

**Anterior interosseous nerve and posterior interosseous nerve involvement in neuralgic amyotrophy**

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**Key words:** anterior interosseous nerve, neuralgic amyotrophy, peripheral nerve palsy, posterior interosseous nerve, radial nerve, neurolysis.

## Highlights

- Neurolysis can be an effective treatment for neuralgic amyotrophy
- Anterior and posterior interosseous syndrome is associated with fewer painful bouts
- Inflammation and fibrosis of nerves cause persistent palsy

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3 **ABSTRACT**  
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6 *Objectives:* The aim of this study was to gain a better understanding of anterior interosseous nerve  
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9 and posterior interosseous nerve involvement in neuralgic amyotrophy.  
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12 *Methods:* In a retrospective chart review, 51 cases (49 patients) with anterior and posterior  
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14 interosseous nerve syndrome were investigated in terms of their symptoms, course of disease, and  
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17 prognosis.  
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22 *Results:* Patients first presented with pain in 52.9% of cases. The location of the pain was distal to  
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25 the shoulder in most cases (85.1%). Sensory involvement was found in 27.5% of patients, and  
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28 patients with pain before paresis had fewer sensory symptoms ( $p = 0.006$ ). Neurolysis significantly  
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30 improved Hand20 scores, but conservative treatment did not ( $p = 0.020$  vs.  $0.204$ ).  
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34 *Conclusions:* Patients with anterior interosseous nerve and posterior interosseous nerve affection in  
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37 neuralgic amyotrophy had less pain. Neurolysis can be superior to conservative treatment in the  
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40 patients with focal constrictions and no spontaneous recovery.  
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## 1. Introduction

Neuralgic amyotrophy (NA) is an acute inflammatory/dysimmune neuropathy involving one or several nerves of the brachial plexus, and is a syndrome characterized by attacks of neuropathic pain and subsequent paresis in the upper extremities [1,2]. However, NA has various underlying mechanisms, phenotypes, and prognoses, and can manifest with involvement of solely the anterior interosseous nerve (AIN) or posterior interosseous nerve (PIN) [3,4]. The lesions of palsy are not confined only to the AIN and PIN [6-11]. Nagano divided AIN palsy into 2 groups [7]. Group I refers to palsy only in muscles innervated by the AIN. Group II include palsy of muscles innervated by the AIN and other muscles innervated by a median nerve, such as the pronator teres. AIN and PIN syndromes involve acute, sometimes painful, and often multifocal peripheral nerve symptom involvement of the upper extremity with a monophasic course. Currently, both syndromes are largely considered as part of NA [12-14]. There is currently no case series of AIN and PIN affection in NA. Therefore, the objective of this study was to determine the characteristics of AIN and PIN syndromes to help clinicians identify and treat patients earlier and more effectively.

## 2. Methods

### 2.1 Patients

We included patients with spontaneous AIN and PIN syndromes, but these syndromes sometimes involved other types of nerve palsy. We included cases with spontaneous median nerve palsy involving the AIN and radial nerve palsy involving the PIN. Palsy is defined as an acute uni- or bilateral monophasic, predominantly motor deficit, in the absence of evidence of an underlying generalized neuropathy. Electromyography (EMG) or magnetic resonance imaging (MRI) shows signs of denervation or reinnervation in muscles innervated by the affected nerves; alternatively, the patients are clinically diagnosed. We conducted a chart review to identify patients who met these criteria in our hospital between April 2004 and April 2014. The Ethics Committee of Nagoya University approved this study and we obtained informed consent.

