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An Unusual Response to *d*-Tubocurarine in a Case of Severe Peripheral Polyneuropathy

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Peripheral polyneuropathy is commonly associated with diabetes, alcoholism, and malignant tumors.[1] We have found no report on anesthetic management of patients with peripheral polyneuropathy. The following is one such case.

REPORT OF A CASE

A 49-year-old woman, admitted for vaginal bleeding, had a medical history of pain and weakness in all four extremities for one and a half years before admission. On examination she had quadriparesis, absence of deep tendon reflexes, ataxia, numbness of the left leg, and moderate atrophy of distal and proximal limb muscles. A recent myelogram and electroencephalogram were within normal limits; cerebrospinal fluid cardiolipin flocculation test was nonreactive. Glucose tolerance test indicated diabetes mellitus. Plasma electrolytes were normal.

Electromyography and peripheral nerve conduction studies demonstrated: 1) inability to record sensory action potentials from any nerve studied except the right sural, which had low-normal amplitude; 2) prolonged distal motor latency of the left peroneal nerve and low-normal motor latency of the right ulnar nerve; 3) slow conduction in right ulnar and median motor fibers; 4) partial denervation of ulnar nerve-innervated muscles; 5) long duration of polyphasic motor unit potentials in scattered muscles. These findings strongly suggested the diagnosis of peripheral polyneuropathy.

A diagnostic dilatation and curettage, uneventfully performed with sodium thiopental and nitrous oxide anesthesia, confirmed the presence of a well-differentiated endometrial adenocarcinoma. Chest x-rays and bone and liver scans were negative for metastases. After a course of pelvic irradiation the patient was scheduled for total abdominal hysterectomy.

Promethazine, 50 mg, and atropine, 0.4 mg, were given im an hour before induction of anesthesia. In addition to the usual monitoring, the patient's right hand was placed in a Twitch Box[2] coupled to a Datascope 865 oscilloscope and Statham writer with a Bell and Howell transducer. A Wellcome peripheral-nerve stimulator was used to deliver supramaximal stimulation to the ulnar nerve.

Thiopental, 250 mg, was given iv, and nitrous oxide, 60 per cent, in oxygen was administered by mask in a semiclosed circuit. Ulnar-nerve stimulation produced a contraction of 0.6 kg, below the normal 2–10 kg.[2] Tetanic stimulation at 30 Hz for 5 seconds produced a sustained contraction of 7.4 kg, well within the normal range of 5–15 kg (fig. 1). Twitch suppression, as well as time to onset and time to peak effect, was normal following incremental 3-mg doses of *d*-tubocurarine (*d*Tc). After 18 mg *d*Tc had been given, the larynx was sprayed with 2 ml of 2 per cent lidocaine and the trachea intubated. Anesthesia was maintained with nitrous oxide, 60 per cent, in oxygen with a supplement of intermittent doses of 0.05 mg, iv, fentanyl every 30 minutes. The total *d*Tc dose during the three-hour surgical procedure was 30 mg. Ventilation was controlled mechanically at a tidal volume of 500 ml and rate of 12/min.

