

Unexplained deaths among injection drug users: a case of probable *Clostridium myonecrosis*

Nancy Williamson, Chris Archibald, Jon S. Van Vliet

A SERIES OF UNEXPLAINED DEATHS ASSOCIATED WITH soft-tissue inflammation and severe systemic sepsis was reported among injection drug users (IDUs) in the United Kingdom and the Republic of Ireland in 2000. Health Canada has identified one reported fatality in an IDU that matched the case definition. Although the cause of the epidemic in the UK and Ireland is not fully understood, contributing factors include injecting into muscle or beneath the skin, rather than directly into a vein, and the use of acid to dissolve the heroin. This single Canadian case is considered to be a sporadic event that occurs at a low background rate among IDUs. These cases serve to remind primary health care providers to be vigilant in cases of soft-tissue infection among IDUs and not to underestimate the potential severity of the situation.

In the spring of 2000, a series of unexplained deaths was first reported among injection drug users (IDUs) in the United Kingdom and the Republic of Ireland. Between Apr. 1 and June 12, 2000, there were about 62 unexplained cases of severe illness, and at least 30 deaths, reported among IDUs.¹ Cases were defined as IDUs who had been admitted to hospital or found dead since Apr. 1, 2000, with soft-tissue inflammation (abscess, cellulitis, fasciitis or myositis) at an injection site and either severe systemic toxicity (total peripheral leukocyte count $> 30 \times 10^9/L$ and sustained systolic blood pressure < 90 mm Hg despite fluid resuscitation) or evidence at autopsy of a diffuse toxic or infectious process, including pleural effusion and soft-tissue edema or necrosis at an injection site. The illness was associated with intramuscular or subcutaneous injection, but not with intravenous injection.² The isolation of *Clostridium novyi* from 2 cases was reported by a British group of researchers in mid-June of 2000,¹ with further *C. novyi* and *C. perfringens* isolations reported in August of that year.³ There was speculation that the unexplained illnesses and deaths were caused by bacterial contamination of heroin supplies.⁴ The most recent update on the epidemic in the UK and Ireland reported that there had been 104 cases, with 35 deaths, of severe systemic sepsis associated with soft-tissue inflammation between Apr. 1 and Aug. 1, 2000. Two *Clostridium* species (*C. novyi* and *C. perfringens*) had been isolated, either separately or together, from 8 cases.³ The outbreak was considered to be over at the end of August: the last case in Ireland was reported in June, that in England and Wales in July and that in Scotland on Aug. 6, 2000.⁵

On June 9, 2000, Health Canada's Bureau of HIV/AIDS, STD and TB sent out an information notice to all provincial and territorial ministries of health regarding these unexplained deaths and asked for reports of similar cases seen anywhere in Canada. During the monitoring period of June 9–Sept. 30, 2000, we received one report that matched the case definition developed from the cases seen in the UK and Ireland.

Case

A 50-year-old male IDU, with a recent history of intramuscular injections of heroin in the buttock, presented to the hospital emergency department in a small community in British Columbia on May 2, 2000, with cellulitis around the injection site. He was admitted to hospital for antibiotic therapy; surgical drainage of the site was attempted, but no pus was found. The area of cellulitis became greatly enlarged and extended down the right leg and into the hemiscrotum. By the morning of May 5, the central area had become purplish and necrotic in appearance. The patient was alert at that time and agreed to be transferred to a regional hospital

Review

Synthèse

At the time of writing, Ms. Williamson was Acting Head, Injecting Drug Use Unit, Division of HIV/AIDS Epidemiology and Surveillance, Bureau of HIV/AIDS, STD and TB, Centre for Infectious Disease Prevention and Control, Health Canada, Ottawa, Ont. Dr. Archibald is Chief, Division of HIV/AIDS Epidemiology and Surveillance, Bureau of HIV/AIDS, STD and TB, Centre for Infectious Disease Prevention and Control, Health Canada, Ottawa, Ont. Dr. Van Vliet is a family physician, Castlegar and District Hospital, Castlegar, BC.

This article has been peer reviewed.

