

CORRESPONDENCE

Acute chorea in a child receiving second dose of human papilloma virus vaccine

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To the Editor,

Since a program of immunization with human papilloma virus (HPV) quadrivalent vaccine Gardasil has began, adverse events' surveillance has started. To date, the most important neurologic adverse events reported are Guillain-Barré syndrome (1), demyelinating diseases (2, 3) and cases of acute disseminated encephalo myelitis (ADEM) (4, 5).

An 11-yr-old girl was admitted in our Child Neurology and Psychiatry Unit presenting generalized choreic movements involving arms, legs and trunk. These were associated with facial grimaces, ataxic gait and dysarthria. The girl is the secondborn sibling of healthy non-consanguineous parents. At the age of 14, her brother started suffering from symptomatic epilepsy as a complication of a surgery he had undergone to remove a fibrillar grade 1 astrocytoma. The girl had always been in good health since she developed the movement disorder. Her symptoms appeared rapidly and persisted for days. We performed accurate anamnestic interview. The patient was born after a full-term pregnancy, by vaginal delivery. No pre-perinatal problems were referred. She had received vaccines following Italian schedule and she had never reported adverse events.

The patient received first dose of HPV vaccine Gardasil on February 25th, 2013. Second Gardasil dose was administered on April 8th, 2013. After 1 month, she developed acute chorea and came to our Unit.

To exclude common causes of chorea in young children, we performed specific blood examinations. Complete blood count, liver enzymes and renal functioning were normal. Considering the hypothesis of rheumatic disease, we dosed antistreptolysin titer and found a value not sufficiently high to justify a rheumatic chorea according to our experience (363 IU/ml). *Streptococcus pyogenes* was not detected in the patient's throat swab specimen. As in rheumatic chorea antistreptolysin titer can also be within normal limits, we performed electrocardiogram and echocardiography and excluded rheumatic carditis. Inflammatory indexes (Erythrocyte sedimentation rate, C reactive protein) as well as serum and 24 h urinary copper and serum ceruloplasmin were normal.

We performed a complete autoimmune screening: immunoglobulins subpopulations, complement C3 and C4 fragments, antinuclear antibodies (ANA), extractable nuclear antigens (ENA), antineutrophils cytoplasm antibodies (ANCA), anti-beta 2 microglobulin antibodies, antitireoperoxidase antibodies, anti-endomysium antibodies, anticardiolipin antibodies, antiphospholipids antibodies (PLP), lupus anticoagulant. All indexes were in the range except for antiperoxidase antibodies

43 U/l (normal range inferior to 35). We underline that thyroid functioning resulted normal and no familiar history of thyro-pathy was reported. Immunoglobulins class E were elevated (1265 IU/ml); we ascribed this data to allergic diathesis (the girl suffers from allergic rhinitis).

Brain magnetic resonance imaging showed normal findings. Finally, we studied a sample of cerebrospinal fluid and obtained normal results. No oligoclonal bands were signaled.

We hypothesized an autoimmune reaction after second dose of Gardasil vaccine (administered 1 month before) and decided to start therapy with oral methylprednisolone 2 mg/kg/die for 4 wk. This was then gradually reduced and completely stopped. The girl started improving after 2 days of therapy and obtained a complete resolution of symptoms within 1 wk. Follow-up visits were carried out monthly after discharge proving a complete recovery.

In this article, we discuss the case of a completely healthy girl before acute choreic signs raising 1 month after the second immunization with Gardasil. We excluded rheumatic disease, other autoimmune disease (i.e., Lupus erythematosus systemic), and other inflammatory processes in central nervous system and copper metabolism disorders. There is a strong temporary association between the administration of vaccine and the appearance of symptoms. As in other cases previously reported (4), symptoms tend to occur after booster vaccination rather than after first application and this is our case. Finally, we believe that prompt answer to steroid treatment could be another element, suggesting that an autoimmune post-vaccine mechanism of action could have caused symptoms. An autoimmune pathogenetic mechanism – that is molecular mimicry – has been postulated for this vaccine's adverse events (6). In particular, it has been observed that Gardasil recombinant proteins and components other than proteins (i.e., Aluminum) have a high antigenicity. Noteworthy, the population eligible for the wide immunization program – girls in pubertal age – is *per se* predisposed to develop autoimmune reactions.

We describe a further case of neurologic complication after Gardasil administration, underlying that surveillance on adverse effect of the vaccine is still needed.

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