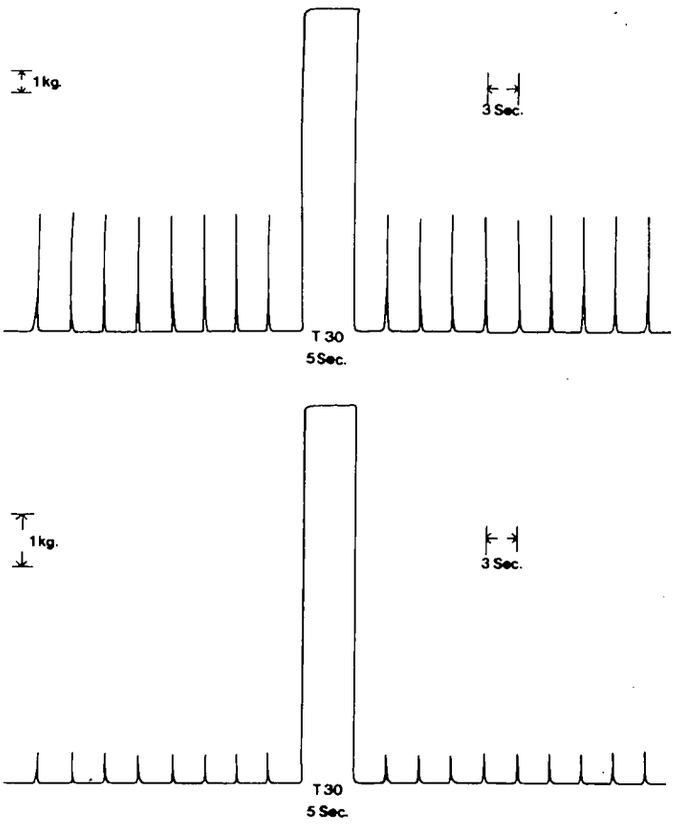

FIG. 1. Before curarization. *Above*, normal response; *below*, patient with peripheral polyneuropathy.

After clinically adequate curarization had been achieved, tetanic stimulation produced muscle contractions with minimal fade and no posttetanic facilitation (fig. 2). Prostigmine, 2.5 mg, and atropine, 1 mg, returned

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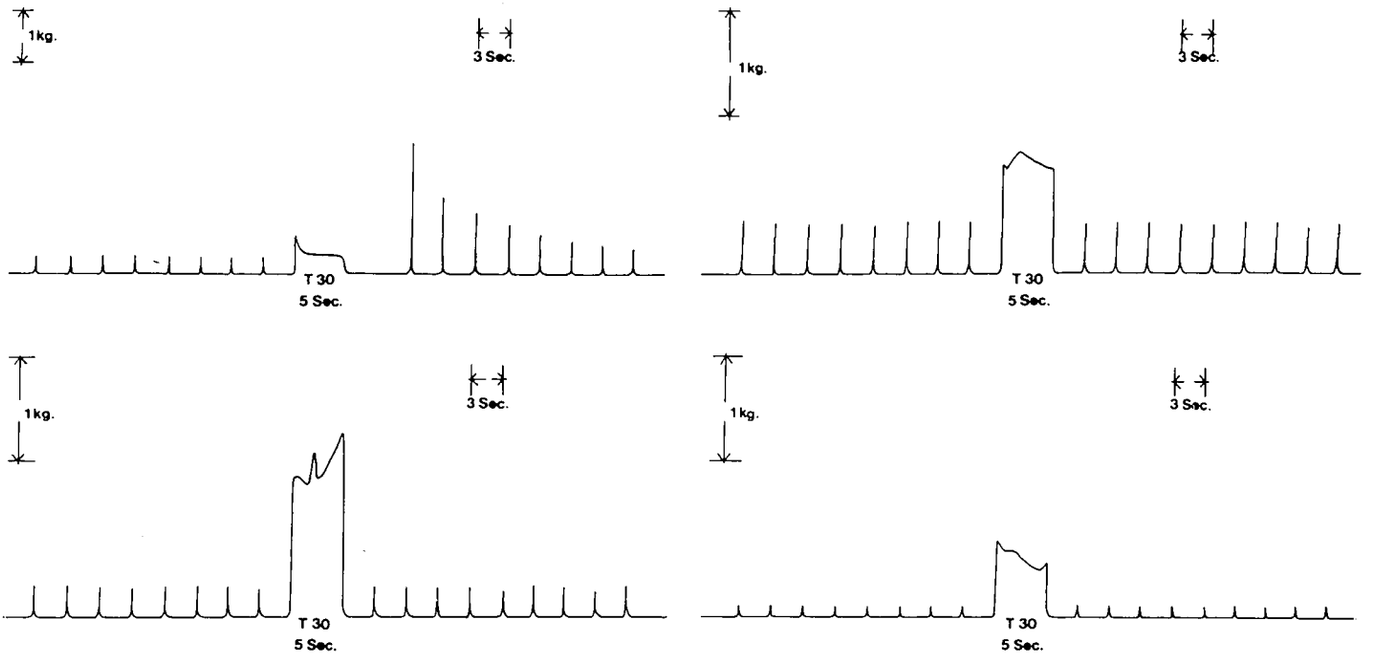

FIG. 2. After curarization.

