Severe but transient parkinsonism after tetanus vaccination

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A 38 year old metal worker with a history of hypertension and hyperthyroidism presented with fluctuating fever and sweating, palpitations, tremor of the upper parts of both legs, and diplopia. These symptoms had been present for five days and had started within hours after he had received the last of three vaccinations for tetanus (TE anatoxal berna, contents: 20 LF tetanus toxoid, 2 mg aluminium phosphate, and 0.1 mg thiomersal, Primmed BV, Almere, The Netherlands). These vaccinations were given because of an injury to his right index finger one month before. There was no family history of movement disorders. Physical examination showed profuse sweating, normal consciousness, a temperature of 37.3°C, symmetric rigidity of all four limbs, and a painful tremor in the upper parts of his legs. Muscle strength, tendon reflexes, and sensation were normal.

Within a week he progressed to severe hypokinetic dysarthria, a mask-like face, and a resting tremor of both hands, and he had bradykinesia and generalised rigidity, together with a cogwheel phenomenon in the arms.

Laboratory examination showed a creatine phosphokinase activity of 2682 U/l (normal <190 U/l) and normal blood concentrations of manganese, copper, ceruloplasmin, and carbon monoxide. His CSF showed 50 lymphocytes (normal range 0-3), slightly raised total protein (0.54 g/l; normal range 0.15-0.45 g/l), normal IgG index (0.43; normal <0.66), and negative serological tests on Epstein-Barr virus, herpes zoster virus, herpes simplex virus, syphilis, Borrelia burgdorferi, and Mycoplasma pneumoniae. Brain MRI was normal. Single photon emission computed tomography (SPECT) with 123I-iodobenzamide (IBZM), specifically binding to the cerebral dopamine receptor (D2), showed a decreased ganglia:cortex ratio, indicating a postsynaptic disorder. Nevertheless, biperidine, levodopa and carbidopa, and pergolide were prescribed, resulting in gradual but impressive clinical improvement within several weeks.

The clinical syndrome was unclear during the first few days after admission, but gradually developed into a hypokinetic rigid syndrome with resting tremor, generalised bradykinesia, and rigidity. This responded well to treatment with levodopa/carbidopa and a dopamine agonist.

Possible causes of a rapidly progressive form of parkinsonism are encephalitis, intoxication, head trauma, tumour, ischaemia, or hydrocephalus. Imaging studies showed no abnormalities, thereby excluding the last three possible causes. Repeated history taking failed to disclose head
trauma. The profession of the patient might suggest poisoning, but blood concentrations of manganese and copper were normal. The CSF showed mild pleiocytosis, but serological testing for various specific microorganisms did not show any recent infection. Radionuclide imaging showed a pattern similar to that seen in progressive supranuclear palsy or multiple system atrophy.2

The sequence of events strongly suggests a relation between the vaccination and the neurological syndrome, although the causal nature is difficult to prove.3 To our knowledge, there are no reports of parkinsonism after tetanus immunisation. Alves et al reported a 5 year old boy who developed a postencephalitic rigid akinetic syndrome 15 days after vaccination for measles with live attenuated virus. Again, cause and effect remained open for debate.4 5

The tetanus vaccine used in our patient does not contain any living microorganisms. However, repeated injections with the tetanus toxoid might have caused hypersensitivity, and also an immunological cross reaction of antibodies with neuronal tissue directly after the last injection. This might also explain the pleiocytosis and raised protein and IgG content in CSF. The alternative explanation is that one of the substances in the vaccine vehicle, thiomersal or aluminiumphosphate, had a neurotoxic effect.

Although we are aware that a causal relation between the vaccine and the hypokinetic rigid syndrome is far from established, we have no better explanation. We wish to record the patient history as a reference, in case analogous patients might be seen in the future.

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