Measles inclusion-body pneumonia: case report of an 18 months old girl autopsy

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Abstract: Objective. The aim of this article is to highlight the main pathological characteristics observed in rare measles virus related deaths, that one may find during autopsy. The diagnosis is usually sustained due to presence of Warthin-Finkeldey giant syncytial cells in lungs and mucosa linings, while external examination characteristics, like Koplik spots, may not be observable.

Case report. We present the case of an 18 months old girl, admitted to the emergency care unit of our hospital with severe respiratory insufficiency, offering no other diagnostic clues for measles virus infection. The rapidity of evolution for this case resulted in, immediate, in-hospital death with no further possibility of revival. The autopsy revealed the presence of Warthin-Finkeldey cells inside the lungs together with liver congestion and cardiac failure.

Conclusion. Although, almost eradicated, measles continues to pose serious problems to medical doctors in both poor and civilized countries, because the disease evolves mutely, eventually, with serious life threatening complications in some patients.

Key Words: measles virus, pneumonia, autopsy, children.

INTRODUCTION

Before the vaccine discovery in 1963, measles virus (MV) infection was a common childhood disease that caused an estimated 135 million cases of MV and more than 6 million MV related deaths, worldwide, annually. Although MV has been eliminated in well developed countries, the rubella virus continues to infect nonimmunized patients that travel abroad of these countries [1]. Measles, an acute infection that is caused by the rubella virus, part of the Morbillivirus genus, in the family of Paramyxoviridae, is highly contagious and usually seen in children. Mainly, the illness is characterized by conjunctivitis, cough, coryza, fever and a macropapular rash that initiates several days after the symptoms appearance. Recovery is the rule, but aggravated complications may occur. In the last years, reports of this disease have increased, as noticed in Spain, Italy, France, i.e. countries with prior good MV control, reporting today infection to older children and adults. In some cases, MV caused severe respiratory distress, even in adult patients, with more than 35 years of age [2]. In some studies, the most afflicted organs are (a) lungs, diagnosed as an interstitial pneumonia due to the presence of lobar alveolar infiltrates or exudates on radiographic examination and (b) the brain, as an encephalitis with a decreased level of consciousness or incidental seizures, sometimes, as far as focal neurological signs. These are associated with elevated serum transaminases, at least twice the normal values, serum creatinine above 1.5 mg/dl, elevated serum lipase and amylase, more than 160-190 U/L. In multiple organ involvement, temperature should rise above 38°C in order to suspect meningeal or brain inflammation, together with cerebrospinal cytologic abnormalities like white blood cell count over 4/mm3 and protein level over 40 mg/dL [3].
CASE REPORT

An 18 months old girl, brought by ambulance, presented to the emergency care unit with dyspnea, aggravated respiratory wheezing, confusion and anxiety. The child’s mother stated that the patient became ill two days before arriving at hospital, having a high vesper fever (40.3°C), with a symptomatic, empirical, treatment with amoxicillin-clavulanic acid and ibuprofen, prescribed by her general practitioner doctor, for no more than 5 day duration. The clinical examination revealed bilateral palpebral edema and secretions containing blood, eliminated through the buccal cavity; with bitten tongue margins. During examination, four minutes after emergency room admission was made, the child status complicated with cardiac arrest, loss of consciousness, with spontaneous elimination of urine and feces. The resuscitation lasted for more than one hour (i.e., 86 minutes), with no reappearance of any life signs. The child was pronounced dead and the body was transferred to the morgue at our pathology department. Serologic and blood tests could not be sampled as death succeeded in a rapid sequence, with no possibility for this manoeuvre to be performed.

At the medical examination, we observed the presence of vulvar region and upper third of the right thigh hyperpigmentation, perioral cyanosis. The brain examination showed no focal lesions, excepting edema and congested meningeal vasculature (Fig. 1a). At internal examination, although the lungs were anatomically normal, during sectional proceedings a significant quantity of blood poured out of the basal lobes (Fig. 1b). Hearth examination proves the presence of enlarged left ventricular and atrial muscular wall, with a higher than normal friability. Inside the peritoneal cavity, a high opalescent liquid quantity was identified (approx. 300 mL). The stomach lining had disseminated hemorrhagic spots, with the pancreas more friable due to increased

Figure 1. Anatomical and histological aspects of diagnostic tissues found during autopsy of a 18 months old female: (a) Brain – observable meningeal vessels congestion; (b) Lung right hilum - in situ sectional aspect revealing tan to white visible flocculent bronchocentric spots accompanied by conspicuous congestion; (c) Kidneys – cortico-medullar junction effacement with disseminated hemorrhagic spots; (d) Lungs - distended capillaries due to congestion with lymphoplasmocytic infiltrates, alveolar space narrowing and the presence of giant-cells (10x10, H&E); (e) Liver - prominent vacuolar dystrophy, lymphocytes, distended capillaries and pericentrilobular atrophy (10x10, H&E); (f) Kidney - wrinkled glomeruli with narrowing Bowmann capsule, discrete chronic inflammatory infiltrate; necrotic epithelium of proximal contort tubuli (10x40, H&E).
edema. Liver was distended, with a pale appearance on macroscopic sectioning, and fatty trans lucid liquid exteriorized. Spleen, with an average anatomical aspect, has largest dimensions within 8 x 4 x 4 cm. The kidneys have higher dimensions bilaterally (i.e., Right: 8/4/3 cm; Left: 9/5/4 cm), hemorrhagic disseminated spots with facile capsule removal and effaced a cortico-medullar junction (Fig. 1c). Adrenals had normal dimensions and weight. The remaining organs were normal with no obvious diagnostic modifications.

