

Acute midbrain syndrome as an adverse reaction to tetanus immunization

G. Schwarz¹, G. Lanzer² and W.F. List¹

¹Department of Anaesthesiology, and ²Department of Internal Medicine, University of Graz, Graz, Austria

Received: 15 March 1988; accepted: 15 May 1988

Abstract. An acute midbrain syndrome III/IV developed twice after tetanus immunization. The occurrence of nearly identical episodes was remarkable, as well as the relatively rapid return to normal consciousness and neurological status after deep coma. Special emphasis is placed upon the chronological relationship of the coma to the immunization and upon immunological tests (tetanus antibody titres) performed to confirm the diagnosis.

Key words: Tetanus vaccination – Coma – Cerebral edema

Even with modern intensive care, infection with *Clostridium tetani* carries a mortality of up to 20% [2]. Prophylactic tetanus immunization provides necessary and very effective protection and only rarely causes side effects. The occurrence of an acute midbrain syndrome requiring intensive care is remarkable as an extremely rare, life threatening complication following tetanus immunization.

Case report

A 21-year-old man injured his left arm in a bicycle accident, suffering contusion and lacerations of the elbow with opening of the olecranon bursa. Surgical treatment was undertaken and simultaneously immunization was given with tetanus vaccine (adsorbed, 0.5 ml) and tetanus antitoxin (250 IE) intramuscularly. There was no past history of allergies and no previous disease of the central nervous system. The patient had received seven tetanus immunizations without complications (the first was diphtheria pertussis-tetanus vaccine, subsequently diphtheria and tetanus) up to 12 years of age. On the seventh day after immunization,

the patient developed headache, tremor and clouding of consciousness. Two days later encephalitis was suspected and the patient was transferred via the neurological department to the intensive care unit (ICU). Upon admission to the ICU, the patient was deeply comatose and unresponsive to pain. Pupillary and corneal reflexes were negative bilaterally, the eyes were divergent. There were spontaneous extensor synergisms; muscle tone and reflexes were increased. Spontaneous respiration was inadequate, there was slight meningism and pyramidal signs were seen.

The patterns was: hyperpyrexia (40–41 °C), blood pressure was 150/70–170/80 mmHg and heart rate 50–60 beats/min. A skull x-ray was normal and a cerebral CT scan showed cerebral oedema (Fig. 1). Dominant delta and subdelta activity with superimposed faster activity were seen on the EEG. The cerebrospinal fluid (CSF) showed 32 cells/mm³ (lymphocytes 83%, monocytes 17%) with no bacteria. Viral serology was negative. Thin-layer and gas chromatography of stomach contents and urine showed no

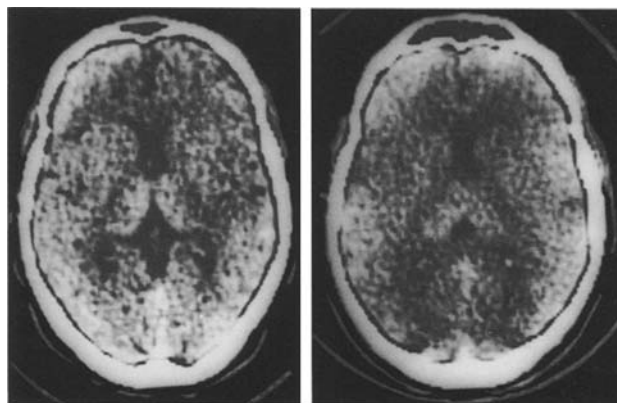


Fig. 1. Cranial CT-Scan. Left: normal (12 h before admission to ICU). Right: brain edema (upon admission to ICU)

evidence of intoxication. The hematocrit value was 41%. The white blood cell count was 12.0/nl. Serum electrolytes, blood glucose, BUN, creatinine and liver enzymes were within normal limits.

Mechanical ventilation was begun and the patient was hyperventilated (pCO₂ 28 mmHg) and sedated with etomidate. Dexamethasone was given. The hyperpyrexia was treated with amidopyrine and physical cooling.

Gentamycin and mezlocillin were given together with immune globulin before it was verified that there was no bacterial infection. Total parenteral nutrition was undertaken via central venous catheter. Cimetidine was given for ulcer prophylaxis.

