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Severe Tetanus with Sympathetic Overactivity in Two Patients

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Tetanus is a nervous system disease caused by tetanospasmin, a toxin produced by *Clostridium tetani*. In Japan, tetanus, which occurs in association with even a slight injury, should always be taken into consideration in the traumatology field, although there are rare cases of tetanus owing to the spread of vaccination, etc. Treatment of spasm and sympathetic overactivity plays an important role in the therapeutic control of this disease. We had an experience of treating two patients suffering from severe tetanus with sympathetic overactivity. For one patient, it took about 15 days to control the disease by continuous administration of phenobartital and diazepam. For the other patient, pancuronium bromide and midazolam were used and fentanyl citrate was added for circulatory dynamic stabilization, and control with a ventilator required about 28 days. Although both patients were cured from the tetanus and discharged, reduced myodynamia required rehabilitation, and delirium and suicide attempts required psychiatric treatment during the recovery period following the anti-spasm therapy. Careful systemic control of tetanus patients is necessary throughout the course of disease as complications to be watched may occur following the anti-spasm therapy as well, although the progress in respiratory control has contributed to the improvement in prognosis of tetanus patients.

Introduction

Tetanus is a nervous system disease caused by tetanospasmin, a toxin produced by *Clostridium tetani*. In Japan, tetanus, which occurs in association with even a slight injury, should always be taken into consideration in the traumatology field, although there are rare cases of tetanus attributed to the spread of vaccination, etc[1)2)]. Treatment of spasm and sympathetic overactivity plays an important role in the therapeutic control of this disease. Complications to be watched occur occasionally following treatment with anti-spasm agents although the progress in respiratory control has improved the prognosis of tetanus patients. We experienced treating two patients having severe tetanus with sympathetic overactivity, and here we report these cases with an overview of the literature.

Case Reports

Case 1: A 70-year-old male

Present disease history: The patient fell down into a drain and developed contused wounds in his lower jaw. The contused wounds were sutured at another hospital. The patient exhibited dysarthria and jaw opening pain immediately after the injury but no radiological examination

was performed. The lower jaw contused wounds healed smoothly, but myalgia from the posterior region of neck to the dorsolumbar region, systemic tonic convulsions, and gait disturbance occurred on November 1, 1993, and opisthotonus and muscle rigidity additionally occurred on November 2. The patient was referred to our hospital on November 3.

Manifestations at admission: The patient was clearly conscious with no vital sign problems. However, jaw opening was limited to an extent equivalent to half a transverse finger, and neck rigidity and allolalia were observed.

Examinations at admission: Hematological examination showed no abnormal findings other than WBC 15,400/μl, CPK 571 IU/l, CRP 3.3 mg/dl. Chest radiography was normal but mandible tomography revealed a fracture and shift of the left articular process.