### 2.2 Clinical data

The severity of the paresis during an attack was defined according to the Medical Research Council (MRC) grade of the affected muscles. The location of the pain, as described by the patients, was classified into 6 different patterns. We classified the distribution of the paresis into anatomical regions according to nerve distribution. The AIN group included muscles innervated by the AIN, the median nerve group included muscles innervated by the AIN and other branches of the median nerve,

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3 the PIN group included muscles innervated by the PIN, the radial nerve group included muscles  
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6 innervated by the PIN and other branches of the radial nerve, and the ulnar nerve group included  
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9 muscles innervated by the ulnar nerve.  
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12 We evaluated conservative and operative treatments and their efficacy. We recommended  
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14 surgery for all patients who presented no recovery signs by 3 months after the onset of symptoms.  
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18 Neurolysis has been shown to have a good outcome for patients younger than 50 years [5]. For  
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20 patients less than 50 years old who agreed to the operation, we performed neurolysis within 2 years  
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22 after the onset. Tendon transfer was performed at more than 2 years after the onset for patients less  
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24 than 50 years old, or at more than 1 year after the onset for patients over 50 years of age.  
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28 Constriction was mostly reported to occur 0–6 cm proximal to the medial condyle in individuals  
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30 with spontaneous AIN syndrome and 1–3 cm proximal to the supinator inlet in cases with PIN  
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32 syndrome [15]. We explored the lesions in the nerves at that site and extended the site proximally  
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34 and distally during operation; however, we did not explore the ulnar nerve. When patients were  
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36 treated by tendon transfer, the final assessment was made immediately before tendon transfer. We  
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38 have used various terms to describe the intraoperative appearance of the explored nerves, and have  
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40 defined them as follows. The term "compression" has been used to describe nerves that demonstrated  
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42 narrowing in the presence of an external compressive object. The term "constriction" describes  
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44 nerves that appear narrow in the absence of any external compression, while "torsion" describes  
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3 nerves that are twisted. "Stiffness" referred to that segment of a nerve that surgically felt stiffer or  
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6 more rigid than the parts of the nerve proximal or distal to it. The term "color change" referred to a  
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9 segment that appeared to differ in color than the parts of the nerve proximal or distal to it.  
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12 Because there is no current standard definition for recovery in NA, some parameters were  
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14 recorded representing residual pain and paresis. Good muscle strength recovery was defined as MRC  
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16  $\geq 4$  and poor muscle strength recovery as MRC  $< 4$  in the affected muscle. The final MRC grade of  
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19 the patients treated by tendon transfer was determined immediately before operation.  
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25 The Hand20 questionnaire was administered (the highest score of 100 represents the worst  
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27 subjective function; 0, the best function)[16]. The Hand20 is an illustrated, 20 short,  
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29 easy-to-understand questionnaire for disorders of the upper limb. The Hand20 questionnaire has  
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32 been validated to be comparable to the Disabilities of the Arm, Shoulder, and Hand—Japanese  
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35 Society for Surgery of the Hand (DASH-JSSH).  
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#### 44 *2.3 Statistical analysis*

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47 The demographic and clinical data available from chart reviews were analyzed using SPSS version  
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50 23 (SPSS Inc., Chicago, IL, USA). We also compared males and females to determine whether there  
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53 were gender-related differences in NA. Differences for both subgroups were tested for categorical  
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56 variables using Pearson's  $\chi^2$  method and an independent Student's *t*-test for continuous variables.  
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3 Differences in the Hand20 questionnaire were tested using Student's *t*-tests, paired *t*-tests, and  
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6 two-way repeated ANOVA. The results are presented the mean  $\pm$  standard error where applicable,  
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9 and the level of significance was set as  $p < 0.05$  in all analyses.  
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### 16 **3. Results**

#### 17 18 19 *3.1 Study population characteristics*

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22 A total of 49 patients (51 cases) were identified retrospectively from our hospital's charts. The study  
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25 population consisted of 32 males and 19 females. The mean age at onset was 44.1 years (median 44,  
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28 range: 13–77 years). Twenty-one cases were affected on the right side and 29 cases on the left. One  
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31 patient presented with bilateral paresis. One patient had recurrence twice. A family history of the  
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34 disease occurred in 2 patients (mother and daughter). The average follow-up time from onset was  
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38 21.7 months.  
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There were no significant differences between males and females in antecedent events ( $p = 0.574$ ), sensory symptoms ( $p = 0.132$ ), or residual symptoms at last visit ( $p = 0.553$ ) but females had more pain before onset than males ( $p = 0.022$ ).

