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## Original Article

Postoperative peripheral neuropathy considered to be induced by surgical stress<sup>☆</sup>Hisao Ishii, Shigeru Kurimoto<sup>\*</sup>, Masahiro Tatebe, Michiro Yamamoto, Katsuyuki Iwatsuki, Hitoshi Hirata

Department of Hand Surgery, Nagoya University Graduate School of Medicine, Aichi, Japan

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## ABSTRACT

**Background:** Most surgeons are unaware that idiopathic neuropathy, which occurs independently of mechanical injury, can present as postoperative peripheral neuropathy. The aim of this study was to reveal the presence of postoperative neuropathy considered to be induced by surgical stress and to make surgeons aware that idiopathic neuropathy can occur postoperatively.

**Methods:** We conducted a survey among orthopedic surgeons regarding patients with postoperative neuropathies of unknown cause. For each case, the type of neuropathy, preceding surgery and anesthesia, patient background, clinical findings, and clinical course were investigated.

**Results:** Seven patients were identified. The mean time from surgery to the onset of neuropathy was 9.3 days (range 1–15 days). Five of the patients fully recovered spontaneously within 1 year, while the remaining two underwent neurolysis. One patient presented with hourglass-like constrictions in the radial nerve. No inflammatory cells were found in the epineurium of the affected nerve.

**Conclusions:** Although it is rare, postoperative idiopathic neuropathy occurs in clinical practice, and it is crucial that surgeons recognize the existence of this neuropathy to elucidate its pathogenesis as well as to reduce the risk of litigation.

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## 1. Introduction

Postoperative peripheral neuropathy is encountered from time to time in daily clinical practice. Cases of these neuropathies in which symptoms do not improve can sometimes lead to medical lawsuits. Although a majority of cases of postoperative neuropathies are attributable to mechanical injuries during surgery, we infrequently encounter neuropathies of unknown cause. Staff et al. reported postoperative neuropathies that are either spatially or temporally segregated from the surgeries as “post-surgical inflammatory neuropathy” and concluded that the inflammatory immune response might be involved [1]. However, awareness of “post-surgical inflammatory neuropathy” is low, particularly among surgeons, who manage postoperative complications.

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<sup>\*</sup> Corresponding author. Department of Hand Surgery, Nagoya University Graduate School of Medicine, 65 Tsurumai-cho, Showa-ku, Nagoya, 466-8550, Japan. Fax: +81 52 744 2964.

E-mail address: [kurimotos@icloud.com](mailto:kurimotos@icloud.com) (S. Kurimoto).

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Therefore, we conducted a survey questionnaire among orthopedic surgeons to reveal and raise awareness of the presence of idiopathic peripheral neuropathies caused by surgical stress, but not mechanical stress, which would normally be treated as usual postoperative complications.

## 2. Materials and methods

We sent questionnaires to the orthopedic departments of 68 hospitals regarding any experience of postoperative neuropathies of unknown cause in the past 10 years. As in the previous report [1], patients who developed peripheral neuropathies within 30 days of a surgery, which cannot be attributed to mechanical injuries during surgery, were included in this study. The types of surgery were not limited to orthopedic surgery; moreover, patients who visited orthopedic departments due to neuropathy after a non-orthopedic surgery were included. Patients with the following characteristics were excluded from the study: those who had the same neuropathy before surgery, those with neuropathy confirmed at the time of awakening from anesthesia, those with neuropathy due to obvious causes, such as mechanical irritation, those with paralysis

considered to be caused by other diseases, such as cerebrovascular disorders and spinal cord diseases, and those who complained of paresthesia or numbness without motor paralysis. For cases satisfying these criteria, age, gender, preceding surgery, type of anesthesia, type of neuropathy, pain, sensory loss, time from surgery to onset of neuropathy, presence or absence of surgery for neuropathy, surgical and pathological findings, and clinical course of neuropathy were additionally investigated. Imaging results (such as MRI and ultrasonography) and results of electrophysiological examination, if performed, were also collected. All participants provided written informed consent, and this study has been approved by the IRB of the authors' affiliated institutions. The authors received no financial support for the research, authorship, or publication of this article. There are no conflicts of interest to declare.

