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# Fatal Mumps Myocarditis Associated with Left Ventricular Non-Compaction

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Statistical Analysis C  
Data Interpretation D  
Manuscript Preparation E  
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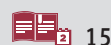
**Patient:** Female, 21-month-old  
**Final Diagnosis:** Mumps myocarditis  
**Symptoms:** Fever • left ear pain  
**Medication:** —  
**Clinical Procedure:** Not applicable  
**Specialty:** Pediatrics and Neonatology

**Objective:** Rare co-existence of disease or pathology

**Background:** Myocarditis is a rare but potentially fatal complication of mumps virus infection. Left ventricular non-compaction (LVNC) is a rare congenital abnormality that can lead to development of low cardiac output, cardiac dysfunction, arrhythmias, or sudden cardiac death. To the best of our knowledge, no autopsy cases of mumps myocarditis with LVNC have been reported in the literature. Here, we report an autopsy case of a 21-month-old girl who died due to mumps myocarditis associated with an undiagnosed LVNC.

**Case Report:** Postmortem computed tomography demonstrated bilaterally enlarged parotid glands. Serum analysis of anti-mumps IgM titer was positive. Macroscopic and histological examinations revealed glandular destruction with massive inflammatory cell infiltration of the enlarged parotid glands and mild inflammatory cell infiltration of the heart, which showed prominent trabeculations and deep intra-trabecular recesses, indicating LVNC. Immunohistochemical analyses showed positive immunostainings for mumps in the cardiac and salivary gland tissues.

**Conclusions:** These findings suggest that mumps myocarditis associated with LVNC contributed to this patient's death. Myocarditis patients with other comorbidities, including LVNC, may be at higher risk of sudden death. Further reports of mumps myocarditis and LVNC are needed to better understand the mechanisms of sudden unexpected deaths in children.

**MeSH Keywords:** Autopsy • Comorbidity • Death, Sudden • Heart Defects, Congenital • Pediatrics • VaccinationFull-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/921177>

## Background

Mumps, an acute viral infection that mainly occurs in the salivary glands, rarely causes death, but it can lead to several severe complications, including orchitis, pancreatitis, meningoencephalitis, and myocarditis. Since myocarditis is a rare complication, which may explain the scarcity of reported cases of fatal mumps myocarditis in the literature [1]. Nonetheless, it is estimated that transient electrocardiographic changes are common in patients infected with the mumps virus [2]. It has been suggested that “subclinical mumps myocarditis” can remain unrecognized, leading to cardiac damage and subsequent fatal outcomes [3]. However, the underlying mechanism of death in mumps myocarditis remains elusive.

Left ventricular non-compaction (LVNC) is a rare congenital abnormality in the structure of the ventricular myocardium, characterized by prominent trabeculae and intra-trabecular recesses [4]. Clinical manifestations of LVNC vary from no symptoms to heart failure, arrhythmias, embolism, and sudden death [5]; however, the etiology of LVNC remains still largely unclear, mainly due to the poor genotype-phenotype association and the poor understanding of ventricular myocardial development [6]. To the best of our knowledge, no cases of fatal mumps associated with LVNC have been reported in the literature.

## Case Report

A 21-month-old Japanese girl was found by her father prone in bed, unresponsive, and not breathing. She was brought to the Emergency Department, where she was declared dead following several attempts at resuscitation.

