Case 1: The need for speed

A 16-year-old girl is referred to your office by her school guidance counsellor. The patient has complained of being in a depressed mood for the past three to four weeks, interspersed with periods of irritability. She has been unable to sleep at night despite feeling excessively fatigued. She has denied any suicidal behaviour, although her teachers note increased absenteeism and feel she has become more isolated in class. She has lost weight in recent weeks, and attributes this to a decreased appetite.

The counsellor notes that a telephone call to her parents revealed that she has been spending more and more time outside of the home. They too have become quite concerned with her behaviour and suspect she is using drugs. She did not return home from school the previous Friday but, instead, arrived home on Sunday morning looking quite disheveled and acting 'wired'. She has denied drug use previously, but has admitted to regular alcohol use with friends.

You meet with the teenager who confirms the above information. A psychosocial screening (obtained using the HEADSS interviewing strategy) reveals that she has recently started dating a new boy at school. She admits to feeling depressed and being unable to sleep, but cannot identify any obvious stressor or trigger. Further questioning reveals that her boyfriend has a 'drug problem', and she eventually discloses information that provides an explanation for the recent changes in her medical and psychological status.

Case 2: Rash, fever and headache….first, do no harm

A 16-year-old healthy boy presented with a two-day history of pruritic painful rash involving his left abdomen and back in a T9 to T10 distribution. In addition, he had a fever, blurry vision, painful eye movements and a headache. The patient had a history of varicella-zoster virus infection without complications when he was eight years of age, and his past medical history was unremarkable. There were no sick contacts, and his vaccinations were current. He had not received the varicella vaccine.

On examination, his temperature was 37.4°C, his heart rate was 72 beats/min, his respiratory rate was 16 breaths/min and his blood pressure was 137/66 mmHg. He was alert with normal neurological findings, except for pain elicited on bilateral upward and extreme lateral gaze. There were clusters of six to eight slightly scabbed, erythematous papules in a left T9 to T10 distribution, with a single vesicular lesion noted over the left upper scapula. The rest of the examination was unremarkable.

Laboratory evaluation revealed a peripheral white blood cell count of 7×10^9/L (neutrophil count of 4.11×10^9/L and lymphocyte count of 2×10^9/L), hemoglobin level of 139 g/L, platelet count of 188×10^9/L and normal chemistry profile with a creatinine level of 62 µmol/L. The cerebral spinal fluid revealed a white blood cell count of 165×10^6/L with 97% lymphocytes, red bood cell count of 105×10^6/L, glucose level of 2.4 mmol/L and protein level of 0.83 g/L. The cerebral spinal fluid polymerase chain reaction was positive for varicella-zoster virus.

Intravenous acyclovir (30 mg/kg/day divided every 8 h) and cefotaxime (2 g taken intravenously every 6 h) were initiated. Intravenous fluid was started at 15 mL/h to maintain vein patency. Despite nursing description of minimal oral intake secondary to nausea, quantitative fluid balance was not documented. On day 2, the patient developed a truncal, erythematous, morbilliform rash. Cefotaxime was discontinued; however, the rash persisted for five more days. On hospital day 4, the patient developed hypertension ranging between 155/80 mmHg and 168/97 mmHg, and his creatinine level had increased to 203 µmol/L.

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CASE 1 DIAGNOSIS: METHAMPHETAMINE ABUSE

The patient admitted to regular use of 'crystal meth' in the weeks leading up to her presentation. She acknowledged that the timing of her drug use correlated with her recent change in mood.

Crystal meth is the crystalline form of methamphetamine. It is a highly potent, inexpensive and addictive stimulant that is typically manufactured in clandestine laboratories. Methamphetamine also commonly goes by the street names speed, ice, tweak, tina and crank. It can be taken orally, snorted, smoked or injected with onset of action occurring immediately (in the case of smoking or injection), or taking as long as 20 min to 30 min when ingested orally (1). The mechanism of action involves blockade of presynaptic reuptake and displacement of stores of various neurotransmitters, including dopamine (most pronounced), noradrenaline and serotonin, resulting in hyperstimulation of postsynaptic neurons with secondary excitatory effects (2). The first noted effect is usually a characteristic 'rush', which is believed to be the result of rapid dopamine release (1). The drug's extended half-life allows a sustained euphoria, or 'high', often followed by a profound crash, which leaves the user desperate to regain the high (2). This predisposes to runs or binges, during which the user may go for days to weeks without sleeping and with minimal nutrition, often resulting in weight loss.