## 3.2 Characteristics of attacks

### 3.2.1 First symptom and paresis

In 52.9% of the cases, the first symptom of the attack was pain (Table 1), which involved only 1 arm in all cases. The locus of the initial pain was variable, including pain in the shoulder (11.1%), whole arm (33.3%), elbow (25.9%), upper arm (18.5%), lower arm (7.4%), and in and/or radiating from the neck (3.7%) (Table 2).

In the attacks characterized by initial pain, the first signs of weakness appeared within 24 h, 1–7 days, and 1–2 weeks in 22.2%, 44.4%, and 18.5% of the patients, respectively. In 14.8% of cases, paresis did not manifest until > 2 weeks later. In terms of distribution of the deficits, the AIN was the most common site (35.3%), followed by the PIN (23.5%), the median nerve (15.7%), the radial nerve (13.7%), the median and radial nerve (3.9%), the PIN and ulnar nerve (3.9%), the AIN and PIN (2.0%), and the radial nerve and ulnar nerve (2.0%) (Table 3).

### 3.2.2 Sensory symptoms

Hypoesthesia and/or paresthesia during an attack were reported in 27.5% of the patients. In 7 cases, although the motor deficit was limited to the AIN or PIN, patients exhibited the sensory symptom in their fingers. The patients with pain before paresis had fewer sensory symptoms than those without pain ( $p = 0.006$ ).

### 3.3 Predisposing factors and medical histories

The patient reported an antecedent event in 41.2% of the attacks, and overuse was the most common (Table 4). In 57.1% of the cases, the event occurred within 1 week prior to the attack. Malignancies were present in 5.9% of cases. The prevalence of diabetes mellitus in our study population was 5.9% versus 11.2% in the general population of Japan in 2011. Seven patients had hypercholesterolemia.

### 3.4 Laboratory findings

Blood analyses were performed in 31 patients (60.9% of total). Liver enzymes were found to be elevated in 7 patients, who had no identifiable organic pathology. We did not perform tests for Hepatitis E virus, because no patients complained of abdominal symptoms.

### 3.5 Electrophysiological study

EMG and nerve conduction studies (NCS) were performed in 14 cases (27.5%). All of these cases showed neurogenic abnormalities in EMG, while 21.4% of cases showed no abnormalities in the nerve that was considered as the lesion in NCS.

### 3.6 Imaging studies

In 27 patients (52.9%), a chest X-ray was performed, which was abnormal in 1 case who showed

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3 consolidation due to pneumonia. We found no elevated diaphragm halves that were due to phrenic  
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6 nerve involvement, and no superior sulcus (Pancoast) lung tumor.  
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10 In 10 cases (19.6%), an MRI scan of the cervical spine was performed. None of the  
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12 abnormalities found could explain the clinical features and course in these patients. In 1 case, an  
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14 MRI scan of the brachial plexus was performed, which demonstrated high intensity in T2-weighted  
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16 images in 1 case who had AIN syndrome on the left side and PIN syndrome on the right side. In 37  
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18 cases (72.5%), an MRI scan of the affected extremity was performed, and demonstrated a high  
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20 intensity in T2 and/or short inversion time inversion recovery images (STIR) in the affected muscles  
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22 in 18 (47.4%) cases, and atrophy in 8 cases (21.1%). In 4 cases (10.5%), MRI showed high intensity  
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25 in the T2-weighted and/or STIR images of the affected nerve (Figure 1).  
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### 34 35 36 37 38 *3.7 Operative findings and pathological findings* 39