Therapeutic progress: The systemic convul-

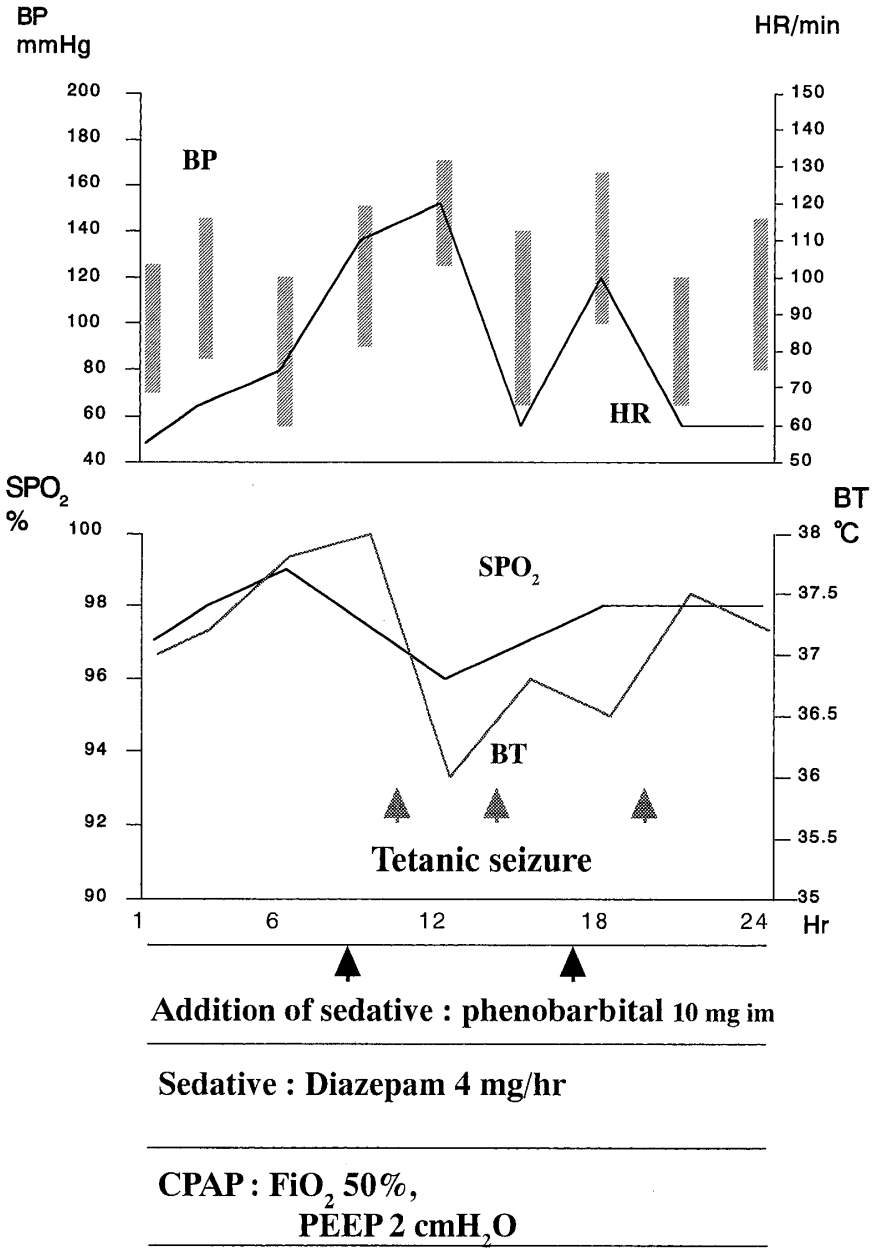

Fig. 1 Diurnal variation (Case 1)

sions and opisthotonus, tachycardia, increased blood pressure and sudoresis which were thought to be manifestations of sympathetic overactivity from the start of admission. Respiration was controlled under endotracheal intubation. The patient was diagnosed as having tetanus, and given 4,500 units of human tetanus immune globulin (TIG), 0.5 ml of tetanus toxoid and antibiotics, and also diazepam. Antibiotics were selected which have sensitivity in sputum-culture (cefazolin sodium 4 g/day × 7 days, gentamicin sulfate 120 mg/day × 3 days, piperacillin sodium 2 g/days × 17 days). Later, tachycardia, increased blood pressure and sudoresis occurred, requiring additional administration of phenobarbital (Fig. 1). Oral ingestion was delayed due to jaw opening impairment resulting from the mandibular fracture, but extubation was conducted on hospitalization day 15, and rehabilitation started because of unavoidable reduced myodynamia during that period. The patient was discharged upon remission of the disease on hospitalization day 55 (Fig.

