

CASE REPORT

An Autopsy Case of Infectious Endocarditis in a Methamphetamine Abuser Usefulness of Microbiological Examination

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Abstract

We present here a case of sepsis due to infectious endocarditis in a methamphetamine abuser. A 32 year-old male presented high fever and abdominal pain last two weeks. He was admitted to the hospital on the diagnosis of infectious endocarditis. In the evening on the day of admission, he suddenly collapsed. Despite of cardiopulmonary resuscitation, his death was confirmed. From the autopsy findings, toxicological analysis and results of the microbiological examination, we concluded that the cause of death was septic shock due to infectious endocarditis, presumably based on the methamphetamine abuse. The result obtained from microbiological examination gave us useful information. We shall have to be on the lookout, not only for acute poisoning, but also for cases of drug abuse related deaths.

Key words: drug abuse – infection endocarditis, methamphetamine – sepsis

Souhrn

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Prezentován případ sepse při infekční endokarditidě v souvislosti s abúzem methamphetaminu. 32letý muž měl po dobu dvou týdnů vysoké horečky a bolesti břicha, byl přijat do nemocnice s diagnózou infekční endokarditidy. Večer v den přijetí náhle zkolaboval. Přes kardiopulmonální resuscitaci u něho nastala smrt. Z pitevních nálezů, toxikologických analýz a výsledků mikrobiologického vyšetření bylo uzavřeno, že příčinou smrti byl septický šok při infekční endokarditidě, pravděpodobně v souvislosti z abúzem methamphetaminu.

Závěr byl stanoven na základě mikrobiologického vyšetření, které poskytlo užitečnou informaci. Při abúzu drogy je na místě usuzovat nejen na akutní otravu, ale také na případy citované smrti.

Klíčová slova: drogový abúzus – infekční endokarditida – methamphetamin – seps

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Introduction

Drug abuse is a one of the severe social problems in developed countries. It has been reported that methamphetamine abuse has a relatively high incidence in modern Japan (25). A

methamphetamine overdose can cause sudden death or abnormal symptoms such as hyperpyrexia, arrhythmia and metabolic acidosis (13, 23). It is also the cause of a lot of complications such as intracranial hemorrhage, infectious endocarditis, pulmonary embolism and sepsis after serial use (5, 6, 13, 16, 21). Here we

report an autopsy case of sepsis with myocarditis originating from infectious endocarditis, a fatal complication presumably arising from intravenous methamphetamine use.

Case report

1. Case history

A 32-year-old Japanese male was admitted to the hospital. His chief complaint was abdominal pain and a continuous high fever over the last two weeks. Intravenous antibiotic therapy was started, as an echocardiography showed vegetation in his mitral valve. In the evening on the day of admission, he suddenly collapsed. Despite cardiopulmonary resuscitation, his death was confirmed. An autopsy was performed about 18 hr after his death.

2. Autopsy Findings

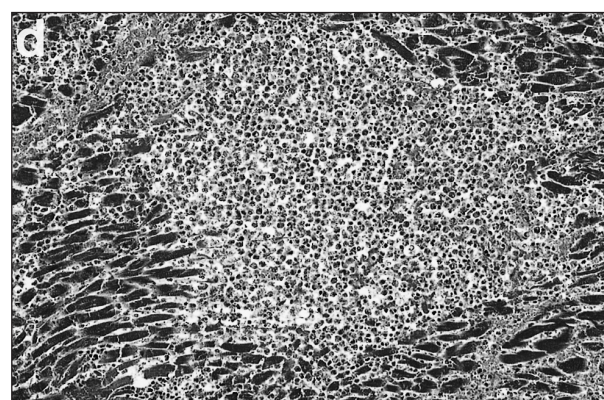
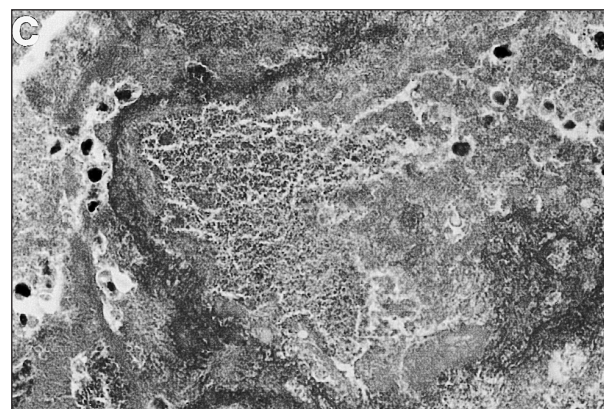
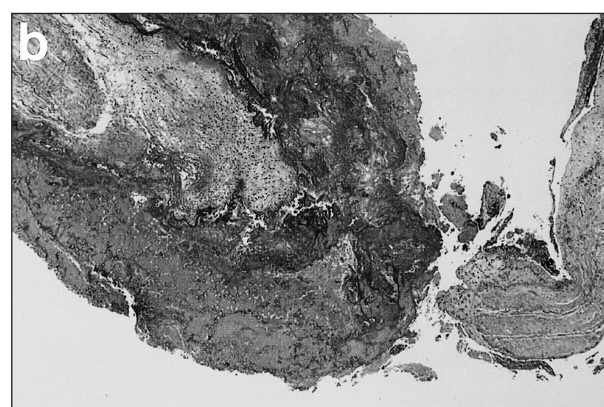
The deceased was a Japanese male, 170 cm in height and 71 kg in weight. There were some old and new track marks and scars on the bilateral antecubital fossa. No other external injury was found.

