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CASE REPORT

Suspected Adverse Event Following Immunization with Multisystem Inflammatory Response in an Infant: A Case Report

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ABSTRACT

Vaccination is a cornerstone of preventive medicine and has significantly reduced childhood morbidity and mortality. Nevertheless, rare but serious adverse events following immunization (AEFI) may occur and require meticulous evaluation. Within hours of receiving a routine vaccination, an 11-month-old male infant experienced acute gastrointestinal distress, seizures, and cardiovascular collapse. We report a suspected serious AEFI. To determine the cause of death, a comprehensive medico-legal autopsy was performed, assisted by histopathology, cytopathology, post-mortem computed tomography (PMCT), and forensic laboratory investigations. The findings of the autopsy showed multisystem involvement, including widespread lymphocytic infiltration throughout several organs, pulmonary edema, and serous effusions. PMCT results, which showed characteristics suggestive of acute respiratory distress syndrome with pleural and pericardial effusions, supported the autopsy. The death was reported as a suspected serious AEFI requiring causality assessment by the AEFI surveillance committee in compliance with World Health Organization guidelines due to the close temporal association with vaccination, the exclusion of other causes of death, and the presence of pathological features suggestive of a multisystem inflammatory

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syndrome driven by immune dysregulation. The importance of forensic autopsy in determining systemic inflammatory reactions in unexplained post-vaccination deaths is highlighted by this case.

KEYWORDS

• Adverse Event Following Immunization • AEFI • Multisystem Inflammatory Syndrome • Forensic Autopsy • Infant Death • Vaccine Safety

INTRODUCTION

Vaccination is one of the most successful public health initiatives as millions of deaths are avoided each year worldwide. Like any of the medical interventions, vaccines may also infrequently be temporally associated with adverse events following immunization (AEFI) despite their established safety profile.[1] World Health Organization (WHO) defined AEFI as any adverse medical event that occurs after vaccination and is not necessarily related to the use of the vaccine.[2] As Serious AEFIs might lead to hospitalization or death, thorough investigation is needed to ensure accurate classification, reinforce surveillance systems, and preserve public trust in immunization programs.[2,3]

Autopsy plays an important role while investigating sudden unexpected and unexplained deaths following vaccination, particularly in infants with minimal clinical histories. Gross postmortem findings, histopathology examination, radiological imaging, and laboratory investigations must be integrated, to differentiate coincidental events from immune-mediated or other pathological processes. This case report discusses a suspected serious AEFI that was investigated by a thorough postmortem medico-legal investigation.

Case History:

A 11-month-old male infant was taken to the primary health center for routine vaccination. At the time of vaccination, the child was in good health. The child was developing normally for his age. He received the booster doses of inactivated poliovirus vaccine (IPV) and pneumococcal vaccine along with first dose of measles-rubella (MR) vaccine, in accordance with the national immunization schedule.

Within a few hours following vaccination, the child developed distress characterized by vomiting, followed by seizures and rapid cardiovascular collapse. Despite medical intervention, the child was declared dead at Government Medical College Hospital, The Nilgiris. Owing to the sudden unexplained death with a close temporal association to immunization, a medico-legal autopsy was ordered. Vaccine vials were seized by the district enquiry officer and forwarded to the Central Drug Testing Laboratory, Chennai, for further analysis as part of the AEFI investigation protocol.

External Examination:

The infant's body (figure 1) weighed 6.1 kg, measured 68 cm in length, and had a body mass index of 15.13 kg/m². According to growth charts from the Indian Academy of Pediatrics, anthropometric measurements were age appropriate. The circumference of the head was 43 cm, chest circumference was 42 cm with a barrel-shaped chest, abdominal circumference was 42 cm with mild umbilical eversion and full flanks. No signs of protein-energy malnutrition evident, and the right thigh circumference was 24 cm.

Figure 1: Body of the deceased infant

A punctured wound suggestive of injection mark with mild swelling was present over the upper one-third of the right thigh. No injection marks, edema, or swelling noted over either upper limb. Bluish discoloration of nail beds was evident suggestive of peripheral cyanosis. No other significant ante-mortem external injuries were noted.

Internal Examination:

Cranial Cavity:

The posterior fontanelle was fused and the anterior fontanelle was membranous, unfused, and mildly depressed. The brain appeared mildly edematous with narrowing of the lateral ventricles. The cerebellum and spinal cord were intact and congested.

