Antiphospholipid Syndrome Following a Diphtheria-Tetanus Vaccination: Coincidence vs. Causality

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COMMENT

Numerous reports have discussed a possible association between vaccines and autoimmune diseases. One of the suggested mechanisms is the "molecular mimicry" theory, according to which an antigen of the vaccine resembles a host antigen, leading to an autoimmune process. Another theory is that immunization may cause the appearance of, or an increase in immune complexes, which may induce vasculitis or exacerbate a preexisting autoimmune disease [1]. Patients with a genetic predisposition for an autoimmune disease may be at higher risk for developing one after a vaccination. Nevertheless, most epidemiologic studies have not found a direct causal link between vaccinations and the onset of an autoimmune disease [2].

Autoantibodies to various phospholipids have been identified in patients with antiphospholipid syndrome, resulting in a wide spectrum of clinical phenomena such as arterial and venous thrombosis, microvascular thrombosis, placental insufficiency, and a variety of other manifestations. Despite the well-established clinical picture, certain pathogenetic issues remain unanswered, especially regarding the initial triggering events leading to a thrombosis.

There is little information on the connection between immunization and antiphospholipid antibodies. In one study, 85 healthy students were vaccinated with a recombinant hepatitis B virus vaccine. One month later, a minor, statistically insignificant rise in antiphospholipid antibodies was detected [3]. Recently, Inic-Kanada et al. [4] showed that mice...
monoclonal antibodies against diphtheria-tetanus toxoid cross-react with β2 glycoprotein and cause adverse pregnancy outcomes when injected in BALB/c mice. These outcomes can mimic the pathogenesis of antiphospholipid syndrome in humans.

Agmon-Levin et al. [5] recently proposed that each component of the vaccine can induce autoimmunity via several mechanisms. Yet, large epidemiologic studies have failed to demonstrate post-vaccination autoimmunity.

Possible causal relationships between vaccinations and autoimmunity have long been discussed, but have not been proven. We present here a patient with clinically and serologically proven antiphospholipid syndrome that manifested a few months after a diphtheria-tetanus vaccine. A possible pathogenic role of the vaccine in the appearance of antiphospholipid syndrome cannot be excluded.

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References

Origin of the human malaria parasite Plasmodium falciparum in gorillas

Plasmodium falciparum is the most prevalent and lethal of the malaria parasites infecting humans, yet the origin and evolutionary history of this important pathogen remain controversial. Liu et al. have developed a single-genome amplification strategy to identify and characterize Plasmodium spp. DNA sequences in fecal samples from wild-living apes. Among nearly 3000 specimens collected from field sites throughout central Africa, the authors found Plasmodium infection in chimpanzees (Pan troglodytes) and western gorillas (Gorilla gorilla), but not in eastern gorillas (Gorilla beringei) or bonobos (Pan paniscus). Ape plasmodial infections were highly prevalent, widely distributed and almost always made up of mixed parasite species. Analysis of more than 1100 mitochondrial, apicoplast and nuclear gene sequences from chimpanzees and gorillas revealed that 99% grouped within one of six host-specific lineages representing distinct Plasmodium species within the subgenus Laverania. One of these from western gorillas comprised parasites that were nearly identical to P. falciparum. In phylogenetic analyses of full-length mitochondrial sequences, human P. falciparum formed a monophyletic lineage within the gorilla parasite radiation. These findings indicate that P. falciparum is of gorilla origin and not of chimpanzee, bonobo or ancient human origin.

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Macrophages need food to fight infection

Starvation or poor nutrition weakens the immune system and makes organisms more susceptible to disease. This reflects in part the need for adequate energy stores. But Mieulet and team provide evidence that sufficient uptake of the amino acid arginine is required for mouse macrophages to respond to bacterial lipopolysaccharide, which binds to Toll-like receptors that initiate innate immune responses. Macrophages deprived of arginine appeared to have a deficit in the activation of mitogen-activated protein kinases (MAPKs) that mediate the immune response. In cultured cells deprived of arginine, the protein kinase TPL-2 (tumor-promoting locus 2, a MAPK kinase kinase) was associated to a greater extent with protein phosphatase 2A, leading to dephosphorylation and inactivation of TPL-2. In mice, deprivation of arginine also reduced MAPK activation and the consequent production of tumor necrosis factor-alpha. Arginine thus appears to have multiple important roles in the innate immune response: It serves as a substrate for the synthesis of nitric oxide as part of cellular response to bacterial infection, and it maintains a key signaling pathway that allows macrophages to fight infection effectively.

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“How easy to be amiable in the midst of happiness and success”
Madame Anne Sophie Swetchine (1782-1857), Russian mystic