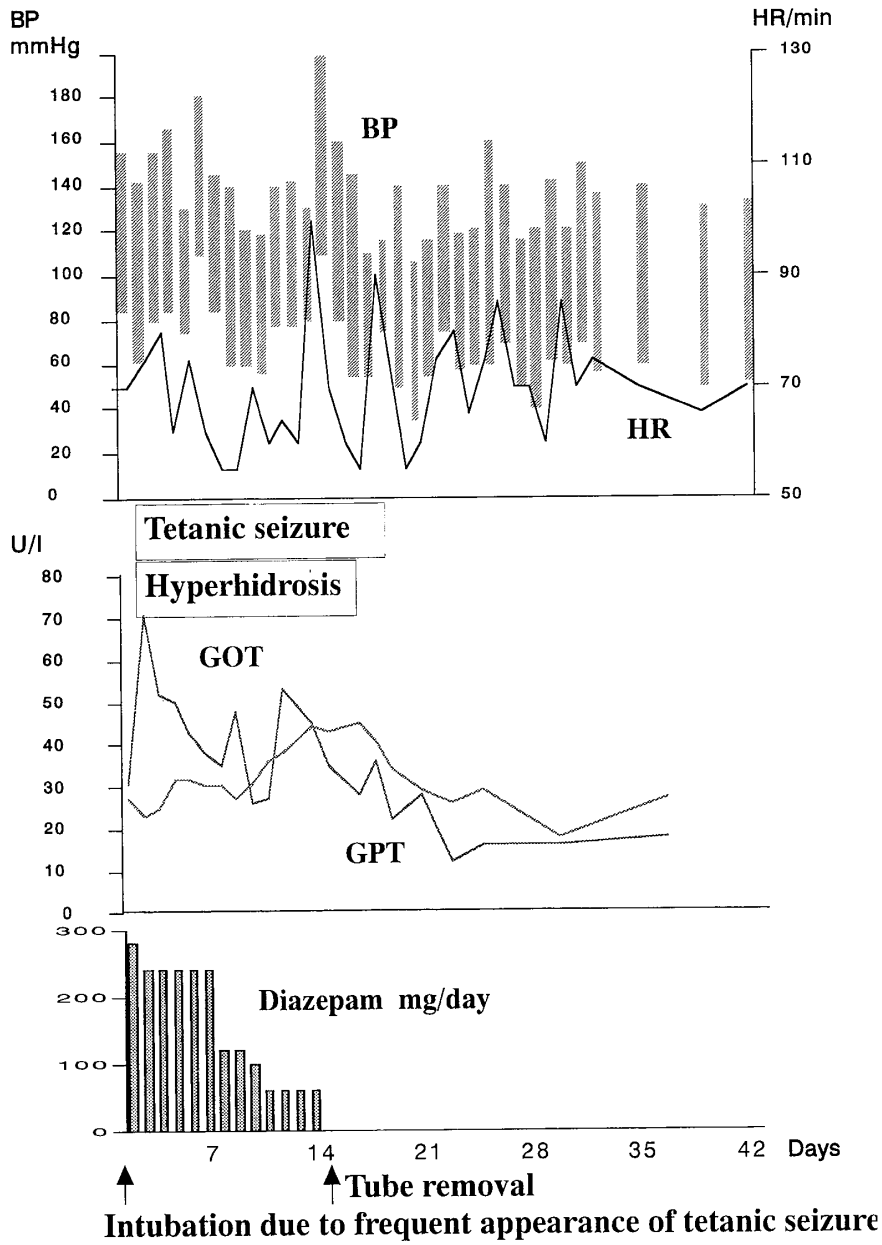

Fig. 2 Clinical course in hospital (Case 1)

2).

Case 2: A 38-year-old male

Present disease history: The patient suffered an abrasion on the face and inside the nasal cavity when he fell down on June 18, 1998. He began to feel a sense of incongruity of the mandibular joint during meals since about June 26 and went to another hospital on July 3. He was referred to our hospital on July 4 since tetanus was suspected owing to jaw opening impairment.

Manifestations at admission: The patient had jaw opening limited to about two transverse fingers and allolalia although his vital signs were normal and no clear causal wound was identified.

Examinations at admission: No hematological abnormalities were observed. No abnormalities were revealed by chest radiography or head CT at the initial admission to the hospital.

Therapeutic progress: Because of manifestations of jaw opening impairment, etc. characteristic of tetanus despite an unclear causal wound, making a diagnosis of tetanus, 0.5 ml of tetanus