Thoracic Cavity:

The thymus was pale and showed petechial hemorrhages at places. The heart was structurally intact and congested. Both lungs were edematous and congested, with petechial hemorrhages over the anterior and posterior surfaces. The pleural cavities contained clear yellow fluid, approximately 25 ml on the right side and 15 ml on the left side.

Abdominal Cavity:

The peritoneal cavity contained approximately 100 ml of dark yellow clear fluid without any peculiar odor. The bowel showed no evidence of intussusception. The liver, spleen, and kidneys were intact and pale. The stomach contained a small quantity of greenish mucoid secretion without peculiar odor, and the gastric mucosa appeared pale.

Ancillary Investigations:

Blood and viscera were preserved and sent for chemical analysis to the Regional Forensic Science Laboratory. For histopathological analysis, tissue samples were kept from the heart, lungs, liver, spleen, kidneys, adrenal glands, mesenteric lymph nodes, brain, spinal cord, thymus, muscle and skin from the injection site, small intestine, and epiglottis. Cytological analysis was performed on bodily fluids, such as pleural fluid, peritoneal fluid, cerebrospinal fluid, and pericardial fluid.

Cytopathology: Pleural, peritoneal (figure 2), and cerebrospinal fluid (figure 3) samples showed a predominance of lymphocytes without eosinophils or cancerous cells.

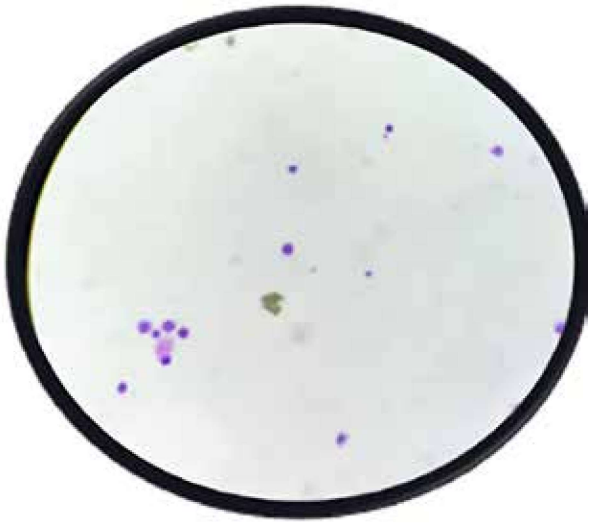

Figure 2: cell cyto-pathology of peritoneal fluid samples shows lymphocyte predominance with no malignant / eosinophilic cells detected

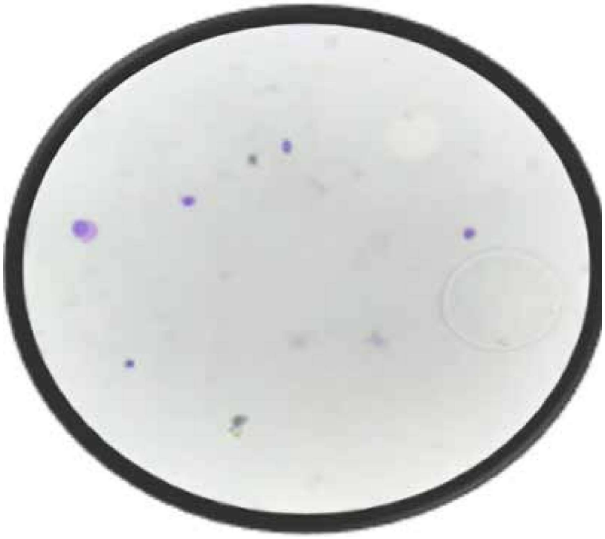

Figure 3: Cell cyto-pathology of Cerebro Spinal Fluid samples shows lymphocyte predominance with no malignant / eosinophilic cells detected

Histopathology: Multiple organs, including the heart (figure 4), lungs (figure 5), brain (figure 6), liver, spleen, kidneys, thymus, adrenal glands, and muscles, were found to have diffuse lymphocytic infiltration. Rather than localized organ-specific pathology, these results were consistent with a systemic inflammatory immune response.