The internal examination revealed remarkable findings. The pericardial sac contained a small amount of a dark yellow colored liquid. The heart weighed 390g, and contained 200 ml of dark red blood with coagulum. There was hemorrhage on the surface of the anterior wall of the left ventricle. The posterior leaflet of the mitral valve showed a vegetation sized approximately 1.5cm x 1.5cm (Figure 1a). The other valves were intact.



Fig. 1. Gross appearance of a vegetation in the mitral valve (a). The vegetation shows polymorphonuclear neutrophil infiltration, coated with massive fibrin (b; HE staining, objective x2), and a bacterial colony (c; HE staining, objective x4) in the posterior leaflet of the mitral valve. Microscopic abscess in the myocardium (d; left ventricle, HE staining, objective x10

The left and right kidneys weighed 240 g and 235 g, respectively, and were slightly edematous. There was a yellowish-colored wedge appearance demarcated by a bleeding zone on its cut surface (Figure 2a, arrow). The left and right lungs weighed 475 g and 565 g, respectively, and were moderately congested. The spleen, which weighed 225 g, showed large infarcts. There was spotty bleeding on the serosal surface of the intestine and mesenterium. No macroscopic findings of fresh myocardial or cerebral infarction presumably due to the embolus originated from the vegetation. The femoral blood was collected for subsequent toxicological examination. The heart blood and swab of the spleen was collected for bacterial examination in a sterile manner.



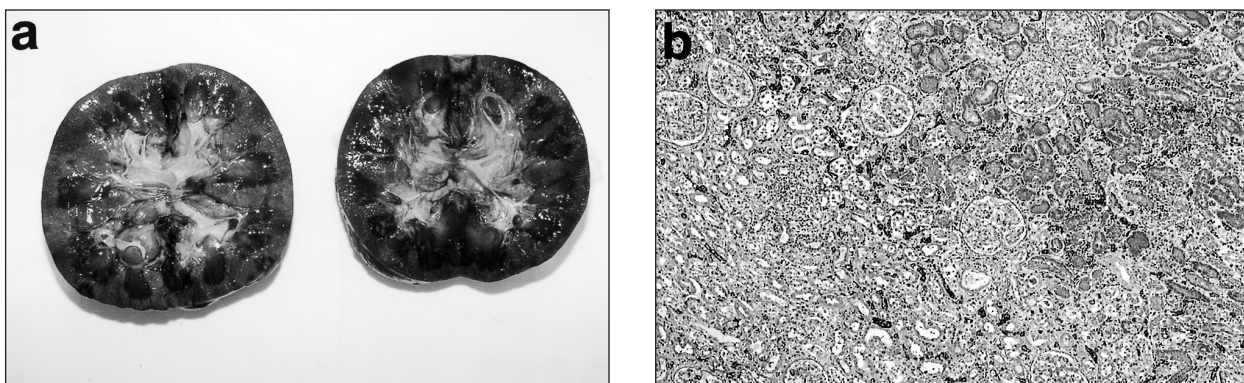


Fig. 2. Macroscopic findings of infarcts, presumably due to the septic emboli. The infarcts were clearly observed on the cut surface of the kidney (a; arrow). Coagulation necrosis demarcated by a hemorrhagic zone with a well-defined margin (b; HE staining, objective x4)