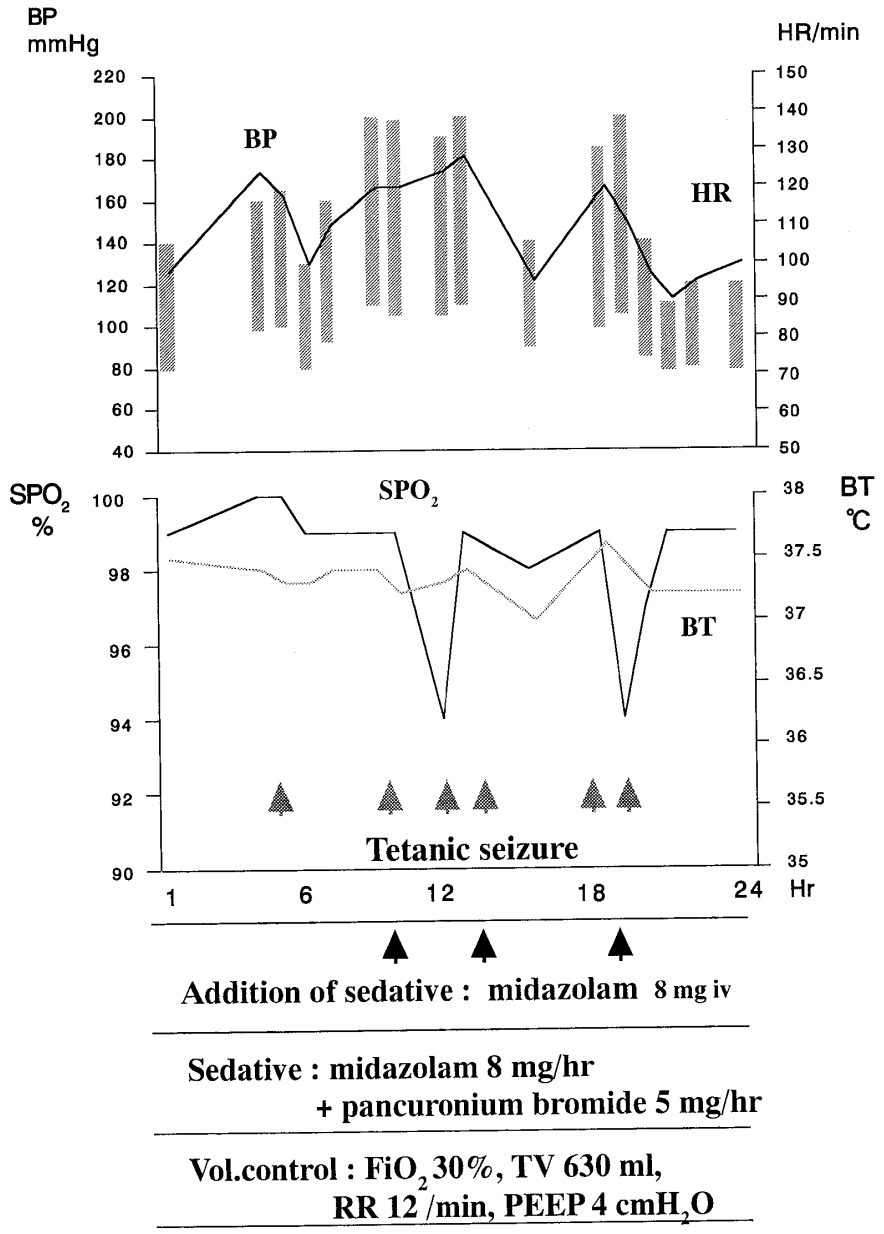

Fig. 3 Diurnal variation (Case 2)

toxoid and 4,500 units of TIG were administered immediately. Immunotherapy and administration of antibiotics were started. Antibiotics were selected which have sensitivity in sputum-culture (cefbuperazone sodium 4 g/day × 6 days, piperacillin sodium 4 g/day × 7 days, cefazolin sodium 2 g/days × 7 days, cefoperazone sodium 2 g/days × 7 days). From the first day of hospitalization, systemic tonic convulsions occurred frequently. Control with a ventilator following endotracheal intubation was started, along with administration of antibiotics (Fig. 3). Muscle rigidity and systemic convulsions occurred despite continuous administration of midazolam and a muscle relaxant during the endotracheal intubation and control with the ventilator. Concomitantly, strong variations of blood pressure and respiratory conditions were observed that required additional administration of drugs (Fig. 4). The dose of midazolam was increased and fentanyl citrate was