### 3. Results

Forty-two (61.8%) of the 68 institutions responded to the questionnaire, and a total of seven patients (three males and four females) were identified who met the criteria (Table 1). The mean age was 58 years (range 39–81 years). Prior to the occurrence of the neuropathies, the patients underwent upper limb surgeries (3 patients), gastroenterological surgeries (3), and dermatologic surgery (1). The patients had been administered general anesthesia (3), spinal anesthesia (1), axillary blocks (2), and local anesthesia (1). The clinical diagnoses of the neuropathies included radial nerve palsy (2), anterior interosseous nerve palsy (1), C5 palsy (2), lumbosacral plexopathy (1), and peroneal nerve palsy (1). The mean time from surgery to the onset of neuropathy was 9.3 days (range 1–15 days). In five cases, the patients fully recovered spontaneously within 1 year (range 2–11 months). Neurolysis was performed in two patients who did not recover, and hourglass-like constrictions of the radial nerve were found in one of them. No inflammatory cells were seen in the epineurium collected during surgery.

### 4. Case presentation

**Case 1.** A 48-year-old male with squamous cell carcinoma of the right auricle underwent tumor resection. One year after the surgery, a tissue expander was inserted in his left distal forearm under general anesthesia to cover the skin defect from tumor resection. However, the insertion site gradually ulcerated, and the expander

was removed under axillary block 3 weeks after insertion. No air tourniquet was used in either surgery. Numbness in the left forearm and hand appeared 15 days after removal of the tissue expander; the next day, the patient exhibited left wrist drop. He was diagnosed with radial nerve palsy since the result of manual muscle testing (MMT) of the wrist and finger extensors was 0, while those of all other muscles, including the triceps brachii, were normal. He complained of numbness in the radial nerve area, although the sensation was normal. Six months of conservative treatment did not improve his palsy, and neurolysis was performed. Two hourglass-like constrictions were seen in the radial nerve 5 cm proximal to the lateral epicondyle of the humerus (Fig. 1). Pathological examination of the epineurium at the site of nerve constriction revealed no inflammatory cells (Fig. 2). The minor infiltration of neutrophils was judged as non-specific acute inflammation by pathologists, most likely induced by mechanical stress on the tissue during the surgery. The muscle strength of the wrist and finger extensors slightly improved from an MMT of 0–2 within 1 year after neurolysis. Subsequently, the patient underwent tendon transfer surgery.

**Case 2.** A 39-year-old male who sustained chronic digital nerve injury of the left little finger underwent nerve repair using collagen conduits under axillary block. Fourteen days after the surgery, the patient noticed that his left thumb could not flex as usual. Results of MMT of the flexor pollicis longus (FPL) and the flexor digitorum profundus (FDP) of the index and middle fingers were both 3, that of the pronator quadratus (PQ) was 4. No complaint of sensory

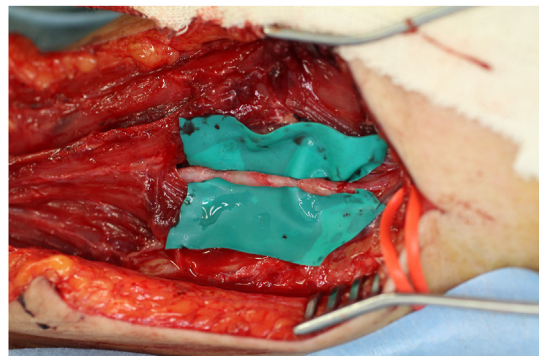
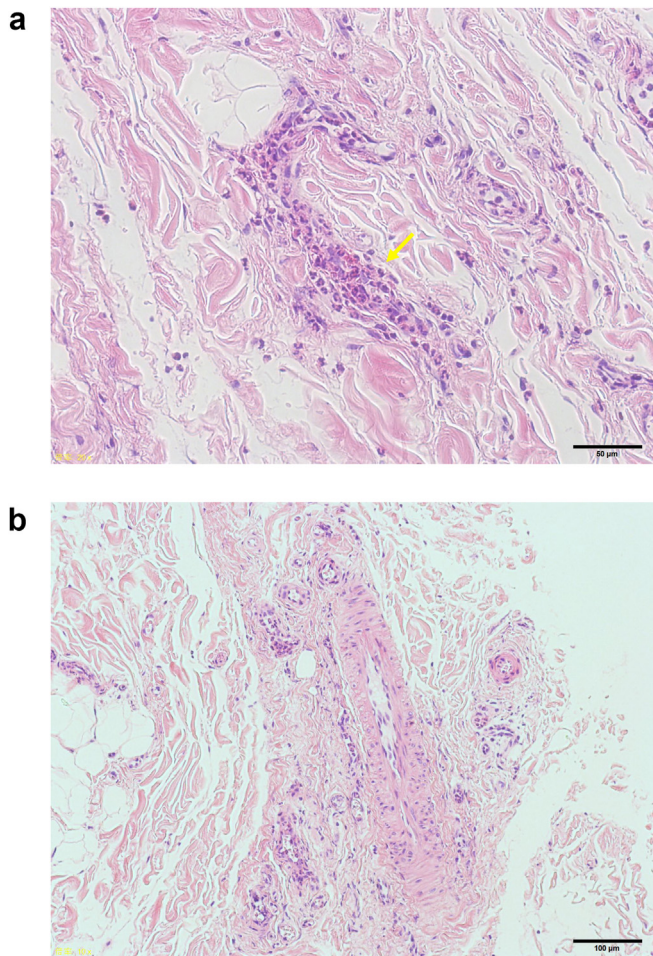


