Outbreak of Tetanus Among Elderly Women Treated with Sheep Cell Therapy

Tetanus is a worldwide disease whose incidence is highest in developing countries. In most Western nations, however, the incidence is less than one case per million population per year [1]. About 60% of the cases occur in persons >60 years [2]. In Argentina, a country with 34 million inhabitants, 10 to 67 cases have been reported yearly in the past decade [1]. We describe an outbreak of tetanus in a population of elderly patients who received sheep cell therapy in Buenos Aires, Argentina, between March and April 1996.

On 14 March 1996, a 63-year-old Argentine woman complained to her relatives of muscle rigidity in her face and legs. She was treated at a medical center for symptoms of high blood pressure and contractures. The patient’s condition gradually worsened, and on 18 March, when she became unable to walk, a diagnosis of tetanus was reached. She died 3 days later. On 22 March, a 54-year-old woman with a clinical diagnosis of tetanus died, and six other women with tetanus were admitted to infectious disease services in two hospitals in the province of Buenos Aires. The following week, four more patients with clinical diagnoses of tetanus were admitted to these hospitals. Of these 12 women, seven subsequently died.

All patients developed the severe generalized type of tetanus; no mild cases or the local or cephalic types of the disease were seen in this patient population. Interviews of the patients and their relatives revealed that all had received intramuscular injections of fetal sheep cells as part of an alternative treatment for rheumatism and arthritis between 8 and 14 days before the onset of symptoms (mean interval, 11 days). All patients had received cell therapy for several years at a single clinic in the province of Buenos Aires. A single pharmaceutical company was the source of the sheep cell preparations. Family members reported that the patients had not previously been vaccinated with tetanus toxoid.

While most patients received the doses of cell therapy at the clinic, the possibility that needles or syringes were shared in the clinic or outside the facility was ruled out. The fetal sheep cells used by the patients were analyzed at three independent infectious disease centers. At the first center, gram staining for Clostridium tetani was not performed. At the second center, the samples were reanalyzed, and positive evidence of anaerobic organisms was found in one of the samples, although the presence of clostridia was not demonstrated. At the third center, rodents and rabbits were inoculated with this sample. These animals subsequently developed the clinical symptoms of tetanus.

About one century has elapsed since the protein neurotoxins produced by clostridia were identified as the cause of the paralytic syndrome of tetanus and botulism [3]. Despite the availability of effective and inexpensive tetanus toxoid vaccines, cases of tetanus continue to occur in most countries. The cases described in this report are consistent with previous cases reported worldwide, which indicate that tetanus occurs primarily among older adults who typically are unvaccinated or have an unknown vaccination history [4].

The potential risks posed by the administration of fresh cells, frozen cells (snap-frozen cell suspensions), or lyophilized cells (sicca cells) are well known (see [5] for a review of transmission of viral infection). Since the administration of heterologous biological material is involved, most of the complications that have been observed have been of the allergic or hyperergic type, resembling experimental allergic encephalomyelitis and experimental allergic neuritis [6]. The use of dried cells has been provisionally banned in several countries; however, these cells are still used in other countries. The tetanus outbreak described herein is, to our knowledge, the first reported outbreak of this disease in a population receiving cell therapy. In addition, this outbreak clearly reveals two serious situations: (1) poor quality control of drugs used in alternative therapies and (2) lack of immunization among the elderly. Since this incident, health authorities have closed both the pharmaceutical company where the fetal sheep cells were manufactured and the clinic.

Several questions remain unresolved. First, it was not possible to determine the total number of individuals exposed to sheep cells in the previous 2 months of the outbreak. Fifty-five clinic patients received prophylactic treatment at hospitals, but this figure might be an underestimate. Second, because of legal reasons, no further details on the contents of the bottles were available. Finally, the time that elapsed before the bottles were submitted to the infectious disease centers (8 to 10 weeks) was too long. In addition, there was possible excessive manipulation of the samples. These two obstacles might have reduced the chances of isolating the putative organism in most bottles.

Tetanus is a totally preventable disease. It may have been forgotten by many people, but it has not been completely eradicated [7]. It is necessary to understand that efforts need to be directed toward universal immunization and compliance with the generally accepted recommendations on wound management. It is ironic that seven relatively healthy women who were seeking treatment to prevent rheumatism died as a consequence of the lack of preventive measures. In the interest of good health and public welfare, this pattern of negligence must stop.

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References