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41 We operated 9 cases of median nerve palsy and 10 cases of radial nerve palsy. We explored both  
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43 nerves below and above the elbow. We found abnormal changes in 94.7% of the cases treated by  
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45 neurolysis; compression was present in 4 cases, constriction in 8 cases, torsion in 1 case, stiffness in  
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47 8 cases, and color change in 7 cases (Figure 2). In 11 cases, pathological examination of the lesion in  
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49 the perineurium and epineurium were performed. Fibrosis was found in 9 cases and lymphocyte  
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51 infiltrates in 1 case (Figure 3). There were no significant differences between pain before onset and  
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3 constriction ( $p = 0.335$ ).  
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10 *3.8 Functional recovery and residual symptoms*  
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12 In 19 cases, neurolysis was performed at 2–12 months (average: 5.5 months), and in 4 cases, tendon  
13 transfer was performed at 12–28 months (average: 21.5 months) from symptom onset. In 72% of  
14 cases treated with neurolysis, recovery of motor function was observed 1 day to 13 months after  
15 surgery (average: 2.9 months). Two patients underwent tendon transfer at 6 and 10 months after  
16 neurolysis. In 71.4% of cases treated conservatively, recovery of motor function took on average 5.4  
17 months. Full muscle strength recovery was observed in 36.8% of cases treated by neurolysis and in  
18 25% of cases who received conservative treatment ( $p = 0.201$ ).  
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35 Of the patients who were followed-up over 1 year or who showed full recovery within 1  
36 year after onset, cases were excluded if their MRC grade exceeded 4 at the first visit or if they  
37 showed signs of recovery within 3 months (neurolysis: 16 cases; conservative treatment: 20 cases).  
38 The percentage of these cases that showed good muscle strength recovery after neurolysis was  
39 62.5%; and of those receiving conservative treatment, 35% ( $p = 0.096$ ). The percentage of patients  
40 with no sign of recovery within the follow-up period was 10.5% after neurolysis treatment and  
41 28.5% after conservative treatment. There was no correlation between age and final MRC grade.  
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57 The patients complained of pain in 9.8% and of sensory symptoms in 7.8% of the cases at  
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3 the last visit. The Hand20 score at the first visit before treatment was on average 62 (27–91) in  
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6 patients receiving neurolysis and 32 (7–65) in those receiving conservative treatment ( $p = 0.047$ ).  
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9 The Hand20 score at the last visit was 24 (1–69) in the neurolysis group and 17 (0–55) in the  
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12 conservative treatment group. Neurolysis significantly improved the Hand20 scores, but  
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15 conservative treatment did not ( $p = 0.020$  vs.  $0.204$ ). However, there was no significant difference in  
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19 the improvement of Hand20 scores between neurolysis and conservative treatment ( $p = 0.144$ ).  
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#### 4. Discussion

Pain preceding the onset of weakness is a common feature of NA: in 90% of the patients, NA was heralded by pain [3]. However, the absence of pain during an attack has also been reported previously [2]. With only 52.9% of patients in the current study presenting with pain at the first visit, our results indicated that pain is a less frequent symptom in AIN and PIN syndromes. However, although sensory symptoms were reported in 27.5% of patients, the patients with motor-specific palsy reported more pain than those with sensory involvement.

Concerning diagnostic tools for NA, MRI detects denervation atrophy and neurogenic edema [17], revealing both denervated muscles and nerve lesions. Our results demonstrated a low rate of detection of abnormalities, because MRI settings could vary. MR neurography should have been required to detect nerve lesions [18]. High resolution ultrasound is able to identify the affected nerve and the site of constriction and nerve torsion (an hourglass-like appearance) to guide surgery [19,20]. However, EMG remains the most commonly used diagnostic test. EMG and NCS are used in combination to detect nerve lesions; both show motor axon loss associated with NA in a different way. Electrophysiology should always form part of the diagnostic work-up of NA patients, as it is the only method for confirming nerve lesions and to reveal its type (axon loss versus demyelination). We performed EMG only in 29.4% of patients and the diagnosis was made on clinical findings.