Methamphetamine abuse has the potential for both acute and chronic health consequences. Acute effects of methamphetamine use parallel those of other stimulants and include euphoria, increased energy, heightened alertness, tachycardia, increased blood pressure, hyperthermia, increased libido, as well as central nervous system effects (eg, insomnia, anxiety, inability to focus, tremors, hallucinations and paranoia) (2). The addictive nature of methamphetamine makes long-term abuse of the drug common. Chronic abuse can result in permanent central nervous system consequences, including confused states, paranoia, hallucinations (auditory and tactile are most common), psychosis and memory loss. Patients are also at risk for the development of cardiomyopathies, stroke, dermatological lesions due to injection site infection or from picking at the skin, poor dentition (meth mouth) and weight loss (2). From a psychosocial standpoint, methamphetamine abuse may also increase the risk of other adverse health consequences, including depression, violent behaviour, blood-borne viruses (HIV, hepatitis B and C) from shared injection equipment and secondarily acquired sexually transmitted infections (2).

The United Nations Office on Drugs and Crime estimated that close to 25 million people worldwide consumed amphetamines in 2005 (two-thirds of whom consumed methamphetamine), surpassing both cocaine and heroin use (3). Globally, amphetamine-type stimulant production appears to have stabilized in recent years, a trend, at least partially influenced by increased monitoring and control measures, although there are suggestions that the number of production laboratories are on the rise (3). The Canadian Addiction Survey 2004 (4) showed that 6.4% of Canadians reported using speed at least once in their lifetime, with less than 1% having used it in the preceding 12 months. This survey, however, did not include high-risk groups, such as street youth and Aboriginal communities in remote areas. Anecdotal information, such as reports of increased hospital admissions, police contacts, numbers of individuals seeking treatment and clandestine laboratories producing methamphetamine point to an increased prevalence of methamphetamine use in the Western provinces (5).

Treatment of methamphetamine ingestion is primarily supportive. Routine laboratory workup should be performed in all patients with methamphetamine intoxication including measurement of electrolytes and creatine kinase levels, to rule out rhabdomyolysis. Patients with acute mood and other psychiatric disturbances may initially be managed nonpharmacologically by decreasing environmental stimuli; although agitated patients may require treatment with a benzodiazepine or an antipsychotic agent (2). Once stable, adolescent patients should be interviewed, assessed and screened (when appropriate) for other high-risk activity. The HEADSS interviewing strategy can facilitate this process because it involves a graduated exploration of psychosocial parameters aimed at identifying specific risk and protective factors in a nonthreatening manner (6). All at-risk youth should be screened for sexually transmitted or injection-acquired infections. Referrals to substance abuse counsellors and other appropriate programs should also be encouraged in cases of ongoing suspected substance abuse.

In the above case, the patient's recent mood disturbance, history of weight loss and sleep disturbance were each believed to be a consequence of her stimulant abuse. The patient was motivated to change her pattern of use and was subsequently referred to a substance abuse program that offered intensive day program support in both an individual and group setting.

CLINICAL PEARLS

- Adolescent patients presenting with depression should undergo a complete history and physical examination, with specific attention paid to psychosocial functioning, substance use history, and recent behavioural changes and/or stressors.
- Methamphetamine is an extremely potent stimulant with an extremely high addictive potential that can cause significant short- and long-term morbidity.
- Patients who present with amphetamine-type stimulant toxicity should be monitored closely, both from a medical (specific attention paid to vital signs and biochemical parameters) and a psychiatric standpoint (agitation and aggression should be treated as needed).

