Legal Medicine 17 (2015) 279–282

Contents lists available at ScienceDirect

Legal Medicine

journal homepage: www.elsevier.com/locate/legalmed

Case report

A case of sudden death after Japanese encephalitis vaccination

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ARTICLE INFO

Article history:
Received 17 September 2014
Received in revised form 4 March 2015
Accepted 7 March 2015
Available online 19 March 2015

Keywords:
Sudden death
Japanese encephalitis vaccine
Psychotropic drugs
Adverse effects
Vasovagal syncope
Fatal arrhythmia

ABSTRACT

Japanese encephalitis (JE) virus is estimated to result in 3500–50,000 clinical cases every year, with mortality rates of up to 20–50% and a high percentage of neurological sequelae in survivors. Vaccination is the single most important measure in preventing this disease. Inactivated Vero cell culture-derived JE vaccines have not been linked to any fatalities, and few serious adverse events after vaccination have been reported. Here, we report a case of sudden death in which a 10-year-old boy experienced cardiopulmonary arrest 5 min after receiving a Japanese encephalitis vaccination. He had been receiving psychotropic drugs for the treatment of pervasive developmental disorders. Postmortem examinations were nonspecific, and no signs of dermatologic or mucosal lesions or an elevation of the serum tryptase level, which are characteristic of anaphylaxis, were observed. A toxicological examination revealed that the blood concentrations of the orally administered psychotropic drugs were within the therapeutic ranges. The patient was considered to have died of an arrhythmia that was not directly associated with the vaccination.

1. Introduction

Japanese encephalitis (JE) virus is estimated to result in 3500–50,000 clinical cases every year, mostly in children younger than 10 years. JE occurs throughout most of Asia and the Western Pacific region and is characterized by the sudden onset of fever, chills, myalgia, and mental confusion, with mortality rates of up to 20–50% and a high percentage of neurological sequelae in survivors [1]. There is no specific antiviral therapy for JE, and vaccination remains the single most important measure in preventing this disease. Mouse-brain derived vaccines had been supplied for decades in Japan. However, the use of mouse-brain derived vaccines has decreased in a lot of countries, because of serious adverse effects, such as anaphylaxis and acute disseminated encephalomyelitis (ADEM), after vaccination in less than 1 per 100,000 people, although the exact cause of ADEM is unknown [2]. Inactivated Vero cell culture-derived JE vaccines have been in use in Japan since 2010, and no fatalities and few serious adverse events after vaccination have been reported to date [3–5]. In the present report, we describe a case of sudden death in which a 10-year-old boy experienced cardiopulmonary arrest 5 min after receiving a JE vaccination.

2. Case history

A mother and her 10-year-old son took her daughter to a pediatrician's office so that her daughter could receive her first injection of JE vaccine. After the daughter had received the vaccination, the mother asked the pediatrician some questions about the JE vaccine and then decided that her son should also receive his first JE vaccination. However, when the son saw the syringe, he began to run back and forth for approximately 5 min. Finally, he was caught on a sofa in the waiting room and the vaccination was administered. After the injection of the vaccine, he was left alone to lie on the sofa. Approximately 5 min later, he was found on the sofa in cardiorespiratory arrest. He immediately received cardiopulmonary resuscitation from the pediatrician and was transferred to an emergency hospital. However, his heart remained still without spontaneous movement and he was pronounced dead 2 h and 30 min after the vaccination. During the resuscitation, he received cardiac massage and artificial respiratory support. He was also administrated adrenaline of 0.6 mg 24 times every 3 min in the emergency hospital but did not receive counter shock.

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http://dx.doi.org/10.1016/j.legalmed.2015.03.003
1344-6223/

The deceased had suffered from pervasive developmental disorders and had received drug therapy for 4 months prior to his death. During the first 3 months of the drug therapy, 3 mg of pimozide and 3 mg of aripiprazole were administered after dinner; 25 mg of sertraline had been added for the last 1 month of therapy prior to the patient's death. He had taken his medications after dinner on the day before his death.

He had received a brief electrocardiogram during a health examination performed approximately 16 months before his death, but no abnormalities were noted.

His sister, who was vaccinated at the same time as the patient, did not experience any adverse events.

In the present case, genetic analysis on the diseases causing fatal arrhythmia was not carried out, because no sudden deaths had occurred among his relatives.

3. Autopsy findings

The deceased was 148.75 cm tall and weighed 73.1 kg. His left upper arm showed a fresh injection mark without erythema and old lineal abrasions, probably caused by scratching. His liver weighed 2270 g and was yellowish. The left and right lungs weighed 440 and 550 g, respectively. Both lungs showed evidence of congestion and edema. The brain was swollen and congestive, weighing 1450 g. However, brain herniation was not observed. The heart weighed 245 g and showed no signs of abnormality, including the coronary artery. The other organs showed no abnormalities, except for congestion and edema.