Fig. 1. Two hourglass-like constrictions in the radial nerve (Case 1).

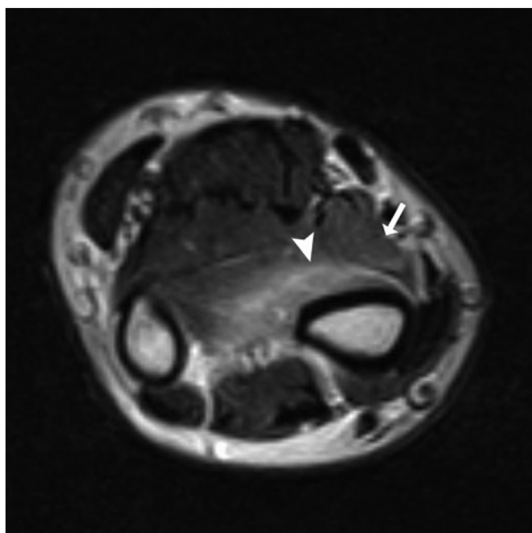
**Table 1**  
Seven cases of postoperative neuropathies considered to be induced by surgical stress.

Case	Age	Sex	Preceding surgery	Anesthesia	Clinical diagnosis of neuropathy	Time from surgery to neuropathy (days)	Sensory disorder	Antecedent pain	Clinical course	Treatment
1	48	M	Removal of tissue expander in Lt. forearm	General	Lt. high radial nerve palsy	15	–	–	Not recovered	Neurolysis
2	39	M	Digital nerve repair in Lt. little finger	Axillary block	Lt. anterior interosseous nerve palsy	14	–	–	Partially recovered	Neurolysis
3	81	M	Tumor resection in Lt. planter	Lumber	Bil. lumbosacral plexopathy	5	–	+	Recovered (at 2 M)	Conservative
4	61	M	Subtotal esophagectomy	General	Lt. peroneal nerve palsy	15	–	–	Recovered (at 11 M)	Conservative
5	73	F	Subtotal esophagectomy	General	Rt. C5 palsy	1	+	–	Recovered (at 3 M)	Conservative
6	39	F	Lt. endoscopic carpal tunnel release	Local	Rt. C5 palsy	14	–	+	Recovered (at 6 M)	Conservative
7	67	M	Total gastrectomy	General	Rt. high radial nerve palsy	1	–	–	Recovered (at 3 M)	Conservative

Lt: left, Rt: right, Bil: bilateral.



**Fig. 2.** Hematoxylin and eosin staining of the epineurium at the site of the nerve constriction (Case 1). (a) Minor infiltration of neutrophils (arrow) diagnosed as non-specific acute inflammation, probably induced by mechanical stress on the tissue during surgery. (b) No inflammatory cells around blood vessels.