CMAJ 2001;165(5):609-11

20 km away to establish central venous access. Upon arrival about one hour later, he was semiconscious, grey in colour and had a barely detectable blood pressure. His blood pressure improved with 2 L bolus intravenous fluids, and débridement of the necrotic area of his buttock was performed. A swab, taken intraoperatively from the muscle tissue, grew *Clostridium perfringens*, which was confirmed by the laboratory at the BC Centre for Disease Control, Vancouver. The patient required inotropic support during the operation. After the operation, he was sent to the intensive care unit in a critical condition, on a ventilator and on maximum doses of dopamine and epinephrine, with a blood pressure of 100/70 mm Hg. His leukocyte count was $100 \times 10^9/L$. He died of apparent sepsis 4 hours after being admitted to the regional hospital. He maintained a low-grade fever throughout his illness and was alert until a few hours before death. The postoperative diagnosis was probable *Clostridium* myonecrosis. No autopsy was performed.

Comments

This is the only case that we are aware of in Canada that matches the case definition developed in the UK and Ireland. There have been no published reports of similar cases from the United States and only one published report of a possible case from elsewhere in Europe (Norway).⁶

The cause of the epidemic in the UK and Ireland is not fully understood. Early speculation centred on the idea that the injected drugs (primarily heroin) were contaminated with bacteria. The subsequent isolation of *Clostridium* species from some cases suggested soil or fecal contamination of the injected drugs or of other material used in the injection process.^{2,4} Investigation continued to determine the cause of the infection, and *Clostridium* species have been isolated from some heroin samples. However, except for one case, the organisms found in the heroin could not be directly linked to these cases (Chris McGuigan, Scottish Centre for Infection and Environmental Health, Glasgow, Scotland: personal communication, 2001). It is believed that contributing risk factors to developing the syndrome include "skin popping" (i.e., injecting into muscle or underneath the skin rather than directly into a vein) and the use of acid to dissolve the heroin, which may contribute to initial skin or muscle damage, or both, and to ideal growing conditions for *Clostridium* and other bacteria.⁵ These cases serve to remind primary health care providers to be vigilant in cases of soft-tissue infection among IDUs and not to underestimate the potential severity of the situation. Prompt and aggressive treatment may be essential in order to prevent the rapid progression from presenting symptoms to severe illness and death. The patient in this case was alert and responsive until shortly before he died.

Whereas it is clear that some IDUs in Canada perform intramuscular or subcutaneous injections, either intentionally (as in the case reported here) or unintentionally,⁷ we have no evidence to indicate that this case is related to the outbreak in

the UK and Ireland. There has been no similar outbreak of unusual deaths among IDUs reported in Canada, and this single case is considered to represent a sporadic event that occurs at a low background rate among IDUs.

Although Canada may have avoided this particular health problem among IDUs, at least for now, it has not avoided the general problem of injection drug use and its significant negative impact on health. It is conservatively estimated that there are between 50 000 and 90 000 IDUs in Canada,⁸ and it is well known that the mortality rate among IDUs is substantially higher than in the general population. For example, a study among IDUs in Italy found that mortality rates ranged from 8 to 45 per thousand person-years,⁹ and this was 5–30 times higher than comparable age-adjusted rates for the general population (depending on sex and HIV status). In Canada, comparing even the crude rates that are available also reveals a stark difference: mortality rates among IDUs in Vancouver are approximately 13–51 per thousand person-years¹⁰ (depending on HIV status) compared with about 7 per thousand person-years in the general population of all ages.¹¹

Another serious health problem for IDUs is HIV infection. It is estimated that at the end of 1999, there were about 11 800 prevalent cases of HIV infection among IDUs in Canada; in addition, during 1999, an estimated 2260 new HIV infections occurred among IDUs in Canada.¹² Given the geographic mobility of IDUs and their social and sexual interaction with nonusers, the problem of injection drug use is one that ultimately affects all of Canadian society. It is hoped that the increased attention given to IDUs as a result of these unusual cases will serve to increase efforts to address this important health and social issue.

Competing interests: None declared.

Contributors: Ms. Williamson contacted provincial and international authorities, performed a literature review, and contributed to the writing and revising of the manuscript. Dr. Archibald initiated the Canadian investigation, contacted provincial and international authorities, and contributed to the writing and revising of the manuscript. Dr. Van Vliet provided clinical information and contributed to the revising of the manuscript.