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CASE 2 DIAGNOSIS: HERPES ZOSTER WITH ASEPTIC MENINGITIS AND ACYCLOVIR-INDUCED RENAL TOXICITY

The renal insufficiency and resultant hypertension was believed to be secondary to acyclovir-induced renal toxicity, and the acyclovir was immediately discontinued. The hypertension and enlarged echogenic kidneys seen on ultrasound had both resolved by one month after discharge.

Herpes zoster (HZ) is uncommon in healthy children. The incidence of HZ ranges between 0.74 per 1000/year in children zero to nine years of age, and 10.1 per 1000/year in adults 80 to 89 years of age. Resulting from the reactivation of dormant varicella-zoster virus (VZV) in the dorsal sensory root ganglia, HZ more commonly affects the elderly and the immunocompromised. Risk factors for HZ in immunocompetent children include intrauterine and infantile (younger than one year of age) VZV, due to decreased specific cellular immunity and subsequent prolonged viremia.

In children, HZ is generally characterized by minimal pain and pruritis. Lesions appear as clusters of vesicles involving sensory dermatomes that crust over the following week. In contrast to adult HZ, postherpetic neuralgia is rare in children. The distribution of HZ is variable and depends on the health status and age of the child; dissemination is more common in immunocompromised individuals. Our patient, although healthy, presented with a rash involving his left, lower thoracic and cervical dermatomes. He also had evidence of central nervous system involvement.

Although rare, aseptic meningitis has been documented in healthy children with HZ infection. Approximately 30% to 50% of HZ patients have pleocytosis in the cerebral spinal fluid. In general, these reports involve children whose primary VZV occurred before one year of age. Our patient, however, developed aseptic meningitis with his HZ, despite having contracted chickenpox at eight years of age. This is an unusual presentation because our patient's history was not suggestive of an immunodeficiency.

The diagnosis of HZ is based on clinical findings, direct fluorescent antigen, Tzanck smear, serology or viral culture. In addition, molecular testing (real-time polymerase chain reaction) can differentiate wildtype from vaccine strains of varicella virus. Once diagnosed, the indications for acyclovir therapy include immunocompromised children, trigeminal involvement of HZ, Ramsay Hunt syndrome and meningoencephalitis. Healthy children with an uncomplicated course of HZ do not usually require antiviral therapy.

Documented adverse effects associated with acyclovir include mild nausea, vomiting, diarrhea and abdominal pain. Rare side effects include neurological, hematological, hepatic and renal toxicity. Several cases of acute renal failure have been reported, usually in the context of fluid restriction to prevent cerebral edema in patients with encephalitis. The combination of ceftriaxone and high-dose acyclovir may further increase the risk of nephrotoxicity. Our patient, without purposeful fluid restriction, developed acute renal failure after four days of intravenous (IV) acyclovir therapy. Cefotaxime was discontinued within 24 h of hospitalization, once cerebral spinal fluid viral polymerase chain reaction results were obtained. Decreased oral fluid intake, combined with inadequate IV hydration, may have contributed to the development of renal insufficiency in our patient. Important factors that have been identified in avoiding nephrotoxicity when using IV acyclovir include, making sure that it is dosed by ideal body mass (and not just body weight), that the patient is optimally hydrated (usually recommend 1.5 times maintenance, unless fluid restricted), and close monitoring of urine output (minimal 1 mL/kg/h), accurate ins and outs, daily weight and serum creatinine. The use of concurrent nephrotoxic agents should be avoided, and the dose of acyclovir must be adjusted for any renal impairment.

Prevention of VZV infection includes the live attenuated VZV vaccine. Licensed for use in Canada in 1998, the varicella vaccine is currently available in all provinces and territories (except Yukon) through routine immunization programs. Children 12 months to 12 years of age currently require one dose in Canada, whereas children older than 12 years of age require two doses, separated by one month. In addition to dramatically reducing the morbidity and mortality of VZV infection in children, vaccination also reduces the risk of HZ compared with wildtype varicella infection (14 cases/100,000 person-years versus 68/100,000 person-years).

CLINICAL PEARLS

- Although uncommon, immunocompetent children can develop HZ with dissemination and central nervous system involvement.
- IV acyclovir treatment in healthy children with HZ should be carefully monitored to avoid acute renal failure.

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RECOMMENDED READING

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