3. Histopathological Examination

The leaflet of the mitral valve was edematous and showed ulceration, polymorphonuclear neutrophil infiltration coated with massive fibrin (Figure 1b), and a bacterial colony (Figure 1c). There was a microscopic abscess in the myocardium of the anterior wall of the left ventricle (Figure 1d). Granulation tissue had also

formed. No findings suggest the acute myocardial infarction. In the kidney, there was a coagulation necrosis demarcated by a hemorrhagic zone with a well-defined margin (Figure 2b). The phagocytosis of erythrocytes was observed in the cervical lymph node (Figure 3). There were an abscess and infarction in the spleen. An abscess was formed in the subcutaneous tissue of the antecubital fossa (Figure 4).



Fig. 3. The phagocytosis of erythrocytes (cervical lymph node, HE staining, objective x20)

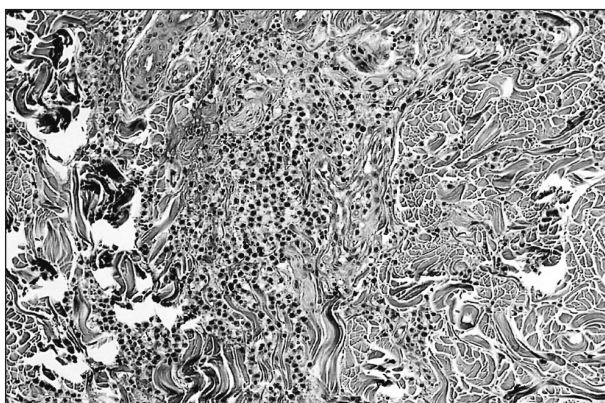


Fig. 4. Abscess in the subcutaneous tissue (left antecubital fossa, HE staining, objective x10)

4. Toxicological Analysis

Screening of the urine sample was performed using a Triage™ Drugs of Abuse panel plus Tricyclic Antidepressants (Biosite Diagnostic Inc., San Diego, USA). It was positive for amphetamines. The concentrations of methamphetamine in the femoral venous blood was 2.9 mmg/ml using GC/MS (26). No ethanol was detected in the blood or urine using head-space gas-chromatography.

5. Microbiological Examination

The bacterial culture of the heart blood was negative. The swab plunged into the cut surface of the spleen in a sterile manner was also cultured, and returned positive for group G streptococci and *Streptococcus mitis* (*S. mitis*). The bacterial culture of the vegetation was not performed.

Discussion

In this case, we observed vegetation in the mitral valve, and a lot of infarcts in the kidney and spleen. Severe lesions of myocarditis and hemophagocytic findings were also observed in the cervical lymph node. Further examination revealed that the smear of spleen culture grew group G streptococci and *S. mitis*, and methamphetamine was detected in his blood. The hemophagocytic finding is associated with active disseminated infections (19). This finding may

also indicate the victim was a severe septic condition. From these findings and the results of the following examination, we conclude that the cause of death was sepsis due to progression of the infectious endocarditis. Intravenous methamphetamine use may be involved in the infectious endocarditis.

It is well known that intravenous drug use is a major risk factor for infectious endocarditis, due to a repeated injections of non-sterile material (2). Intravenous drug users are 300 times more likely to die suddenly with infectious endocarditis than non- intravenous drug users (2). Infectious endocarditis is more likely to occur on the right side of the heart among intravenous drug users than among non-addicts (3, 12). The incidence of right-side infectious endocarditis in intravenous drug users ranges from 23 % to 76 %, as reported by various institutes (2–4, 9, 10, 15). The variance may depend on various factors such as selection bias, reporting bias, variations in diagnostic definitions or differences in sample size (15). However, the left-side valves are frequently affected in intravenous drug users (10, 15). Also left side endocarditis is usually accompanied by multi-organ infarcts (2). In the present case, the mitral valve was severely damaged, and we also observed a lot of infarcts in the kidney and spleen. Myocardial abscesses occur as a complication of either overwhelming sepsis or of infective endocarditis (14). The free wall myocardial abscess may result from septic coronary artery embolism (1).