Previous pathological studies of NA and AIN/PIN syndrome described mononuclear

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3 inflammatory cell infiltration of the nerves [21-23]. In our study, most cases showed fibrosis instead.  
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6 This difference may be reflective of the phase of the inflammatory process. Nevertheless, fibrosis is  
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8 thought to underlie the observed nerve constriction, which is of clinical significance, as residual  
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10 symptoms of NA may be due to this constriction and/or other nerve changes.  
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16 Recently, constriction of the affected nerve has been reported in patients with NA  
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18 [19,24,25]. Good muscle strength recovery after neurorrhaphy or autografting for constriction has  
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20 been seen in several studies [5,26-30]. In addition, our results suggest that neurolysis can be superior  
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22 to conservative treatment for countering the mechanical constriction of nerves by fibrosis. In terms  
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24 of surgical treatment, it should be made clear that neurolysis is useful only if severe constriction  
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26 (with or without nerve torsion) is present (at the site where neurolysis will be carried out), and there  
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28 is no spontaneous recovery. In patients with spontaneous recovery, imaging studies show swollen  
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30 nerves with or without incomplete focal constrictions. Regarding the waiting period for spontaneous  
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32 recovery before surgery is indicated, the distance between the site of constriction and the muscles to  
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34 be reinnervated should be taken into account. The difference between conservative and operative  
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36 treatment was not statistically significant in this study; however, operative treatment tends to be  
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38 superior to conservative therapy in such severely affected patients. Our study population was small  
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40 and the nerve fascicular lesion may have been more proximal than where we explored [18]. Our  
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42 study was a retrospective study. A prospective randomized control study is needed to confirm  
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6 Pasonage and Turner have described NA, but there were two cases without pain [1]. Van  
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9 Alfen has shown that 10% of the patients with neuralgic amyotrophy have no pain before onset [12].  
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12 Painless NA is therefore 1 category of the condition [12,14]. AIN and PIN syndromes are largely  
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15 considered part of NA [12-14,31]; however, from the point of view of AIN and PIN syndromes,  
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18 about 50% of patients experience no pain. Therefore, use of the term “neuralgic” should be  
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22 reconsidered, and this should be recategorized.  
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## 28 **5. Conclusion**

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31 Overall recovery of NA is less favorable. Neurolysis can be superior to conservative treatment for  
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35 patients showing no spontaneous recovery and those with nerve constriction in NA.  
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6 physicians.  
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9 The authors declare that they have no conflict of interest.  
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**Table 1. Characteristics of attacks**

<b>First symptom</b>	Pain	Paresis	Sensory	Discomfort	<b># Cases</b>
	52.9%	33.3%	7.8%	5.9%	51
<b>Time from prodrome to paresis</b>	< 24 h	1–7 days	1–2 weeks	> 2 weeks	<b># Cases</b>
	20%	60%	6%	14%	35

**Table 2. Location of pain**

<b>Location</b>	<b>% Cases</b>	<b># Cases</b>
Neck and back	3.7	1
Shoulder	11.1	3
Whole arm	33.3	9
Elbow	25.9	7
Upper arm	18.5	5
Lower arm	7.4	2

**Table 3 Nerve involvement**

<b>Involved nerve</b>	<b>Percentage</b>	<b>Cases</b>
AIN	35.3	18
PIN	23.5	12
MN	15.7	8
RN	13.7	7
MN and RN	3.9	2
PIN and UN	3.9	2
AIN and PIN	2.0	1
RN and UN	2.0	1

AIN: anterior interosseous nerve, PIN: posterior interosseous nerve, MN: median nerve, RN: radial nerve, UN: ulnar nerve