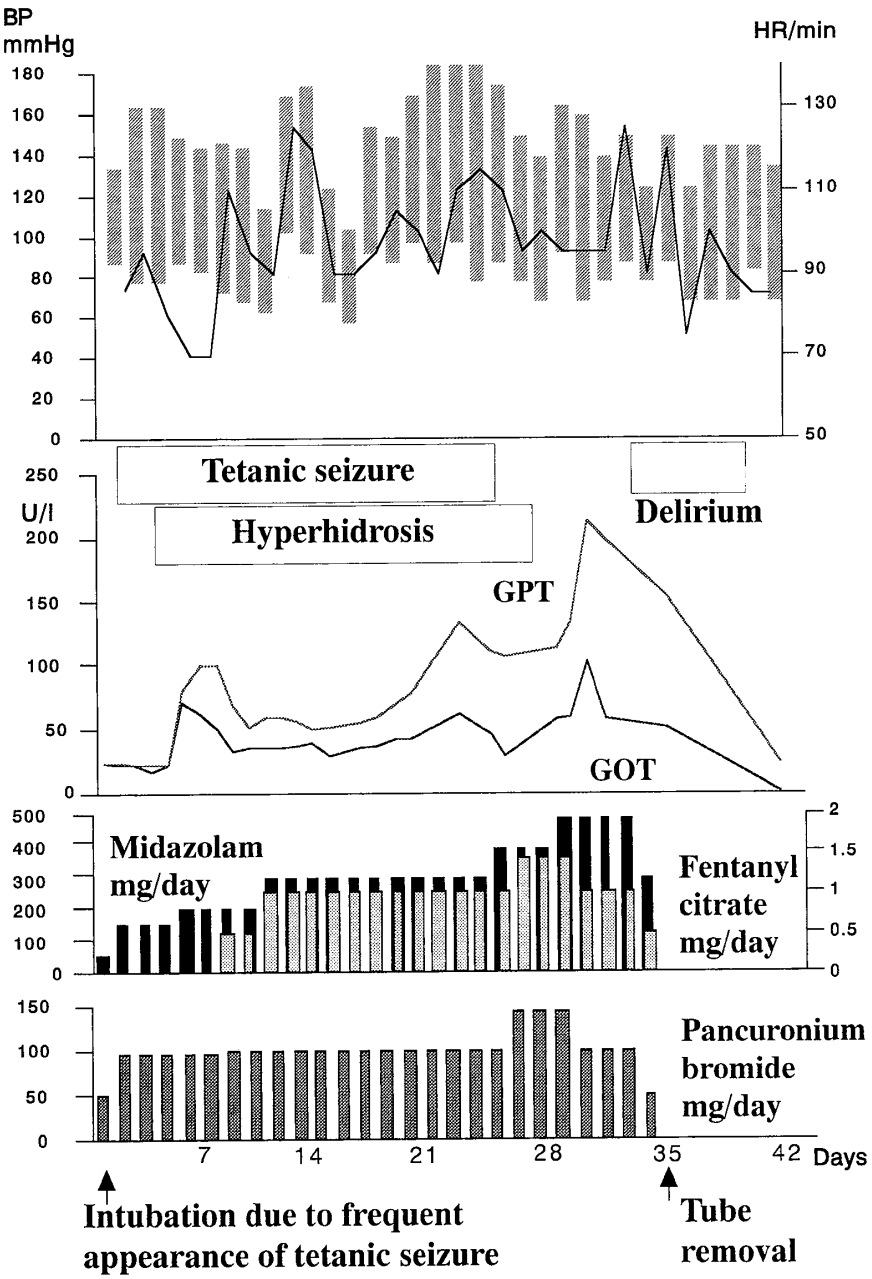

Fig. 4 Clinical course in hospital (Case 2)

administered additionally because of sharp variations in the persistent systemic convulsions, respiratory dynamics and hemodynamics. The patient progressed to the recovery stage approximately 28 days later, but delirium and suicide attempts were observed during the recovery stage and required psychiatric treatment for about 8 days. Finally, the patient had stable mental state and recovery of myodynamia and was discharged on day 44 despite persistent slight hepatic dysfunction.

Discussion

Tetanus is a neurotoxic disease caused by tetanospasmin, a toxin produced by *Clostridium tetani*[1)2)]. The neurotoxin is very strong and increases the motor neuron excitation, leading to manifestations of muscle rigidity, etc. Severe cases exhibit strong respiratory and circulatory system variations due to abnormal excitation of the autonomic nervous system and some patients die of respiratory insufficiency, circulatory insufficiency, etc.

The clinical manifestations and progress of tetanus are classified into the following three stages: the first stage, namely, the incubation period until stiff shoulders and jaw opening impairment such as incongruous sense of the neck become manifest; the second stage called onset time of manifestations ranging from jaw opening impairment to systemic rigidity; and the stage of acme. Patients with the onset time of less than 48 hours and with severe respiratory and circulatory system variations, like our two patients, are regarded as severe cases.

The important therapeutic modalities for tetanus include administration of preventive tetanus toxoid, local cleaning debridement for cases with clear infected wounds, and administration of antibiotics, toxoid, TIG. It has been reported that a history of trauma is not clear in 10% to 30% of patients[1)]. Detection of *Clostridium tetani* is no more than 5～30% in even the patients having clear wound[3)]. In one of our patients as well, there was no causal wound except very slight abrasion, and another pateint noticing a wound could not be detected *Clostridium tetani*. Prevention and early treatment are not necessarily easy. It is not a few that jaw opening impairment and tonic seizure make a decisive factor of diagnosis. Consequently, treatment is often started in the second stage called onset time with manifestations ranging from jaw opening impairment to rigidity like in our patients. Treatment in the stage of acme is mainly respiratory and circulatory maintenance. The mortality of patients with onset time of less than 48 hours has been reported to range from 60 % to 80%. Sympathetic overactivity, that is, sudden change of the circulatory system caused by the action of tetanospasmin on the sympathetic nerves, accounts for the majority of causes of death[1)4)]. Administration of diazepam and a muscle relaxant is a basic therapy for the control of this stage[4)～8)]. Furthermore, various approaches, including continuous epidural anesthesia[9)], spinal anesthesia[10)11)], and introduction of inhalational narcotics[12)], are employed. Anti-convulsion therapy and sedation by continuous administration of diazepam alone produced relatively good control in one of our two patients, because of his advanced age. However, in the other patient who received anti-convulsion therapy and sedation by administration of midazolam and pancuronium bromide, it was necessary to increase the doses of the drugs, with additional administration of fentanyl citrate.