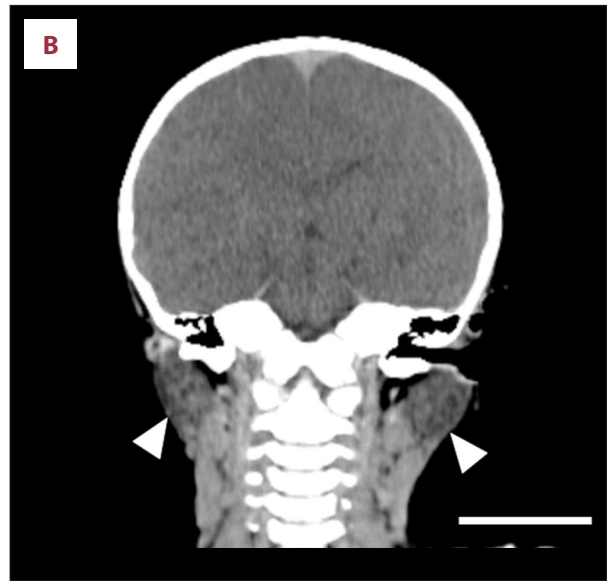
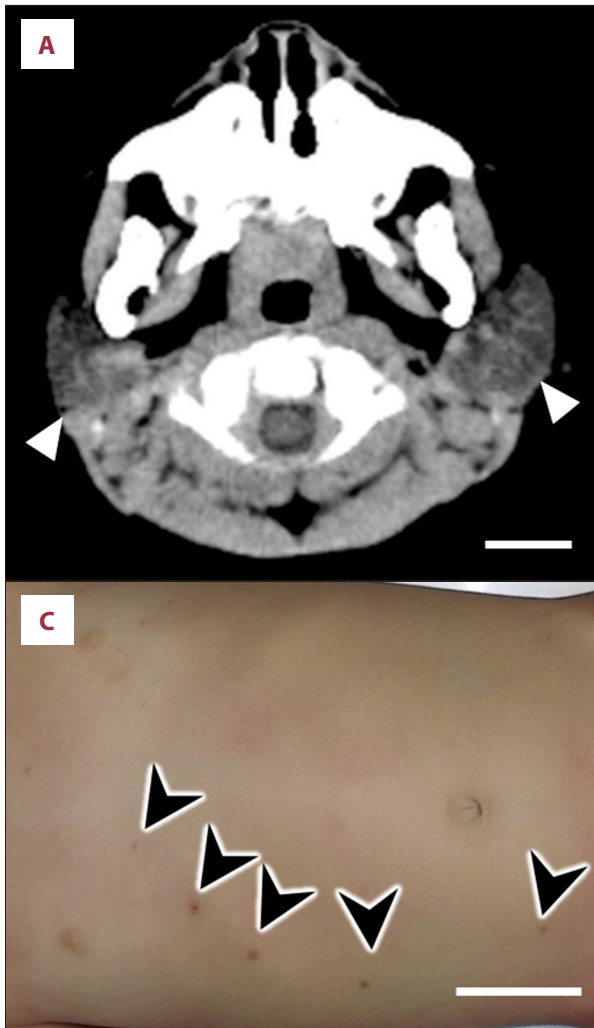
Nine days prior to her death, she had fever and her mother brought her to the primary care physician. Because she had red blisters on her trunk (a typical presentation of chicken pox) and her temperature was 37.8°C, she was diagnosed with varicella and treated with valacyclovir, which is an antiviral agent for varicella. Three days later, the physician told her mother that the virus infection was almost cured because her temperature had decreased to 36.9°C, and almost all the blisters had turned into scars. Subsequently, she resumed going to the children's nursery. On the morning of her death, she had a fever of 37.6°C; however, her skin was normal color and the all blisters on her trunk had turned into scars. She was active and ate breakfast by herself at the time. After arriving at the nursery, she had mild fatigue but she ate lunch. Two hours after lunch, she complained of pain in her left ear and her temperature was reported to be 39.6°C. Her mother picked her up and brought her to the primary care physician, who examined her and found that swelling of the cheeks under the ears,

pharyngitis, and a nasal discharge. However, her skin color was normal, all blisters turned had into scars, and no signs of dehydration were identified. The physician diagnosed her with mumps following these findings and based on her brother's mumps infection, and prescribed a nonsteroidal anti-inflammatory drug (acetaminophen) and gastrointestinal medication (Bifidobacterium). Subsequently, the child was returned home. After coming back home from the hospital, her mother gave her food but the child did not eat. Since she had severe fatigue and loss of appetite, her mother asked her to rest. Upon her father's return from work and on checking on her 1 hour later, she was found lying in bed not breathing and was subsequently brought to the hospital in an ambulance. However, she could not be revived and was declared dead after 1 hour of attempted resuscitation.

