, such as microcephaly and lethargy, eye involvement with chorioretinitis and optic nerve atrophy, prematurity and low birth weight, and sensorineural hearing loss

Diagnosis

- Serology: IgM has high rates of false positivity. Positive IgG indicates prior infection, which is useful for risk stratification in transplant recipients
- NAAT (in immunocompromised hosts)
- Viral cultures
- pp65 antigenemia (in immunocompromised hosts)

Usual Treatment

- Immunocompetent host: Supportive symptomatic management, antivirals not indicated
- Immunocompromised host: IV ganciclovir in moderate-to-severe infection; oral valganciclovir in mild infection. IV foscarnet or cidofovir for resistant virus. IV immunoglobulins as adjunctive therapy in refractory cases; other experimental drugs (brincidofovir, maribavir, letermovir)
- Surgical: For complications of end-organ damage, such as repair of GI perforation.

Prevention

- Oral valganciclovir in high-risk solid organ transplant recipients
- Preemptive monitoring with NAAT in stem cell, bone marrow, and umbilical cord transplant recipients

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Destruction of retina	Decreased visual acuity, blind spots	Funduscopy; white and red lesions	Ophthalmology evaluation
CV	Myocarditis; LV dysfunction	CHF symptoms, palpitations	Irregular rhythm, displaced PMI, S_3	ECG, ECHO, heart biopsy
RESP	Pneumonitis; impaired gas exchange	Dyspnea, nonproductive cough	Wheezes, crackles, hypoxemia	CXR, ABG, bronchoscopy + biopsy
GI	Viral infection of organ	Hepatitis/cholangitis: • Right upper quadrant pain • Jaundice, itching, acholic stools Esophagitis: Dysphagia, odynophagia Colitis: Diarrhea, abdominal pain Gastritis: Pyrosis, anorexia, epigastric pain	Signs of hepatic failure, fetor hepaticus, asterixis, jaundice, bruising, painful liver, nonspecific abdominal pain	Liver function tests, ERCP, EGD, US, NAAT, ± biopsy
HEME	Bone marrow suppression	Fever, fatigue	Petechiae, pallor, tachycardia	CBC with differential
CNS	Encephalitis	Motor or sensory abnormalities, altered mental status	Motor weakness, sensory abnormality, cerebellar ataxia, abnormal tests of cortical function	CT, MRI, lumbar puncture

Key References: Rafailidis PI, Mourtzoukou EG, Varbobitis IC, et al: Severe cytomegalovirus infection in apparently immunocompetent patients: a systematic review, *Virol J* 5:47, 2008; Crumpacker C: Cytomegalovirus. In Bennett J, editor: *Mandell, Douglas, and Bennett's principles and practice of infectious diseases*, ed 8, Philadelphia, PA, 2015, Elsevier, pp 1738–1753.

Perioperative Implications

Perioperative Preparation

- Evaluate for signs of pulmonary, cardiac, hepatic, CNS, bone marrow, and/or adrenal dysfunction.

Monitoring

- Routine
- May need drug dose adjustment if hepatic/renal dysfunction present

Airway

- May require high FIO_2 and PEEP if pneumonitis present

Preinduction/Induction

- Avoid tachycardia/hypotension.

Maintenance

- Follow CO, PCWP, SaO_2, and BP.

Extubation

- No special concerns

Postoperative Period

- Monitor for clinical signs of disease progression.

Adjuvants

- No special concerns

Dandy-Walker Syndrome

David Johnson | Lee A. Fleisher

Risk

- Multiple genetic factors; mostly sporadic with limited familial inheritance
- Range: 1:10,000-30,000 newborns

Perioperative Risks

- Variable phenotypic expression and organ involvement
- Increased incidence of additional developmental abnormalities
- Depend upon severity of disease and comorbidities, which may include elevated ICP; craniofacial, cardiac, and renal malformation; seizure disorder; respiratory depression; nausea; and vomiting

Worry About
- Hydrocephalus with elevated ICP and possible seizures
- Pt's ability to cooperate and follow commands
- Aspiration risk
- Ventilation challenges because of craniofacial abnormalities
- Postanesthetic respiratory depression
- Multiorgan disease resulting in cardiac and urogenital abnormalities

Overview
- Dandy-Walker complex represents a group of related congenital disorders of brain development, including Dandy-Walker malformation, mega cisterna, and Dandy-Walker variant.
- Includes congenital brain malformation involving a hypoplastic cerebellum with variable defects in formation of the cerebellar vermis, enlargement of the fourth ventricle, and cyst formation in the posterior fossa.
- Commonly associated conditions with variable severity include hydrocephalus, defects in corpus callosum formation, developmental delay, and abnormalities of the heart, urogenital tract, and bones. There may be associated developmental syndromes including PHACIES, spina bifida, and others, which may complicate management. Careful Hx and physical exam are required to identify comorbidities.
- ICP and seizure management are primary concerns.
- Rostral brain involvement may predispose pt to apnea following anesthetic.