Continuous epidural anesthesia and spinal anesthesia pose problems including the impossibility of keeping the tetanus patient in appropriate position due to muscle rigidity during tube indwelling and opisthotonus, as well as induction of convulsions upon inserting the needle[13)], and expected long-term tube indwelling. Infection con-

trol of the indwelling site in the tetanus patient exhibiting sudoresis state will also be problematic. In our patients as well, indwelling of an epidural tube was not carried out due to frequent occurrence of convulsive rigidity attacks following the introduction of anti-convulsion therapy as well. Instead, administration of midazolam was selected, which produced no opacification when mixed with other drugs and provided early arousal. The efficacy decreased gradually, and the doses of not only midazolam but also pancuronium bromide needed to be increased with additional administration of fentanyl citrate.

Each of midazolam and fentanyl citrate has been reported to cause psychiatric symptoms such as delirium following administration of a high dose or during the withdrawal period following long-term administration. For tetanus against which administration of a high dose or long duration of an anti-convulsion agent is expected to be necessary, the anti-convulsion therapy and systemic maintenance treatment mainly with diazepam play a major role. We thought that attention should be paid to the aforementioned complications in employing those therapies.

The tetanus patients who have to be kept bedridden for a long period cannot avoid reduction of myodynamia. The second patient, because of being in his prime, recovered in about 21 days to a level that he could lead a normal daily life without any trouble, despite 28-day long-term administration of midazolam, pancuronium bromide and fentanyl citrate. It took about 30 days for the first patient to recover despite 15-day administration of the drugs. Because of his advanced age, the manifestations were controlled under spontaneous respiration by continuous administration of diazepam alone without using pancuronium bromide, etc despite endotracheal intubation. If treatment with a muscle relaxant was also needed due to severe rigidity attack, withdrawal from the ventilator would have needed a recovery period of longer duration.

The tetanus patients requiring long-term anticonvulsion therapy may suffer from complications which need special medical attention according to the disease severity and patient age. Careful systemic control is necessary throughout the course of disease.

Conclusions

We experienced two cases of severe tetanus and sympathetic overactivity, and reported them with an overview of the relevant literature.

The vital prognosis in respiratory and circulatory control has been improved with medical progress. Tetanus patients requiring long-term anticonvulsion therapy, however, may suffer from complications which need special medical attention according to the disease severity and patient age. Careful systemic control is necessary throughout the course of disease.

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Sympathetic overactivity を伴った重症破傷風の2例

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中川（ナカガワ）　隆雄（タカオ）[1)2)]・須賀（スガ）　弘泰（ヒロヤス）[1)]・出口（デグチ）　善純（ヨシズミ）[1)]・木村（キムラ）　俊久（トシヒサ）[1)]・鈴木（スズキ）　忠（タダシ）[2)]

破傷風は，*Clostridium tetani* の産生毒素 tetanospasmin に起因する神経系疾患である．今日我が国では，予防接種の普及等により稀となった反面，軽微な外傷でも発症する本疾患は，外傷領域においては常に念頭に置くべき疾患である．その治療管理において痙攣，sympathetic overactivity に対する対処が重要となる．今回我々は sympathetic overactivity を伴った重症破傷風の2例を経験した．1例に対しては phenobartital, diazepam 持続投与下の管理を約15日間要し，また他の1例は pancuronium bromide, midazolam を使用すると共に，循環動態安定のため fentanyl citrate を追加し，人工呼吸器管理期間は約28日を要した．いずれも軽快退院したものの，抗痙攣療法後の回復期に，筋力低下によるリハビリテーション，あるいはせん妄・自殺企図がみられ精神科的治療を要した．呼吸管理の進歩により生命予後は改善されたものの，抗痙攣療法後にも注意すべき合併症があり，全経過を通じ慎重な全身管理が必要である．