She had been born at 37 weeks of gestation without any complications. She had no noticeable antecedents and there was no history of sudden death in the family. No abnormal electrocardiographic changes, including signs of long QT syndrome, were recorded in her medical records or baby health checkup. At 4 days after her birth, she underwent metabolic disease screening tests, including phenylketonuria, homocystinuria, maple syrup urine disease, galactosemia, congenital hypothyroidism, congenital adrenal hyperplasia, and other metabolic diseases such as fatty-acid metabolism disorder (a total of 20 diseases), and the all screening tests were negative. No abnormal findings were detected at 1-week, 1-month, and 6-month health checkup screenings. She had never had any signs of arrhythmias, including dizziness, breathlessness, and palpitations. Her parents were non-smokers. She was vaccinated according to the routine Japanese vaccination schedule, but she did not receive mumps vaccination, which it is voluntary in Japan.

To determine the cause of death, postmortem computed tomography (CT) and an autopsy were performed 37 hours following her death. A postmortem CT scan revealed a bilateral swelling of the parotid glands (Figure 1A, 1B). No definitive trauma such as bone fractures or hematoma were identified on the body. A complete postmortem examination was carried out following the interpretation of the CT findings. Her body weight was 11.7 kg and her height was 84.0 cm, which are within the normal range for her age [7]. External examination revealed no serious body injuries (e.g., abrasions or bruising) except for the presence of scabs on the abdomen (Figure 1C) and scalp, which were believed to be scars due to varicella infection (chickenpox). Consistent with the CT findings, a bilateral swelling was found under the ears.

Internal examination of the body revealed enlarged parotid and mandibular glands (Figure 2A, 2B). The heart weight (68.0 g) was normal for her age. The horizontal section of the heart showed prominent trabeculations (data not



**Figure 1.** Postmortem computed tomography images. (A) A coronal section of the cervical region showing the bilateral swelling of the parotid glands (indicated by the white arrowheads). Bar=2.0 cm. (B) An axial section of the cervical region. Bar=5.0 cm. (C) The skin of the abdomen showing multiple small scars (highlighted by the black arrowheads), indicating typical chicken pox scars. Bar=10.0 cm.