Microscopic examination showed the presence of Warthin-Finkeldey cells inside the lungs, within an lymphoplasmocytic sepal infiltrate, capillary hyperemia and flattened peripheral alveolar spaces (Fig. 1d). Liver sections showed disseminated lymphocytes, mainly around portal spaces, significant vacuolar dystrophy, similar to a high degree steatosis, around centrilobular veins space. Discrete periportal fibrosis is notable (Fig. 1e) with marked capillaries hyperemia. Spleen shows marked hyperemia with depletion of immunologic population of white pulps, penicillar arterial wall thickening and microscopic capsular disruptions. The timus was normally located with average aspect, corresponding to the age of the child. Kidney sections proved enlarged, wrinkled glomeruli, Bowmann space narrowing; enlarged vas recta were visible, more prominent near the cortico-medullar junction. The proximal contort tubules have epithelial coagulative necrosis, with cariorrhesis phenomenon. Furthermore, inside the tubuli lumina, one may observe the presence of a basophilic amorphous substance, consistent with some degree of proteinuria (Fig. 1f). The pancreas showed scant chronic diffuse inflammatory infiltrate, and interstitial edema with focal exocrine epithelial necrosis inside the acini. The tongue biopsies from the traumatized margins mentioned earlier shows marked vacuolar dystrophy inside the intermediate strata of the epithelium, together with marked stromal lymphocytic infiltrate (Fig. 2). The myocardium was normal with slight edema and cariorrhesis, having no features of acute, localized, ischemia.

The final death diagnostic sequence was hemorrhagic pneumonia with hypoxia, subsequent cardiac arrest, acute anuria and congested liver.

**DISCUSSIONS**

On electron microscopy, MV virions are pleomorphic spheres that have dimensions between 100 to 250 nm. They have a inner nucleocapsid that is a coiled helix of protein and RNA, within an envelope that has two types of surface projections. These projections include the hemagglutinin (H) and fusion (F) proteins. Unlike many other known viruses, the expression of neuraminidase (N) is not encountered in MV. The molecular weight of the single-stranded RNA that encodes the proteins of the virus is 4.5 kDa. The major receptor for MV virus is the signaling lymphocyte activation molecule (SLAM, CDw150), usually attachable to the wild type. The SLAM protein complex is frequently expressed on T and B lymphocytes and antigen-presenting cells, which accounts for the wild type virus on lymphotropic and immunosuppressive effects. The vaccine type virus uses CD46 as a receptor, known as the complement regulatory protein. Epithelial cells that expresses extracellular metalloproteinase inducer – i.e., CD147 – facilitates aerosol transmission of the virus [4]. The role of histopathology in MV related pneumonia is achieved in autopsy resulted specimens, initially in unclear cases. Therefore, thickened alveolar sepa with multinuclear, syncytial giant cells with both intracytoplasmic and intranuclear eosinophilic inclusions, known as Warthin-Finkeldey cells, that are characteristic for MV infection are found on tissue sections sampled from an autopsy [5]. These syncytial structures are formed as a result of a SLAM independent mechanism, as some studies may suggest [6]. Nevertheless, epithelial cells of the upper respiratory tract are swollen with areas of metaplasia, perivascular lymphocytic infiltrates. In the epidermis within the maculopapular rash the pathologist may find vacuolar and hyperkeratosis modifications in the cells strata. Sometimes, in deaths related to MV, the histologic diagnosis might be sustained due to lymphoid tissue modifications, that also encompasses the presences of giant cells [7]. As an aid tool for diagnosis, during the first days of the prodromal stage, in specimens retrieved from the Koplik spots, giant syncytial cells may be uncovered in cytopathological techniques. Also, the samples from accessible epithelial surfaces located in pharynx, bulbar conjunctiva, nasal and buccal mucosa offers the possibility for giant cell cytologic detection. However, in patients vaccinated with Schwarz strain, live, attenuated MV, the giant cell formation remains inconspicuous [8].

**CONCLUSIONS**

Although many other different causes are implied in children death, MV infections could become
a frequent cause, especially, with a higher likelihood for MV outbreaks in civilized countries. Thus, a rapid, clinical examination is mandatory before any emergent diagnosis, especially when infectious diseases are suspicioned. In MV related deaths, autopsy diagnosis becomes further difficult with unclear pathogenic processes for the unwise examiner, while characteristic lesion may illuminate the matter, with no immunohistochemically confirmation to be required allowing the formulation of a definitive diagnosis.

Conflict of interest. The authors declare no conflict of interests.

We certificate that the procedures and the experiments we have done respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2000, as well as in accordance with the national law.

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References