Clinical Note

An adult patient with rubella encephalitis

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Encephalitis is a complex and severe neurological syndrome and the identification of its etiologic agents is useful to determine the treatment strategy and anticipate the illness course. However, according to many studies, the etiologic agent was not identified in 48-63% of encephalitis' cases.[1] Rubella is a rare etiologic agent, causing encephalitis only in one in 5000-6000 cases during previous epidemics.[2] Rubella encephalitis (RE) almost always occurs in unvaccinated children and accounts for 2.9-7.4% of childhood encephalitis according to recent studies, even though rubella has become very rare after universal childhood vaccination.[3] We present an uncommon case of RE in an immunocompetent unvaccinated adult patient to highlight the likelihood of its occurrence in the adult population even without clinical evidence of rubella infection.

A 65-year-old man who presented with fever (temperature up to 39°C), vomiting, and drowsiness during the previous 10 days was admitted to the Neurological Department. On neurological examination the patient was in a lethargic condition, able to utter words only occasionally and follow simple commands, while he opened his eyes and had a flexing motion after a painful stimulus. There were neither focal neurological signs nor neck stiffness, and his recent medical history was free of any symptoms and signs of infection. Routine laboratory data, ECG, and x-rays of the chest were all normal. The CSF analysis was as follows: cells 10/mm^3 (lymphocytic cell profile), protein 60mg/dl, glucose 55mg/dl, while CSF culture for common bacteria, cocci and fungi were negative. The EEG showed generalized high-amplitude θ and δ activities, predominantly in the frontal areas. Cranial MRI revealed focal areas of high signal intensity on FLAIR and T2-weighed images with indistinct margins, close to the lateral ventricles, in the frontal lobes, corpus callosum, and the white matter of temporoparietal region (**Figure 1**). The T1-weighed MRI image after gadolinium demonstrated diffuse heterogeneous enhancement of the lesions. These findings were compatible with diffused parenchymal encephalitis. Specific IgM antibodies for Ebstein-Barr virus, cytomegalovirus, herpes simplex virus type 1 and 2, coxsackie, varicella zoster virus, adenovirus, *Toxoplasma gondii, Borrelia burgdorferi, Mycoplasma pneumoniae, Listeria monocytogenes, Brucella, Candida albicans, Aspergillus fumigatus*, and *Cryptococcus neoformans* using an ELISA technique were not detected in the serum and CSF. Gene probe for tuberculosis was also negative in the serum and CSF. In contrast, the ELISA revealed that titers of Rubella specific IgM and IgG antibodies in serum were 33.6 (0-20 IU/ml), 178 (0-9 IU/ml). Both were negative in the CSF. Rubella RNA was not isolated in the serum or in the CSF using polymerase chain reaction. Later, rubella IgM antibody serum titers showed a significant reduction; 26.7 on the fifteenth day, and 15.7 on the thirtieth day, while IgG antibody serum titers increased: 256 on the fifteenth day, and 261 on the thirtieth day.

Initially, the patient was treated with dexamethasone and acyclovir and after the serologic results we stopped acyclovir and followed symptomatic therapy. Twenty days after admission his fever and vomiting remitted, but the level of consciousness remained unchanged. The CSF, EEG, and MRI examinations were repeated and showed no significant change. Three months later the patient died of severe nosocomial infections.

In this report we present a case of RE in an adult, unvaccinated for rubella. This diagnosis was confirmed by the identification of positive IgM antibodies against rubella in serum, the progressive reduction of these titers in sequential measurements, and the parallel increase of IgG antibody titers, even though there was no evidence of recent rubella infection.[2,3] Encephalitis is a rare complication of rubella infection and usually occurs in unvaccinated children as mentioned above. Only few

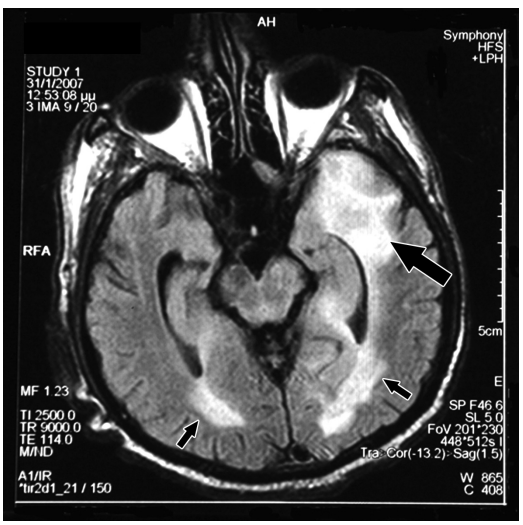

Figure 1 - Axial fluid-attenuated inversion recovery (FLAIR) MRI showing high signal intensity areas with indistinct margins in the white matter of left temporal region.

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cases of RE have been observed in the adult population, as in our patient. Clinical signs of encephalitis may begin 4-7 days after skin eruption,[2] but rubella may be manifested subclinically even without rash in 25-50% of the cases.[2,4] It is noteworthy that during the atypical course of the disease, development of encephalitis is very rare, which we also observed in our patient.[4] In RE patients, rubella specific antibodies and viral nucleic acid have rarely been isolated from the CSF, because the virus is scarce in acquired rubella infection.[2] Although our patient died, sequelae following recovery from RE are very rare.[4,5] The pathogenesis of RE is not yet completely known, although some researchers accept the absorption of rubella to the nerve cells after penetration of the virus into the nervous system via a permeable "inflamed" blood brain barrier. After the direct penetration of the virus into the nervous system the spectrum of the clinical syndrome depends on the host immune response.[5] Finally, other postrubella neurologic complications are myelitis, optic neuritis, Guillain-Barré syndrome, peripheral neuritis, and carotid artery thrombosis.[5]

In conclusion, since a number of adults have not been vaccinated against rubella for various reasons, we should take into account rubella as a cause of encephalitis even when the typical rash is absent.

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References

1. Glaser CA, Honarmand S, Anderson LJ, Schnurr DP, Forghani B, Cossen CK, et al. Beyond viruses: clinical profiles and etiologies associated with encephalitis. ***Clin Infect Dis*** 2006; 43: 1565-1577.
2. Frey TK. Neurological aspects of rubella virus infection. ***Intervirology*** 1997; 40: 167-175.
3. Xu, Y, Zhaori G, Vene S, Shen K, Zhou Y, Magnius LO, et al. Viral etiology of acute childhood encephalitis in Beijing diagnosed by analysis of single samples. ***Pediatr Infect Dis J*** 1996; 15: 1018-1024.
4. Guler E, Davutoglu M, Guler S, Citirik D, Karabiber H. Encephalitis in a child during atypical course of rubella. ***Infection*** 2009; 37: 65-66.
5. Chang DI, Park JH, Chung KC. Encephalitis and polyradiculoneuritis following rubella virus infection. ***J Korean Med Sci*** 1997; 12: 168-170.

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