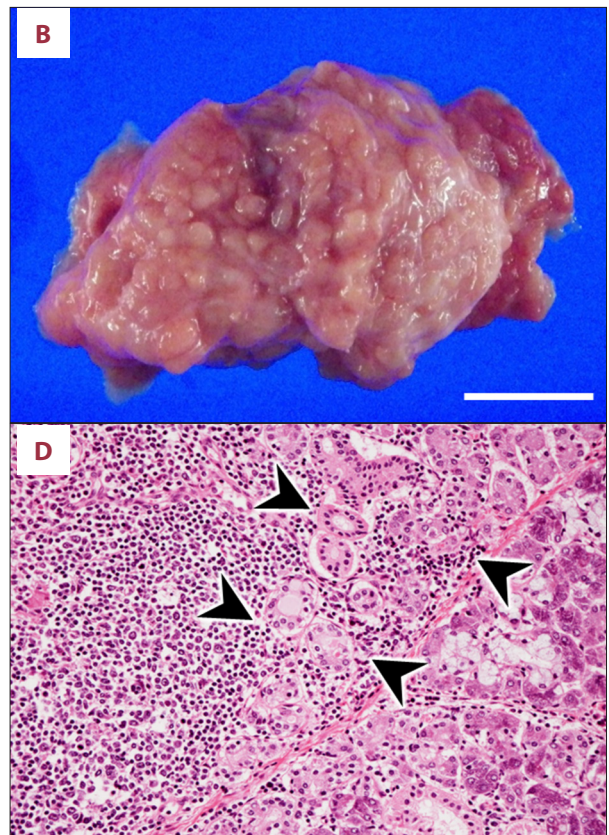
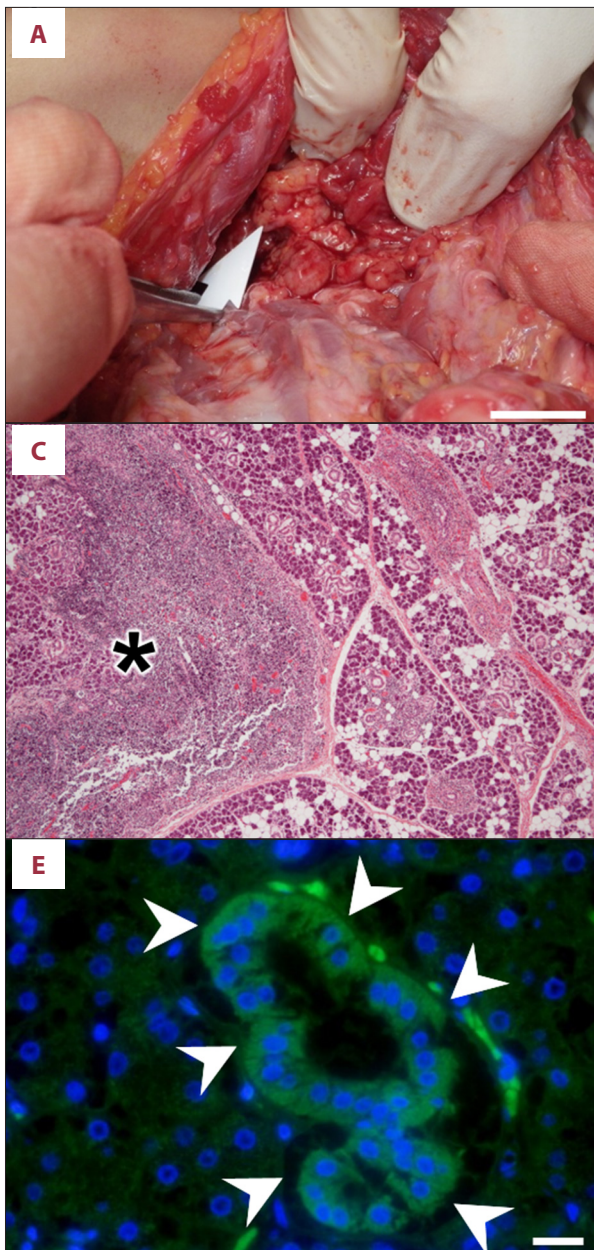
shown). No abnormal findings were detected in the brain with regard to weight (1124 g), signs of hemorrhages, and cerebrospinal fluid. No pathological lesions were detected in other organs, including the lungs, pancreas, liver, kidneys, spleen, and uterus. No drugs, toxins, or alcohol were detected in serum and urine samples using high-performance liquid chromatography. Screening tests were negative for hepatitis B and C, respiratory syncytial-, influenza-, adeno-, rota-, and noroviruses in addition to *Streptococcus pneumoniae* and *Haemophilus influenzae* type B. The anti-mumps IgM titer in the serum sample from the Emergency Department was positive. To confirm the presence of mumps virus infection, genetic tests were performed using buccal swabs and cerebrospinal fluid samples from autopsy, by inducing the samples to MDCK, FL, RD-18S, Vero cells, and neonatal ddY mice; however, the virus genome could not be detected by these tests, probably due to the degradation of the genome resulting from the long postmortem time. No external injuries indicating child abuse were identified.

Histological examinations of the parotid and the submandibular glands revealed glandular destruction with massive inflammatory cell infiltration, which were mainly lymphocytes (Figure 2C, 2D). Immunohistochemical analyses using anti-mumps antibody (Chemicon, MAB84, 1: 1000) showed positive immunostainings in the salivary gland tissue (Figure 2E). The heart showed inflammatory cell infiltration in the interstitial space, consisting of lymphocytes and neutrophils (Figure 3A). Positive immunostaining for mumps was also detected in the heart (Figure 3B).

In line with the macroscopic examination, histological examination of the heart showed prominent trabeculations and deep intra-trabecular recesses and a pathological non-compacted-to-compacted ratio  $>2$ , which is an indicator of LVNC (the ratio=2.3), and it also revealed mild endocardial fibrotic changes, a typical histological finding of LVNC (Figure 4A, 4B). No pathologies were detected in the brain and meninges, including meningitis, and no pathological lesions were detected in other organs.

