Sudden death of a male child with varicella after anti-MMR vaccination

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Abstract: Varicella is a common and extremely contagious disease of childhood. It has usually no major complications and healing is complete. Severe infections may be observed on immuno-compromised patients and in adults. Bacterial infections, pneumonia, myocarditis or brain damage are among potentially fatal complications. We report a special case with multiple and rare complications of varicella in a previous healthy 13 months boy, soon after vaccination against MMR and with abrupt evolution to death.

Key Words: varicella, myocarditis, interstitial pneumonitis, encephalitis.

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Varicella is a common and extremely contagious disease of childhood. The etiologic agent is varicella-zoster virus (VZV) which is also responsible for shingles (Herpes zoster). Usually, it has no major complications and healing is complete, but infection of an immunocompromised host may be associated with a high degree of morbidity and mortality. Bacterial infections, pneumonia, myocarditis or brain damage are among potentially fatal complications.

Case report

A thirteen month male child presents an unequivocal rush eruption consistent with varicella diagnosis one day after vaccination against measles, mumps and rubella (MMR). His previous medical history included a hospital infection with Klebsiella pneumonia at birth, healed after 9 months. Twelfth days later after the generalized eruption of varicella, he suddenly presented vomiting and hypertonia of the left upper limb followed by cardio-respiratory arrest due to ventricular fibrillation.

After resuscitation the child was hospitalized in the Intensive Care Unit of Emergency County Hospital Constanta. Despite of intense care and specific treatment, he had succumbed five hours later. Post-mortem examination revealed an exanthema over the face, trunk and limbs represented by typically skin lesions of late stage of varicella (Figure 1).

Also, macroscopic examination revealed pleural effusion (250ml of serous liquid) and areas of congestion and edema of both lungs (Figure 2).

Histopathological aspect consisted with diagnosis of severe interstitial pneumonitis characterized by a serous exudate and dust-cells in the alveoli associated with thick alveolar walls secondary to hyperemia, areas of hemorrhage and chronic inflammatory infiltrate (lymphocytes and plasma cells) (Figure 3).

Examination of the heart showed dilated cardiomyopathy (7/5/3cm) with non hypertrophied and slightly mottled myocardium (Figure 4).

It was observed interstitial edema, hyperemia and moderate polymorphous inflammatory infiltrate (lymphocytes, monocytes and rare neutrophils.) on
Figure 1. Typically skin lesions for varicella (late stage).

Figure 2. Postmortem examination of lungs – areas of necrosis and hemorrhage.

Figure 3. Interstitial pneumonitis-microscopic aspect: thick interalveolar septae due to a moderate lympho-plasmocytes infiltrate, hiperemia and interstitial hemorrhage(col HE 40x).

Figure 4. Sub-acute viral myocarditis – macroscopic aspect: the heart is dilated (inset), but not hypertrophied and presents a slightly mottled myocardium.

Figure 5. Sub-acute viral myocarditis – microscopic aspect: the ventricular myocardium presents a moderate and diffuse polymorphous inflammatory infiltrate and interstitial edema (col HE 40x).

Figure 6. Subacute encephalitis – histopatologic aspect: fibrillar gliosis and abundant limfo-plasmocytes infiltrate (Col HE 40x).
microscopic examination with final diagnosis of subacute interstitial myocarditis diagnosis (Figure 5). Macroscopic examination of brain revealed massive congestion and histopathological analysis established sub-acute encephalitis diagnosis with abundant, diffuse lymphocytes and monocytes infiltration associated with fibrillar gliosis (Figure 6). Other macroscopic findings were: ascites (300ml serous liquid), hypertrophy of the tymus and acute hemorrhagic gastritis.

Serologic testing for antibody (immunoglobulin -Ig) against MMR and VZV were negative both for IgG or IgM. Postmortem samples of blood and cerebrospinal fluid (CSF) were analyzed by enzyme-linked immunosorbent assays (ELISA), a highly sensitive and specific method. Determination of VZV-DNA by polymerase chain reaction (PCR) was also negative.

Discussion
Varicella is a common disease of childhood like MMR, with an average incubation period of 15 days and usually characterized by a self-limiting evolution. Incidence of varicella decrease from 237.5 cases per 100 000 in 2005 [1] to 169 cases per 100 000 in 2010 in Romania [2], mostly due to monovalent or combined vaccine availability. Rarely, severe complications can appear and may lead to death, especially at immunosuppressed patients or in adults.

However, cases have been reported with fatal potential in previous healthy persons without a clear explanation for this severe evolution [3]. Pneumonia, myocarditis, neurological manifestations (encephalitis, cerebellitis, Reye’s syndrome) or secondary bacterial infection are seldom complications of varicella with life threatening potential [4-7].

The most frequent complication of varicella regarding central nervous system is cerebellar damage, encephalitis being rare. Encephalitis was recorded with an incidence of 1/33000 cases [8] and a mortality rate of 5-10% [9]. The symptoms may include hypertonia or hypotonia, ataxia, hemiparesis and even seizures or coma [10]. Pneumonia is another frequent complication of chickenpox. It can affect both immunocompetent and immunosuppressed patients but the most severe evolution with respiratory failure was observed in neonates and adults [11].

The rate of mortality is between 10-30% but is higher in adults reaching up to 50%, as has been reported by some studies [12,13]. Lung damage usually occurs in the first days (1-6) after skin eruption. Histologically interstitial pneumonia is frequently observed, characterized by diffuse alveolar damage [14]. Myocarditis is an unusual complication of varicella but long known, with a greater preponderance in young adults. The condition is severe, causing arrhythmias and progression to dilated cardiomyopathy and is associated with a high morbidity and mortality [15]. Therefore, each child with chickenpox and acute cardiac decompensation should be suspected of myocarditis and treatment should be promptly established.

In summary, our report brings attention to a special case with multiple and rare complications of varicella in a previous healthy 13 months boy, soon after vaccination against MMR and with abrupt evolution to death. The child vaccination against MMR during the incubation period of VZV weakened immune system and this could explain the severe evolution of the disease and the absence of both antibody against MMR or VZV. From this case we can conclude with recommendation that each vaccine should be done not only after a careful clinical and physical evaluation but also after a thoroughly epidemiological investigation.

References