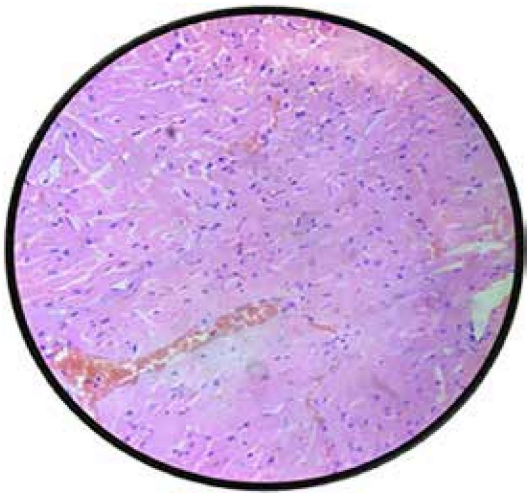

Figure 4: Section of heart shows diffuse lymphocytic infiltration

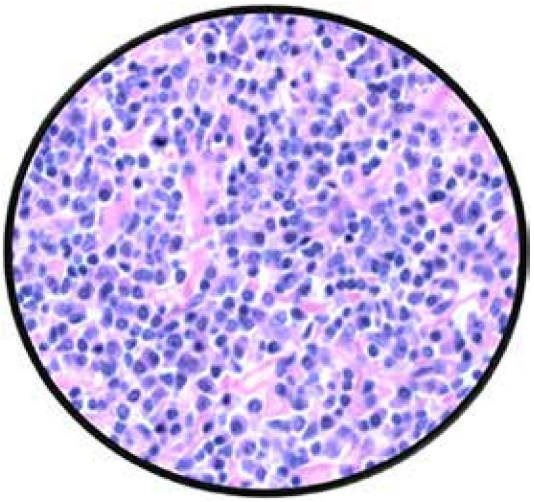

Figure 5: Section of lungs shows diffuse lymphocytic infiltration

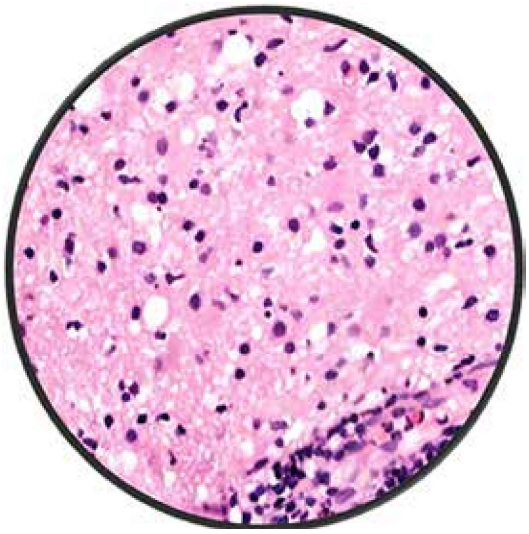

Figure 6: Section of brain shows diffuse lymphocytic infiltration

Post-Mortem Computed Tomography:

PMCT performed prior to autopsy demonstrated diffuse ground-glass opacities in both lung fields, suggestive of acute respiratory distress syndrome-like changes (figure 7). Bilateral pleural effusions and pericardial effusions (figure 8) were noted, with greater effusion on the left side. Moderate free fluid was present in the abdomen and pelvis. Minimal subcutaneous fat stranding with small air pockets was noted over the upper and lateral aspect of the right thigh, corresponding to the injection site.

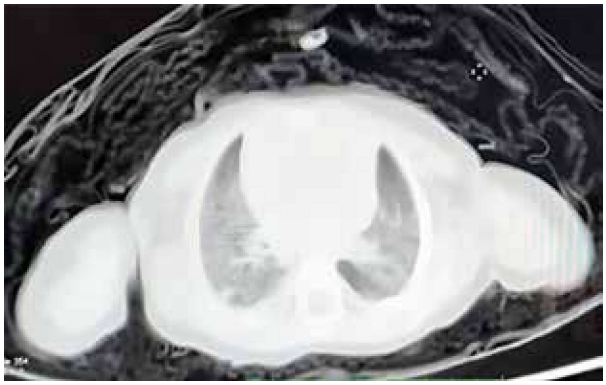

Figure 7: Diffuse ground glass opacities noted in bilateral lung fields and features suggestive of ARDS changes