## Discussion

In the present case, based on autopsy findings, we believe the direct cause of death was mumps-induced myocarditis,

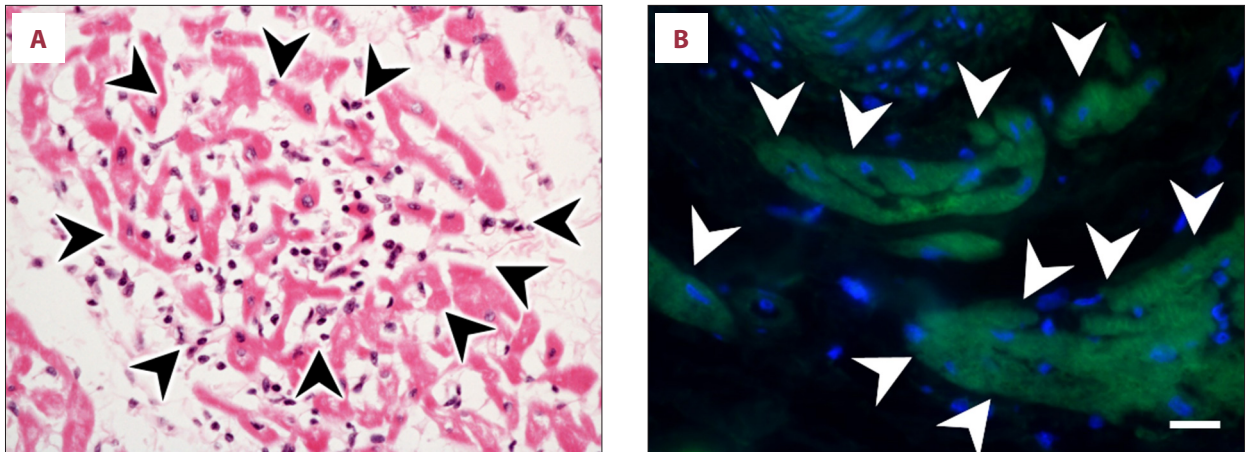


**Figure 2.** Macroscopic and histological findings of the parotid and mandibular gland. (A) The parotid gland is indicated by white arrow. Bar=1.0 cm. (B) The excised specimen showing the enlarged submandibular gland. Bar=1.0 cm. (C) Histological findings of the parotid gland showing lymphocytic infiltration (indicated by an asterisk). Original magnification  $\times 200$ . (D) Histological finding of the mandibular gland showing glandular destruction with lymphocytic infiltration (indicated by arrowheads). Original magnification  $\times 400$ . (E) Immunohistochemical analysis for mumps in the parotid gland. White arrows highlight positive-staining cells in parotid duct (green). Nuclei were stained with 4',6-diamidino-2-phenylindole (DAPI; blue). Bar=20  $\mu\text{m}$ .

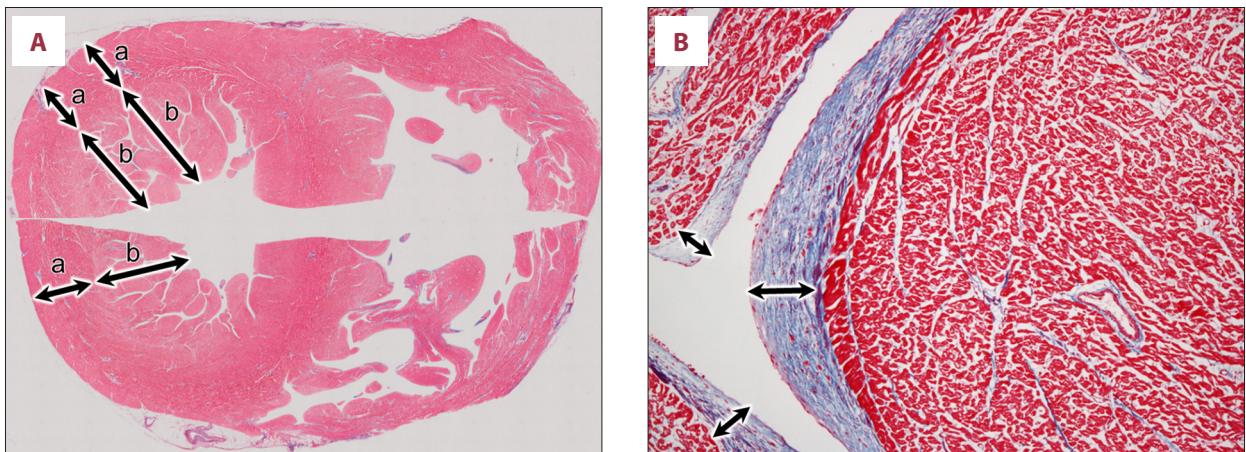
including swelling and inflammation of the salivary glands, positive IgM titer for mumps virus, positive immunostainings for mumps in the cardiac and the salivary gland tissues, and the sibling's history of mumps infection before the death of the patient. Furthermore, we believe that LVNC contributed to her death. Considering that the patient's condition had been relatively stable until immediately before hospital admission, the cause of death may have been fatal arrhythmias caused by mumps-induced myocarditis in the background of LVNC.