Above, left, normal response. Twitch suppression 90 per cent. Tetanic contraction fades from 1 to 0.5 kg force. Posttetanic facilitation is present.

Above, right, patient with peripheral polyneuropathy. Twitch suppression 15 per cent. Tetanic contraction with minimal fade; no posttetanic facilitation.

Below, left, patient with peripheral polyneuropathy. Twitch suppression 50 per cent. Tetanic contraction with minimal fade; no posttetanic facilitation.

Below, right, patient with peripheral polyneuropathy. Twitch suppression about 85 per cent. Tetanic contraction with minimal fade; no posttetanic facilitation.

the force of muscular contraction to pre-curarization levels.

DISCUSSION

Polyneuropathy is seen in 30–40 per cent of diabetic patients and 5 per cent of patients who have oat-cell carcinoma of the lung.[3] Ovarian, uterine (body and cervix), and rectal tumors are also associated with peripheral polyneuropathy.[1] Paresthesias, sensor loss, ataxia, and areflexia, as well as hypotonia, weakness, muscle atrophy, and paralysis, are possible. These symptoms may appear before any clinical evidence of tumor is present.[1] Nerve conduction is slow, and fibrillation action potentials and small potentials on voluntary effort are seen in electromyography. Pathologic changes include diffuse patchy myelin degeneration extending along many nerve segments. Transmission failure at the neuromuscular junction,[4] as well as denervation of muscle fibers, may also occur in peripheral polyneuropathy.[5]

In managing this patient, we avoided succinylcholine to prevent hyperkalemia.[6] Control twitch height was abnormally low, but the response to *d*Tc, in terms of time to onset, time to peak effect, percentage suppression, rate of recovery, and response to prostigmine, was within normal limits, suggesting normally functioning neuromuscular junctions.

The response to tetanic stimulation after curarization was most unusual. Contractions with minimal or no fade and with no posttetanic facilitation were consistently seen. Eaton, Lambert,[7] and Wise[8] described action potential facilitation during high-frequency (50 Hz) tetanic stimulation in non-curarized patients who had bronchial adenocarcinoma associated with the myasthenic syndrome. Unlike our patient, these individuals were extremely sensitive to *d*Tc and had definite neuromuscular junction disease.

Variations of tetany and posttetanic facilitation are determined by factors controlling release, mobilization and synthesis of acetylcholine (ACh). Readily releasable ACh is gradually depleted during tetanic stimulation. Early stimuli release larger amounts of ACh per stimulus than later stimuli. The

quantity of ACh released by each subsequent stimulus decreases, and the level finally reached depends upon frequency and duration of stimulation, as well as rate of mobilization and synthesis of ACh.[9] Tetanic stimulation also accelerates ACh mobilization and synthesis, an effect that lingers after the tetanic stimulation ceases, and is the cause of posttetanic facilitation.[9]

Usually the amount of ACh released per impulse greatly exceeds the minimum quantity needed to evoke muscular response, and therefore the decline in ACh release with repetitive stimulation causes no fade.[9] When, however, neuromuscular transmission is partially blocked by muscle relaxant, reduction in ACh release may result in transmission failure and fade. Since rate of ACh depletion is directly proportional to frequency of tetanic stimulation,[10] transmission failure occurs only when tetanic frequency is sufficiently high.

We speculate that in severe peripheral polyneuropathy, diseased peripheral nerves do not propagate all impulses of a tetanic stimulation, and therefore reduce tetanic frequency to a rate too slow to exhaust ACh stores or to stimulate ACh mobilization and synthesis in the neuromuscular junction. This explains the absence of fade and posttetanic facilitation in our patient.

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