**Fig. 3.** Hyperintense signal in the flexor pollicis longus (arrow) and the pronator quadratus (arrowhead) on T2-weighted MRI (Case 2).

impairment was observed. MRI demonstrated a hyperintense signal in the FPL and PQ on T2-weighted images (Fig. 3), and the patient was diagnosed with median nerve palsy (anterior interosseous nerve palsy). After 7 months follow-up, the strength of the index and middle finger improved, although weakness in the FPL remained, and neurolysis was performed. Hardening of the median nerve was observed at the anterior interosseous nerve bifurcation. No hourglass-like constriction of nerves was observed. Pathological examination of the epineurium revealed only scarring, and no inflammatory cells were seen.

**Case 3.** An 81-year-old male with hemangioma of the left sole underwent tumor resection under lumbar anesthesia. Pain and numbness in bilateral lower extremities and urinary retention appeared on the fifth postoperative day, following which, bilateral leg paralysis and gait disturbance occurred. Results of MMT of the right quadriceps (Q-ceps), anterior tibialis (TA), extensor hallucis longus (EHL), and the flexor digitorum profundus (FDP) of the index and middle fingers were all 4, those of the left Q-ceps, TA, and EHL were 3-. There was no description of the strength of the hamstrings. Deep tendon reflexes were reduced in the right knee and ankle and absent in the left knee and ankle. A thoracolumbar MRI showed no significant abnormalities, such as epidural hematoma. Steroids were administered intravenously for 3 days, after which muscular strength recovered completely, and urinary retention disappeared 2 months after surgery.

**Case 4.** A 61-year-old male with esophageal cancer underwent subtotal esophagectomy under general anesthesia. His medical history included mild hemophilia. Numbness in the left forefoot and left-sided foot drop appeared 15 days after the surgery. Results of MMT of TA and EHL were 3 and 4, respectively. Deep tendon reflexes in the left knee and ankle were normal. No Tinel sign was found over the peroneal nerve. Lumbar MRI revealed no significant abnormalities. He was diagnosed with incomplete peroneal nerve palsy, and mecobalamin was administered orally for 7 months. All neuropathic symptoms had disappeared 11 months after the surgery.

**Case 5.** A 73-year-old female with esophageal cancer underwent subtotal esophagectomy under general anesthesia. On waking from anesthesia, she did not complain of neurological symptoms. The next evening, she was unable to raise her right arm. Spine surgeons examined and diagnosed right C5 palsy since the results of MMT of the deltoid, biceps brachii, triceps brachii, and wrist and finger extensors/flexors were 1, 0, 5, and 5, respectively. She had hypesthesia in the right C5 and C6 dermatomes, with no neuropathic pain. Cervical computed tomography and MRI showed only degenerative changes and no canal or foraminal stenosis. Her neuropathic symptoms gradually improved and completely recovered spontaneously in 3 months.

**Case 6.** A 39-year-old female with left carpal tunnel syndrome underwent endoscopic carpal tunnel release under local anesthesia using an air tourniquet. Two weeks after the surgery, the patient was unable to raise her right (opposite side from the surgery) arm. Before that, she felt pain from right shoulder to arm. The result of MMT of the deltoid was 2+, whereas results of MMT of the trapezius, biceps brachii, triceps brachii, and wrist and finger extensors/flexors were all 5. No complaint of sensory impairment was noted. Deep tendon reflexes of the biceps, triceps, and brachioradialis were normal. Cervical MRI revealed no abnormalities that can possibly lead to the palsy. No medication was administered; she recovered completely in 6 months.

**Case 7.** A 67-year-old male with gastric cancer underwent total gastrectomy under general anesthesia. The patient complained of no neurological symptoms on waking from anesthesia; however, he exhibited right wrist drop the next day. He experienced no numbness or pain. He was diagnosed with incomplete high radial

nerve palsy, since results of MMT of the wrist and finger extensors were 0 and 2, respectively, whereas results of MMT of all other muscles, including the triceps brachii, were normal. Cervical MRI showed only degenerative changes and no cause for the palsy. Mecobalamin was administered for 3 months, and he recovered completely.