Myocarditis is defined as an inflammation of the myocardium, which is often triggered by viral pathogens such as coxsackieviruses and adenoviruses [8]. The Dallas criteria for the diagnosis

of myocarditis based on endomyocardial biopsies was applied as a histological diagnostic reference [9]. It differentiates between active myocarditis, which is defined as an inflammatory infiltrate of the myocardium with myocyte necrosis, and borderline myocarditis, which is defined as an inflammatory infiltrate of the myocardium without myocyte necrosis. In the present case, although no apparent myocyte necrosis was observed, the histology of the heart showed a mild but compelling inflammatory cell infiltration in the interstitial space (Figure 3A) [10]. Moreover, consistent with her clinical history, postmortem CT, macroscopic, and histological examinations revealed bilateral swelling of the parotid and mandibular glands with glandular destruction and inflammatory cell



**Figure 3.** Histological findings of the heart. (A) An inflammatory focus (indicated by black arrowheads) composed of lymphocytes and neutrophils in the heart. Original magnification  $\times 400$ . (B) Immunohistochemical analysis for mumps in the left ventricle. White arrows highlight positive-staining cells in cardiomyocytes (green). Nuclei were stained with 4',6-diamidino-2-phenylindole (DAPI; blue). Bar=20  $\mu\text{m}$ .



**Figure 4.** Histological finding of the heart wall. (A) The prominence of the non-compacted area (indicated by arrow b) and a thin compacted area are shown (indicated by arrow a) in the left ventricle. The ratio of non-compacted to compacted myocardium is 2.3 ( $>2$  indicates left ventricular non-compaction). (B) Azan staining of the left ventricle showing endocardial fibroelastosis (indicated by arrows).

infiltrations (Figure 2A–2D), the positive IgM titer for mumps virus, and the positive immunostainings for mumps in the cardiac and the salivary gland tissues (Figures 2E, 3B). Taking all these findings into consideration, we determined the cause of death to be mumps-induced myocarditis.

Mumps myocarditis was first reported by Pujol et al. in 1918 [11]. Its incidence reached 15% in the mid-1950s, but after the mumps vaccine became available, it dramatically declined to 4% [3]. Most cases of mumps myocarditis show a sub-clinical course in patients, but there are a few reports of fatal cases, including those in patients who were not neonates. The mechanism of death in mumps myocarditis is believed to be related to arrhythmias and cardiac dysfunction [2].

We also believe that the present case had a pre-existing undiagnosed LVNC that may have caused a vulnerability to arrhythmia, further leading to the lethal arrhythmia induced by acute mumps myocarditis [12,13]. Mortality rates of patients with LVNC range from 5% to 47% [14]; the wide range may be explained by lack of awareness of LVNC, variable disease severity, and confounding effects of comorbidities [15]. With regard to the mechanisms of LVNC-related death, Muraoka et al. reported that myocardial dysfunction and comorbidities such as congenital heart disease can contribute to life-threatening events, including arrhythmia [5]. We considered that the cause of death may be fatal arrhythmias caused by myocarditis in the background of LVNC rather than congestive heart failure, because the patient's condition had been relatively stable until immediately prior to hospital admission.

## Conclusions

Myocarditis is a rare complication of mumps. Myocarditis patients with other comorbidities, including LVNC, may be at higher risk of sudden death. Further reports of mumps myocarditis and LVNC are needed to understand the mechanisms of these sudden unexpected deaths in children.

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## Conflict of interests

None.