The lethal level of methamphetamine in blood has been reported to be 3.0 $\mu\text{mol/dl}$ (4.48 $\mu\text{mg/ml}$) (17). In this case, the blood concentration of methamphetamine was less than the lethal level, but, nevertheless of a severe toxic concentration. However, no confusion or other psychiatric symptoms were reported before his death. From the macroscopic cutaneous finding and histological finding of the subcutaneous tissue of the antecubital fossa, we speculate that he had been a serial intravenous drug user for a relatively long time, and may have developed a tolerance.

The group G streptococci and *S. mitis* were detected from the spleen culture, but the blood culture was negative. This may be due to the administration of antibiotics that had been started. Prior administration of antibiotics reduces the incidence of positive blood cultures (22). The spleen culture is a reliable indicator of septicemia during life (11). Group G streptococci are part of the normal flora of the skin, pharynx, vagina and gastrointestinal tract (8, 24). They colonize the skin and it may be introduced by repeated injections, since most intravenous drug users do not cleanse their skin before injection (12). There are a few reports of bacteremia or in-

fectious endocarditis caused by group G streptococci in intravenous drug users (8, 20, 24). The immune system suppression may also have been a factor in the pathogenesis of bacteremia (8). He had no history of any of the causes of immunosuppression, such as alcoholism, diabetes mellitus or neoplasm. Drug abuser are a major risk group for the acquired human immunodeficiency virus (HIV) (18). However, the serological test for HIV infection was not performed in this case.

S. mitis is classified as a *Streptococcus viridans* group, which is the normal flora of the oral cavity (7). This is a common microorganism involved in infectious endocarditis, and it could cause infectious endocarditis without intravenous drug use. However, for the addicts, there is the theoretically heightened potential risk of infection when solutions such as tap water or saliva are used to clean equipment and dissolve agents (12). From these findings, we speculate that his death was strongly related to his intravenous methamphetamine abuse. In this current case, we employed microbiological examination of the specimens obtained at autopsy, which gave helpful information for the diagnosis of sepsis.

There have been a lot of reports concerning to infectious diseases in intravenous drug addicts in western countries (12). Medical complications related to drug abuse in the USA are increasing (12). In Japan, as the incidence of drug abuse is lower than that of western countries, we believe that resulting complications of intravenous drug use, such as infectious endocarditis, are rare. However, there is no detailed data about the incidence, because no national surveillance is conducted. Methamphetamine is the most commonly abused drug in Japan, and the number of arrests for illicit use of methamphetamine has been gradually increasing in recent few years (25). As amphetamines are most often injected by drug users (12), there is a potential risk of drug-related infection. Drug abuse related deaths may increase with the increase of drug abuse in Japan.

In conclusion, we have presented here a case of sepsis, presumably related to intravenous methamphetamine use. The result obtained from microbiological examination gave us useful information. In the future, we shall have to be on the lookout, not only for acute poisoning, but also for cases of drug abuse related deaths, such as the present case.

References

1. Anguera I, Quaglio G, Ferrer B, Nicolas JM, Pare C, Marco F, Miro JM. Sudden death in staphylococcus aureus-associated infective endocarditis due to perforation of a free-wall myocardial abscess. Scand J Infect Dis 2001;