## 5. Discussion

Prior to the report on “post-surgical inflammatory neuropathy” by Staff et al. [1], peripheral neuropathy associated with surgery has often been reported. In 1990, Nagano et al. described 5 of 17 patients with anterior interosseous nerve palsy who complained of preceding pain after undergoing surgery 1 week to 2 months before the onset of palsy [2]. Van Alfen reported 115 of 246 patients with neuralgic amyotrophy (Parsonage-Turner syndrome) who had an antecedent event, 16 of which were surgeries. Furthermore, 15 of these 16 patients developed neuralgic amyotrophy within 2 weeks of surgery [3]. It is well known that delayed deltoid and/or biceps brachii muscle weakness, called C5 palsy, occurs after cervical decompression surgery. The most cited pathogenic mechanism of postoperative C5 palsy is the extradural tethering effect; however, its etiology has not been elucidated. There are some reports suggesting that C5 palsy is caused by neuralgic amyotrophy or brachial neuritis [4,5]. Some cases of Guillain-Barré syndrome have also been reported after surgery, including mandibular, lung, spine, and pelvic surgeries [6–11]. Thus, although relationships between some neuropathies and history of surgery have been reported, it is not well known that idiopathic paralysis occurs after surgery. Five of our 7 cases occurred within 1 year before the survey and were still being treated at the time of the survey, despite inquiring for experience of surgeons within the past 10 years. Therefore, it is possible that some past cases disappeared from the list because the attending physicians had transferred to other facilities, or because the doctors had forgotten past cases. Simultaneously, some doctors noticed that the patient's paralysis was not due to mechanical injury while participating in this study. This suggests the possibility that many previous cases were treated without being diagnosed as postsurgical idiopathic neuropathies. Because postoperative paralysis is a serious complication that causes a doctor-patient problem, it is crucial to make surgeons aware of postoperative neuropathy that is independent of mechanical stress.

In the cases in this study, pathological examination did not reveal the presence of inflammation. In contrast, Staff et al. found inflammatory cells in the nerve biopsies of 21 of 23 patients suspected of having post-surgical inflammatory neuropathy, and they excluded the remaining 2 cases from their study [1]. This may suggest that our cases were not cases of “inflammatory” neuropathy. In our cases, biopsies were performed with neurolysis at 6 months or more, not immediately after onset, so it is possible that inflammation had subsided at the time of biopsy. Furthermore, Staff et al. performed nerve biopsies, whereas only the epineurium of the affected nerve was examined in our cases, which could contribute to the differences in results. Focal, multifocal, and diffuse neuropathy have been reported in post-surgical inflammatory neuropathy, whereas 6 of 7 patients in this study had single-limb involvement. Staff et al. detected inflammatory changes in biopsies of the cutaneous nerve, not the paralyzed motor nerve [1]; it is considered that systemic stress response causes paralysis of more vulnerable nerves, which leads to phenotypic differences. Although only 2 of our 7 patients experienced pain preceding the paralysis, most of our patients did not have a sensory impairment, and their neuropathy can also be classified as neuralgic amyotrophy. The

possibility that an immune response is involved in neuralgic amyotrophy has previously been pointed out [12]. Post-surgical inflammatory neuropathy may be considered to be neurological amyotrophy associated with surgery and not another disease entity.

In our 2 cases (Cases 5 and 7), paralysis occurred the day after surgery, before a primary learned immune response would be expected to develop. In the study of Staff et al. approximately half of the patients (16/33) developed neuropathy within 1 day after surgery; they deduced that the stress of surgery combined with genetic predisposition and subclinical pre-existing inflammation or neuropathy triggered the inflammatory neuropathy.

This study was conducted with the aim of clarifying the occurrence of postoperative neuropathies considered to be induced by surgical stress; hence, it was a questionnaire survey regarding the experience of surgeons in the past 10 years. In our 68 affiliate hospitals, where we perform 45,000 orthopedic surgeries per year, it was impossible to determine the occurrence frequency, as this study included patients who visited our orthopedic surgery departments for treatment of neuropathies after undergoing surgeries in other departments or other hospitals. In addition, since this was a retrospective study, the available data are limited, and the pathogenesis has not been elucidated. With the aim of solving these problems and establishing effective treatment options, we are currently performing a prospective study of all surgical cases in our facilities.

In this survey, we found 7 cases of postoperative neuropathies considered to be induced by surgical stress. Not only to provide effective treatment but also to avoid medical lawsuits, it is important to spread the recognition of postoperative neuropathy not due to mechanical stress to surgeons.

## Declaration of competing interest

None.

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