After three days of treatment there was a remarkably rapid recovery of consciousness and neurological status. An abortive meningoencephalitis with midbrain signs was suspected. The patient was asymptomatic by the 14th day. A causal relationship with the preceding tetanus immunization was not established.

Two and a half years later the patient required treatment after an accident with open injuries of the limbs. Again, tetanus vaccine (adsorbed 0.5 ml i.m.) was administered. Eight days later, a comatose state developed with signs of an acute midbrain syndrome III/IV which was very similar to the first presentation. There was also unilateral paralysis of the facial nerve and mild meningism. Similar treatment to the first episode was given and consciousness returned after two days. CSF studies and toxicological and serological findings again provided no definitive result and an allergic-hyperergic event subsequent to tetanus immunization was postulated. Immunological studies were performed after the acute illness. The most outstanding finding was a tetanus antibody titre of 16.0 IE/ml (protective level 0.01 IE/ml) [4]. The IgE concentration was elevated at 30 g E/ml. The pattern of the lymphocyte subpopulations was altered (elevation of Leu 7⁺/11⁻ cells to 40% with decrease of the Leu 7⁻/11⁺ cells to 7%, Leu 7⁺/11⁺ coexpression was seen in 42% of the lymphocytes).

Discussion

In addition to a generalized reaction (fever, malaise), tetanus immunization has been described as producing side effects in the skin, cardiovascular and locomotor systems, respiratory tract and nervous system. Among the latter, mono- and polyneuropathies are most common [1].

What is remarkable about this patient is on the one hand that the brain was the organ primarily affected and on the other the recurrence of the event in nearly the same form after two and a half years. In both episodes the clinical picture was dominated by the features of an acute midbrain syndrome III/IV. The

chronological course was also similar, with the illness beginning on the 7th and 8th days respectively after tetanus immunization. After each incident, normal consciousness returned after a short period (two and three days, respectively, after treatment onset) and recovery was complete.

The pathological mechanisms were assumed to be immunological reactions to tetanus vaccination (localized vasculitis mediated by immune complex or cerebrally accentuated systemic vasculitis) and need further investigations. The pathomorphological substrate was expressed by an allergic cerebral oedema. This has also been reported after smallpox vaccination, antibiotic therapy, injection of x-ray contrast media, serum and bee stings [3]. Allergic oedema masquerading as post vaccination encephalitis following smallpox vaccination is clinically similar to this case [3]. In contrast to encephalitis, the prompt response to treatment suggests that allergic oedema was largely responsible for the symptomatology. As this report shows, the differential diagnosis of coma (with negative serology and toxicology) occurring soon after a tetanus immunization must include a postvaccination allergic event involving the central nervous system. The occurrence of monocytes in the CSF may represent an early stage of immunologic stimulation (complement stimulation by immune complexes). Tetanus antibody titre testing helps to clarify the situation. In this case the tetanus antibody titre was 1600 times greater than the protective level and this was interpreted as an indication of a hyperimmune reaction to the tetanus vaccine. The value of the altered pattern of the lymphocyte subpopulations was not definitive as the serological testing was not done during the acute illness. Skin testing may have a "booster" effect and was avoided because of the severe clinical conditions of the patient. As the postvaccination reactions may recur every time a booster immunization is required, the patient should be warned and perhaps given a card to carry detailing the potential complications.

References

1. Korger G, Quast U, Dechert G (1986) Tetanus vaccination – tolerance and avoidance of adverse reactions. *Klin Wochenschr* 64:767
2. List WF (1981) Immediate treatment of tetanus with high doses of human tetanus antitoxins. *Notfallmedizin* 6:731
3. Vich V (1968) Contribution on the problem of allergic cerebral oedema following smallpox vaccination, that imitates a postvaccinal encephalitis. *Z Arztl Fortbild* 62 (21):1183
4. Wolters KL, Dehmel H (1942) Final studies on tetanus prophylaxis with active immunization. *Z Hyg u Infektionskr* 124:326

Dr. G. Schwarz
Department of Anaesthesiology
A-8036 Graz – LKH
Austria