References

- Greater Glasgow Board of Health, Scottish Centre for Infection and Environmental Health, Djuretic T. *Clostridium novyi* is likely cause of 'serious unexplained illness' as cases continue to be reported. *Eurosurveillance Wkly* 2000;4(24):000615. Available: www.eurosurv.org/update/ (on Web page, select Archives and then the appropriate issue) (accessed 2001 July 27).
- US Centers for Disease Control and Prevention. Unexplained illness and death among injecting-drug users — Glasgow, Scotland; Dublin, Ireland; and England, April–June 2000. *MMWR Morb Mortal Wkly Rep* 2000;49(22):489–92.
- Andraghetti R, Goldberg D, Smith A, O'Flanagan D, Liefucht A, Gill N. Severe systemic sepsis associated with soft tissue inflammation (previously reported as 'serious unexplained illness') in injecting drug users in Scotland, Ireland, England, and Wales. *Eurosurveillance Wkly* 2000;4(31):000803. Available: www.eurosurv.org/update/ (on Web page, select Archives and then the appropriate issue) (accessed 2001 July 27).
- US Centers for Disease Control and Prevention. Update: *Clostridium novyi* and unexplained illness among injecting-drug users — Scotland, Ireland, and England, April–June 2000. *MMWR Morb Mortal Wkly Rep* 2000;49(24):543–5.
- Glasgow Outbreak Control team. Scottish Centre for Infection and Environmental Health. Glasgow drug injector infection outbreak. Glasgow (Scotland): The Centre; last updated 2001 July 19. Available: www.iduoutbreak

- .abelgratis.com (accessed 2001 July 27).
6. Maagaard A, Hermansen N, Heger B, Bruheimand M, Meidell NK, Hoel T, et al. Serious systemic illness among injecting drug users in Europe: new case in Oslo. *Eurosurveillance Wkly* 2000;4(37):000914. Available: www.eurosurv.org/update/ (on Web page, select Archives and then the appropriate issue) (accessed 2001 July 27).
 7. Hankins C, Palmer D, Singh R. Unintended subcutaneous and intramuscular injection by drug users [letter]. *CMAJ* 2000;163(11):1425-6. Available: www.cma.ca/cmaj/vol-163/issue-11/1425a.htm
 8. Fischer B, Rehm J, Blitz-Miller T. Injection drug use and prevention measures: a comparison of Canadian and Western European jurisdictions over time. *CMAJ* 2000;162(12):1709-13. Available: www.cma.ca/cmaj/vol-162/issue-12/1709.htm
 9. Zaccarelli M, Gattari P, Rezza G, Conti S, Spizzichino L, Vlahov D, et al. Impact of HIV infection on non-AIDS mortality among Italian injecting drug users. *AIDS* 1994;8(3):345-50.
 10. Tyndall M, Currie S, Pitchford M, Craib KJP, Hogg RS, Patrick DM, et al. *Incidence rates of HIV-1 infection and mortality in the VIDUS Cohort: results at 30 months* [abstract C311]. Toronto (Ont): Canadian Association for HIV Research; 1999.
 11. *Deaths and death rate, Canada, the provinces and territories*. Ottawa: Statistics Canada; updated 2001 July 30. Available: www.statcan.ca/english/Pgdb/People/Population/demo07a.htm (accessed 2001 July 27).
 12. Geduld J, Archibald C. National trends of AIDS and HIV in Canada. *Can Commun Dis Rep* 2000;26(23):193-201.

Correspondence to: Dr. Chris Archibald, Bureau of HIV/AIDS, STD and TB, Health Canada, Rm. 0108B, Brooke Claxton Building, Tunney's Pasture, AL 0900B1, Ottawa ON K1A 0L2; fax 613 946-8695; chris_archibald@hc-sc.gc.ca

CMAJ

for the best of Canadian medicine

3000 volunteer reviewers from across North America are the foundation for CMAJ's thorough, criterion-based review process. The editorial staff includes scientific consultants with expertise in statistics, experimental design and epidemiology.

**CMA Member
Service Centre**
tel 888 855-2555 or
613 731-8610 x2307
fax 613 236-8864
cmamsc@cma.ca
www.cma.ca/cmaj

ASSOCIATION
MÉDICALE
CANADIENNE



CANADIAN
MEDICAL
ASSOCIATION