Microscopically, no evidence of an inflammatory reaction was observed in the subcutaneous tissue around the injection mark in the left upper arm. The epiglottis showed signs of edema and the slight infiltration of lymphocytes and plasma cells. However, mast cells were not observed. The lungs showed signs of congestion and edema, but no inflammatory reactions were observed around the bronchioles. The brain exhibited edema and a loss of granular cells in the cerebellar cortex, probably caused by hypoxemia during resuscitation. The liver showed signs of severe fatty degeneration of the hepatocytes with large fat droplets and periportal fibrosis with an active moderate inflammatory reaction comprising a mixed population including neutrophils, lymphocytes and macrophage (Fig. 1). The diagnosis was non-alcoholic steatohepatitis. The heart exhibited high frequencies of contraction band necrosis and 23 foci/100 mm^2 of myofibril break-up of the cardiac myocytes throughout the left ventricular myocardium (Fig. 2). The atrioventricular node artery of the right coronary artery showed signs of intimal fibrosis (Fig. 3), and the narrowing of the lumen was less than 50%. However, the other areas of the coronary artery showed no signs of abnormality.

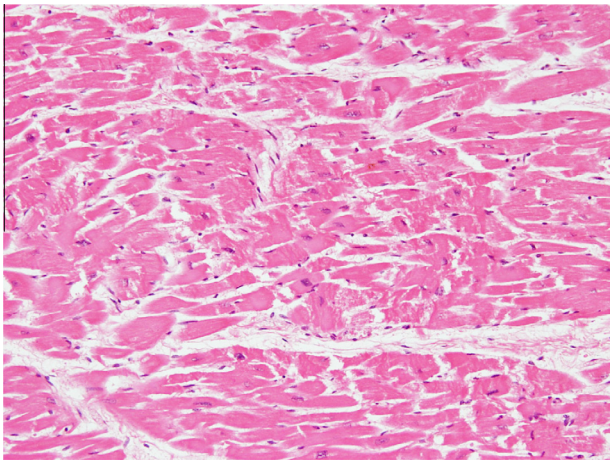

Fig. 2. The photograph showed myofibril break-up of the cardiac myocytes in the left ventricular myocardium. In the lesions, the cardiac myocytes fell into contraction band necrosis (hematoxylin–eosin, 110×).

4. Postmortem laboratory findings

The serum sample was prepared from blood obtained from the right atrium. The concentrations of tryptase, C-reactive protein, and nonspecific IgE were 8.1 μg/mL, 0.13 mg/mL (cut-off value, <0.30 mg/mL), and 440 IU/mL (cut-off value, <173 IU/mL). Acylcarnitine analysis by tandem mass spectrometry of serum metabolites revealed no special abnormalities.

5. Toxicological findings

A Triage® kit (Biosite Inc., San Diego, CA, USA) was used for the screening of drugs, and the results were negative.

For the detection of psychopharmaceuticals, a liquid chromatography–tandem mass spectrometry (LC–MS/MS) was applied. Briefly, the procedure is shown as follows. Plasma samples were purified using liquid–liquid extraction with acetonitrile/ethylacetate (4:1); the purified residues were reconstituted with 100 μL

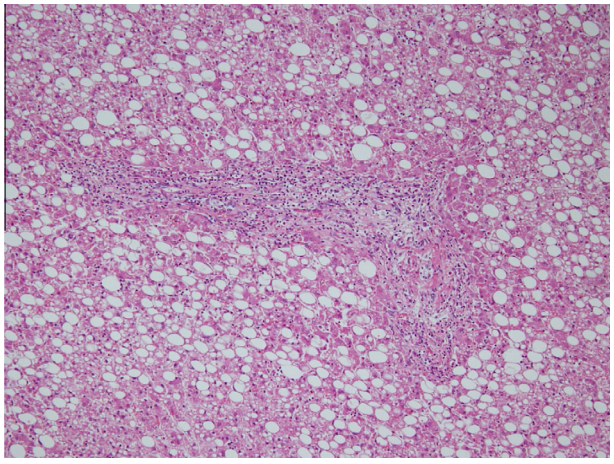

Fig. 1. The photograph showed severe fatty degeneration of the hepatocytes with large fat droplets and periportal fibrosis with an active moderate inflammatory reaction (hematoxylin–eosin, 60×).

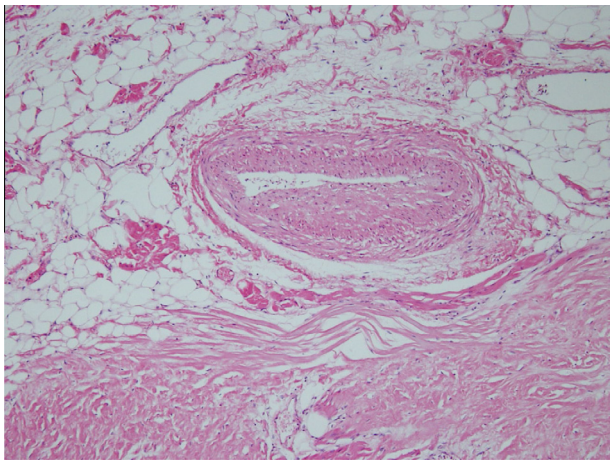

Fig. 3. The photograph showed intimal fibrosis of the atrioventricular node artery (hematoxylin–eosin, 60×).