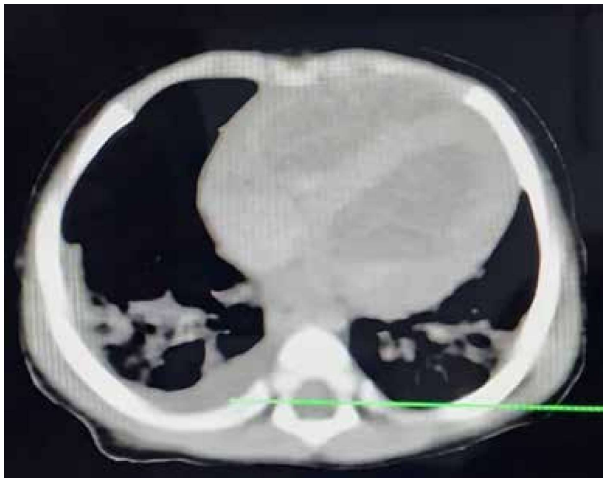

Figure 8: Bilateral pleural effusion noted with pericardial effusion. (Left side have more effusion than right side)

DISCUSSION

The clinical course and pathological findings in this case are suggestive of a multisystem inflammatory syndrome (MSIS) temporally associated with immunization. Multiple organ systems may be affected by systemic

immune activation in such hyperinflammatory states, which are characterized by elevated inflammatory markers, organ dysfunction, and dysregulated immune responses.[4] While these syndromes are most commonly described following infectious triggers, similar immune-mediated inflammatory responses have been hypothesized in temporal association with immunization, although a causal relationship cannot be assumed solely based on temporal proximity.[3,5]

In the present case, diffuse lymphocytic infiltration was observed across multiple vital organs, including the heart, lungs, brain, liver, kidneys, thymus, spleen, adrenal glands, and skeletal muscle, suggesting systemic immune activation rather than localized pathology. A cytokine-mediated inflammatory cascade with increased vascular permeability and capillary leak is supported by the presence of serous effusions within the pleural, pericardial, and peritoneal cavities as well as pulmonary edema and ARDS-like changes on post-mortem imaging. Such widespread inflammatory involvement is consistent with multisystem immune dysregulation described in hyperinflammatory syndromes.[4]

Several immunopathological mechanisms have been proposed to explain the development of systemic inflammatory syndromes in susceptible individuals. Host factors, including underlying immune regulatory variability, may influence the intensity of immune responses following antigenic exposure.[5] Additionally, immune activation following exposure to vaccine components or adjuvants has been hypothesized in rare instances to trigger autoimmune or inflammatory phenomena in predisposed individuals.[6]

Hypersensitivity-type immune responses and excessive activation of innate and adaptive immune pathways represent additional proposed mechanisms. Adjuvants are designed to enhance immunogenicity; however, they may rarely be associated with exaggerated immune activation and systemic inflammatory manifestations.[6] Molecular mimicry has also been suggested as a theoretical mechanism, whereby immune responses generated against antigenic components may cross-react with host tissues.[6]

T-cell dysregulation and cytokine-driven inflammation are key features of multisystem inflammatory syndromes, contributing to endothelial injury, increased vascular permeability, and multi-organ dysfunction.[4] In this case, the lymphocyte predominance in body fluids which was observed in cytological examination supports a cell-mediated immune response rather than an eosinophilic or IgE-mediated hypersensitivity reaction.

Importantly, there was no evidence of infection, sepsis, trauma, poisoning, or congenital anomaly which is sufficient to explain death was noted during the postmortem examination. The temporal association with immunization and by excluding all other differential causes and supportive pathological findings, makes the event to be considered within the spectrum of a suspected serious adverse event following immunization (AEFI). However, further thorough systematic evaluation is required as temporal association alone is insufficient to establish the causation.[2,3,7]

Public Health and Legal Implications:

To strengthen vaccine safety surveillance and maintain public trust, transparent reporting and thorough systematic investigation of serious AEFIs are important. While highlighting that rare adverse outcomes are appropriately contextualized without undermining the overwhelming benefits of vaccination, postmortem examination provides objective, unbiased evidence essential for public health decision-making, legal scrutiny, and policy formulation.

CONCLUSION

The importance of comprehensive postmortem evaluation in unexplained infant deaths occurring after immunization is discussed in detail in this case report. Integration of gross autopsy findings, histopathology, cytology, and PMCT supported classification of the death as a suspected serious AEFI with multisystem inflammatory response. Identifying MSIS as a potential immunopathological mechanism underscores the cruicial role of forensic medicine in vaccine safety monitoring and public health.

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