## G105 Vaccine Death: A Rare Case of Anaphylactic Shock After Hexavalent Immunization

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After attending this presentation, attendees will learn of a rare case of fatal anaphylactic shock after hexavalent (against diphtheria, tetanus, pertussis, poliomyelitis, Haemofilus influenzae type B and hepatitis B) immunization in a three month-old female white infant is presented. The aim of the paper is to alert scientific community on reactogenicity of recent hexavalent formulation of vaccine.

This presentation will impact the forensic community and/or humanity by demonstrating that any death that occurs within a few days of vaccination to be autopsied using immunohistochemical stainings, toxicological analysis on urine and blood specimens and detection of femoral blood concentration of mast-cell Beta-tryptase to rule out anaphylactic shock.

This case presentation concerns a first-born child, delivered at the 41st week of gestation by caesarean delivery, with a birth weight of 3.400 g and Apgar scores of 9-10. The mother related no significant family history, an unremarkable pregnancy and good heath of the baby, who was bottle-fed. At three months of age the female infant received a hexavalent immunization during a morning clinic visit. The mother stated that a few hours after the immunization the baby had difficulty feeding. Early in the afternoon the clinical condition of the baby got worse with the onset of severe dyspnea, so she was immediately taken to the emergency department of the local hospital. A state of shock with critical acute respiratory failure was diagnosed. The baby appeared pale and unresponsive. The baby was hypotensive (systolic pressure 50 mmHg) and tachycardic (180 bpm) with an undetectable diastolic pressure. Laryngoscopy was unremarkable. Laboratory tests revealed the presence of hyper-eosinophylia and metabolic acidosis (pH 7.154) with blood desaturation (pO2 75.9 mmHg) and compensatory hypocapnia. Repeated administrations of adrenaline by aerosol were given along with intramuscular corticosteroids. Despite the aggressive intervention the infant died two hours after arriving at the hospital.

A complete postmortem examination was performed two days after the death. External examination was unremarkable, except for the immunization puncture site on the left thigh. The body was of a three month old, well-developed and well-nourished, white infant with a body weight of 4930 gr and body length of 55 cm. Internal examination was unremarkable except for lungs presenting white foam in the main bronchi. Histological examination revealed mild cerebral oedema, and a shock histomorphology of the main organs (lungs, liver and kidneys). Immunohistochemical analysis revealed the presence of numerous degranulating mast-cells in the pulmonary parenchyma. Toxicological analysis of blood and urine specimens for therapeutic and non-therapeutic drugs were unremarkable. Postmortem measurement of mast cell b- tryptase in femoral blood was determined using the AA5 antibody ELISA; high concentrations, more than 10 ug/l were recorded (11.3 ug/l).

Adverse events following immunization are defined as medical incidents that take place after an immunization. Serious adverse events after vaccination have generally been defined as those adverse events that result in permanent disability, hospitalization or prolongation of hospitalization, life threatening illness, congenital anomaly or death. They are generally associated with the inherent properties of the vaccine (vaccine reaction) or some error in the immunization process (program error). The event could also be totally unrelated but only temporally related to immunization (coincidental event). The use of combination vaccines is an ideal way to simplify the simultaneous administration of multiple vaccines, reducing the number of injections, and may also be the most effective way of ensuring high compliance rates to complex immunization schedules. Recently, parental concern about polivalent vaccines has become increasingly prevalent. Hexavalent vaccine has been developed for primary booster vaccination of infants against diphtheria, pertussis, tetanus, poliomyelitis, Haemophilus influenzae type B and hepatitis B. Post marketing study confirmed the safety and immunogenicity of hexavalent vaccine as an alternative to other licensed vaccines. Members of the European Agency for the Evaluation of Medical Products in 2003 investigated whether there might be a link between hexavalent vaccines and some cases of sudden infant deaths occurred after immunization. It was concluded that there was no significant benefit/risk profile of these products, and, therefore, no changes in the present conditions of use were recommended. SIDS, viral infection, metabolic disorders, allergic reactions or airway obstruction were plausible but were not definitely proven to have been the cause of death. Vaccine associated anaphylaxis is a rare occurrence with only few cases reported despite the million of doses administered, giving a relative risk of 0.65 cases per million doses. It is not always clear which component of vaccine is involved in the

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anaphylactic reaction (antigens, preservatives, adjuvants, manufacturing residuals). Postmortem measurement of mast cell β-tryptase in serum is the only possible means of diagnosing or confirming death due to anaphylactic shock because autopsy findings after acute anaphylactic death are generally non-specific; a cutoff value of 10 ug/l has been established to be optimal, with a sensitivity of 86% and specificity of 88%.

**Hexavalent Vaccination, Mast-Cell Beta Tryptase, Anaphylaxis**

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