33:622–625. – 2. **Burke AP, Kalra P, Li L, Smialek J, Virmani R.** Infectious endocarditis and sudden unexpected death: Incidence and morphology of lesions in intravenous addicts and non-drug abusers. *J Heart Valve Dis* 1997; 6:198–203. – 3. **Chambers HF, Korzeniowski OM, Sande MA** with the National Collaborative Endocarditis Study Group. *Staphylococcus aureus* endocarditis: Clinical manifestations in addicts and nonaddicts. *Medicine* 1982; 62:170–177. – 4. **Chambers HF, Morris DL, Tauber MG, Modin G.** Cocaine use and the risk for endocarditis in intravenous drug user. *Ann Intern Med* 1987; 106:833–836. – 5. **Chaudhuri C, Salahudeen AK.** Massive intracerebral hemorrhage in an amphetamine addict. *Am J Med Sci* 1999; 317:350–352. – 6. **Cherubin CE, Sapira JD.** The medical complications of drug addiction and the medical assessment of the intravenous drug user: 25 years later. *Ann Intern Med* 1993; 119:1017–1028. – 7. **Clancy CF.** *Streptococcus*. In: O'Leary WM editor. *Practical handbook of microbiology*. Boca Raton: CRC press, 1990, pp. 103–106. – 8. **Craven DE, Rixinger AI, Bisno AL, Goularte TA, McCabe WR.** Bacteremia caused by group G streptococci in parenteral drug abusers: Epidemiological and clinical aspects. *J Infect Dis* 1986; 153:988–992. – 9. **Dressler FA, Roberts WC.** Infective endocarditis in opiate addicts: analysis of 80 cases studied at necropsy. *Am J Cardiol* 1989; 63:1240–1257. – 10. **Faber M, Frimodt-Moller N, Espersen F, Skinhoj P, Rosdahl V.** *Staphylococcus aureus* endocarditis in Danish intravenous drug users: High proportion of left-sided endocarditis. *Scand J Infect Dis* 1995; 27:483–487. – 11. **Gresham GA, Turner AF.** *Post-mortem procedures*. London: Wolfe Medical Publications Ltd, 1979. pp. 121–130. – 12. **Haverkos HW, Lange WR.** Serious infections other than human immunodeficiency virus among intravenous drug abusers. *J Infect Dis* 1990; 161:894–902. – 13. **Karch SB.** *The Pathology of Drug Abuse*, 2nd ed. Boca Raton: CRC Press, 1996, pp. 199–230. – 14. **Kim H-S, Weilbaecher DG, Lie JT, Titus JL.** Myocardial abscesses. *Am J Clin Pathol* 1978; 70:18–23. – 15. **Mathew J, Addai T, Anand A, Morrobel A, Maheshwari P, Freels S.** Clinical features, site of involvement, bacteriologic findings, and outcome of infective

endocarditis in intravenous drug users. *Arch Intern Med* 1995; 155:1641–1648. – 16. **Moriya F, Hashimoto Y.** A case of fatal hemorrhage in the cerebral ventricles following intravenous use of methamphetamine. *For Sci Int* 2002; 129:104–109. – 17. **Nagata T.** Signification of methamphetamine concentration in body fluids and tissues. *Jpn J Legal Med* 1983; 37:513–518. – 18. **Nahass RG, Weinstein MP, Bartels J, Gocke DJ.** Infective endocarditis in intravenous drug users: a comparison of human immunodeficiency virus type 1-negative and positive patients. *J Infect Dis* 1990; 162:967–970. – 19. **Risdall RJ, Brunning RD, Hernandez JL, Gordon DH.** Bacteria-associated hemophagocytic syndrome. *Cancer* 1984; 54:2968–2972. – 20. **Smyth EG, Pallett AP, Davidson RN.** Group G streptococcal endocarditis: two case reports, a review of the literature and recommendations for treatment. *J Infect* 1988; 16:169–176. – 21. **Takasaki T, Nishida N, Esaki R, Ikeda N.** Unexpected death due to right-sided infective endocarditis in a methamphetamine abuser. *Legal Med* 2003; 5:65–68. – 22. **Tunkel AR, Kaye D.** Endocarditis with negative blood cultures. *New Engl J Med* 1992; 326:1215–1217. 23. **Uchima E.** Physiologic studies on acute methamphetamine poisoning. *Jpn J Legal Med* 1984; 38:814–826. – 24. **Vartian C, Lerner PI, Schlaes DM, Gopalakrishna KV.** Infections due to Lancefield group G streptococci. *Medicine* 1985; 64:75–88. – 25. **Wada K.** The current status of drug abuse and dependence in Japan. *Jpn J Alcohol & Drug Depend* 1998; 33:587–596. – 26. Working group for forensic toxicology of the Japanese society of Legal Medicine. *Manual for forensic toxicology analysis of the Japanese Society of Legal Medicine*, Tokyo: Japanese Society of Legal Medicine; 1999. p. 26–31.

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