Etiology
- Believed to be the result of multifactorial gene mutations. TUBA1A has been identified as a major driver, resulting from mutation of tubulin transport proteins. Inheritance is mostly sporadic, with a small familial association.

Usual Treatment
- Depends upon disease presentation. Hydrocephalus is often treated with ventriculoperitoneal shunt, medication for seizures, physical therapy for muscular involvement, occupational therapy, and education for learning disabilities.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Craniofacial abnormality, macrocephaly, micrognathia, macroglossia, occipital meningocele, nystagmus			
CV	Varied cardiac abnormalities, including Tetralogy of Fallot	SOB, poor exercise tolerance, "Tet spells"	Cyanosis, heart murmur	CXR, ECG, angiography
RESP	Medullary control of respiratory center		Apnea	
RENAL	Urogenital malformation	Urinary tract infections		UA
CNS	Intracranial pressure, developmental delay, CN palsy	N/V, seizure	Palsy, altered mentation	CT
MS	Abnormal vertebrae, prominent occiput, frontal bossing, cleft palate, truncal ataxia, muscle spasticity		Ataxia	CT

Key References: National Institutes of Health: Genetic and rare diseases information center. <https://rarediseases.info.nih.gov/gard/6242/dandy-walker-complex/resources/1>, 2016 (Accessed 12.04.16.); Shweta M, Rao S, Ladi SD, et al.: Dandy Walker syndrome: case report, *Innov J Med Health Sci* 4(1):309–311, 2014.

Perioperative Implications

Preoperative Preparation
- Identify organ involvement, aspiration risk, and anatomic defects.

Monitoring
- Standard monitoring
- Arterial line if cardiac dysfunction warrants

Airway
- Craniofacial abnormalities may compromise ventilation and intubation.
- Macrocephalus may be managed with a shoulder bag to improve positioning.
- Rapid sequence induction if aspiration risk exists.

Induction
- Avoid increased ICP with smooth induction, normocapnia, and muscle relaxants.
- Preop ventriculoperitoneal shunt may be needed before other surgeries.
- Succinylcholine may need to be avoided because of renal disease or elevated ICP.
- Cognitive impairment may render pt uncooperative.
- pt may have CV disease.

Maintenance
- Pt may have CV instability.
- Monitor for seizure activity; maintain normocapnia.

Extubation
- Anticipate challenges with reintubation.
- Pt may be at risk of apnea and delayed spontaneous ventilation due to diminished respiratory drive.

Adjuvants
- Shoulder bag, video laryngoscope, and fiberoptic laryngoscope

Postoperative Period
- Monitor respiratory status closely.
- Monitor for seizure activity; avoid increased ICP.

De Morsier Syndrome

Ashley R. Valentine | Jeffrey R. Kirsch

Risk
- For live births: 1:10,000; equal male to female prevalence
- Associated with younger maternal age
- May not be identified until later in life

Perioperative Risks
- Reduced cortisol stress response in undiagnosed or untreated pts. Hormone tests may be normal in nonstress conditions.
- Treatment of one hormone deficiency (e.g., hypothyroidism, or hypothyroidism and adrenal insufficiency) may unmask another or others (e.g., adrenal insufficiency, DI).

Worry About
- Unrecognized hypothalamic/pituitary axis deficiencies
- Neurocognitive disorders causing agitation, seizures, or confusion in periop period

Overview
- Highly phenotypically variable disorder diagnosed when at least two of three features are present: ONH, midline/CNS neuroradiographic abnormalities (may include absence of the septum pellucidum), and/or hypothalamic/pituitary abnormalities.
- ONH is third most common cause of any vision impairment in children <3 y in USA.
- ONH associated with other neuro abnormalities (e.g., developmental delay, autistic spectrum disorder, epilepsy, disrupted circadian rhythm).
- Hypothalamic/pituitary hormone abnormalities can develop at any age and may include growth hormone deficiency (most common), hypothyroidism, ACTH deficiency, and DI (least common).
- Limb abnormalities (e.g., syndactyly) and MSK abnormalities (e.g., spastic quadriparesis, hypotonia) also may be present.

Etiology
- Majority of cases are sporadic, and less than 1% have currently identifiable genetic mutation.
- Environmental risk factors may include antenatal drug/ETOH use and low socioeconomic status.
- Genetic mutations in HESX1, SOX2, SOX3, or OTX2 may be causal.
- See also Adrenal Insufficiency, Hypopituitarism, Hypothyroidism, and Seizure.

Usual Treatment
- Pts followed at least every 6 mo for growth and development
- At least annual vision evaluation and treatment as indicated
- Endocrine function followed for life because hypothalamic/pituitary abnormalities can develop at any age
- Supportive services tailored to individual pt's needs (e.g., occupational, speech, developmental, and/or physical therapy; neuropsychology; ophthalmology)
- Genetic counseling for families with identifiable genetic mutation
- May need surgical correction of associated strabismus or orthopedic deformities