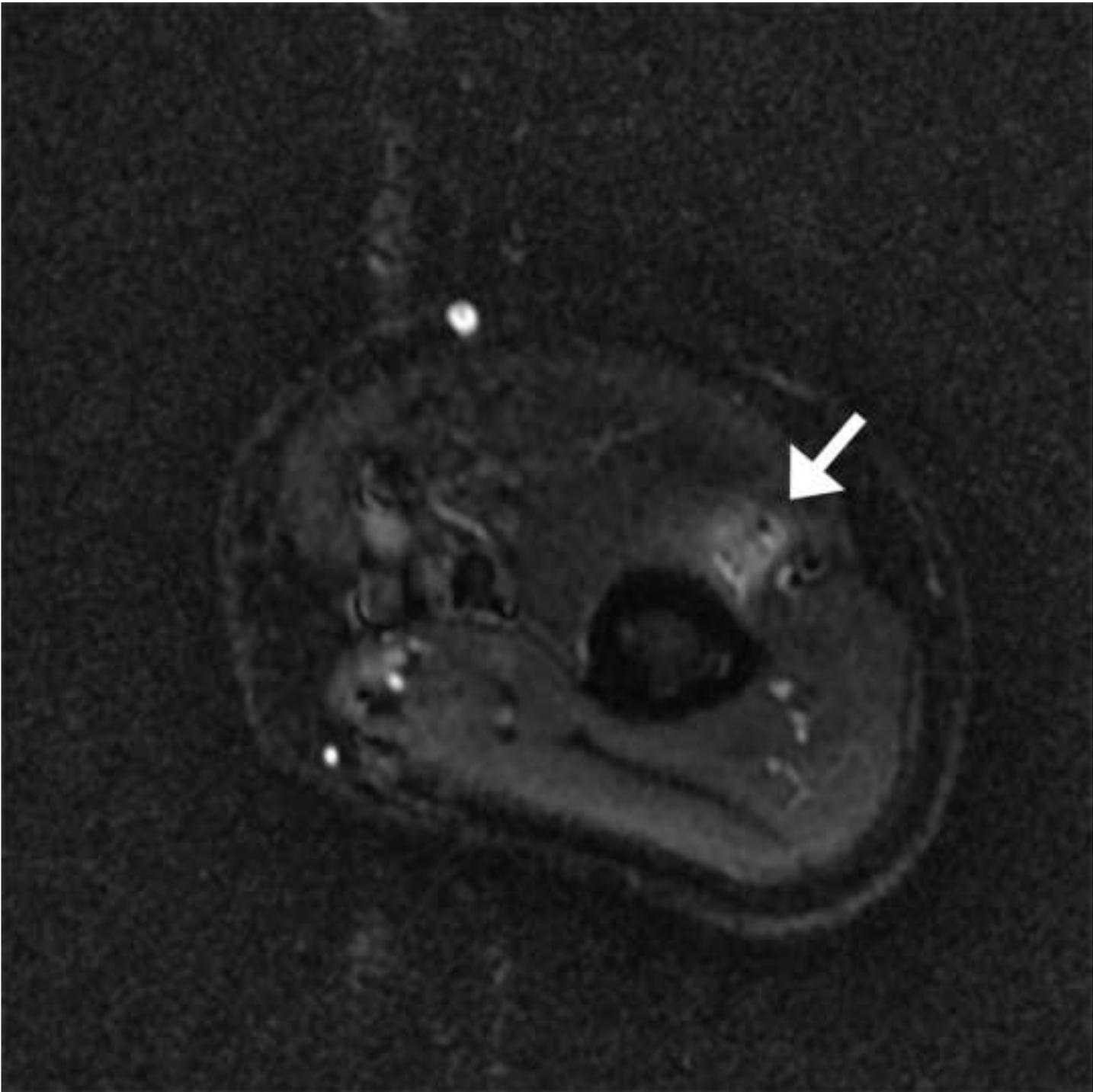
**Table 4 Antecedent events**

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<b>Antecedent</b>		
<b>event</b>	<b>Percentage</b>	<b>Cases</b>
Over use	21.6	11
Operation	9.8	5
Infection	5.9	3
Trauma	2.0	1
Other	2.0	1

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Figure(s)  
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**Figure 1.** MRI of an affected extremity in a patient with radial nerve palsy. The brachioradialis, extensor carpi radialis longus, extensor carpi radialis brevis, supinator, extensor pollicis longus, abductor pollicis longus, and extensor digitorum were affected, but the triceps brachii were not affected. Sensory disturbance was present at the web of skin between the thumb and index finger. A short inversion time inversion recovery image showing radial nerve high intensity at 50 mm above the lateral condyle (white arrow).

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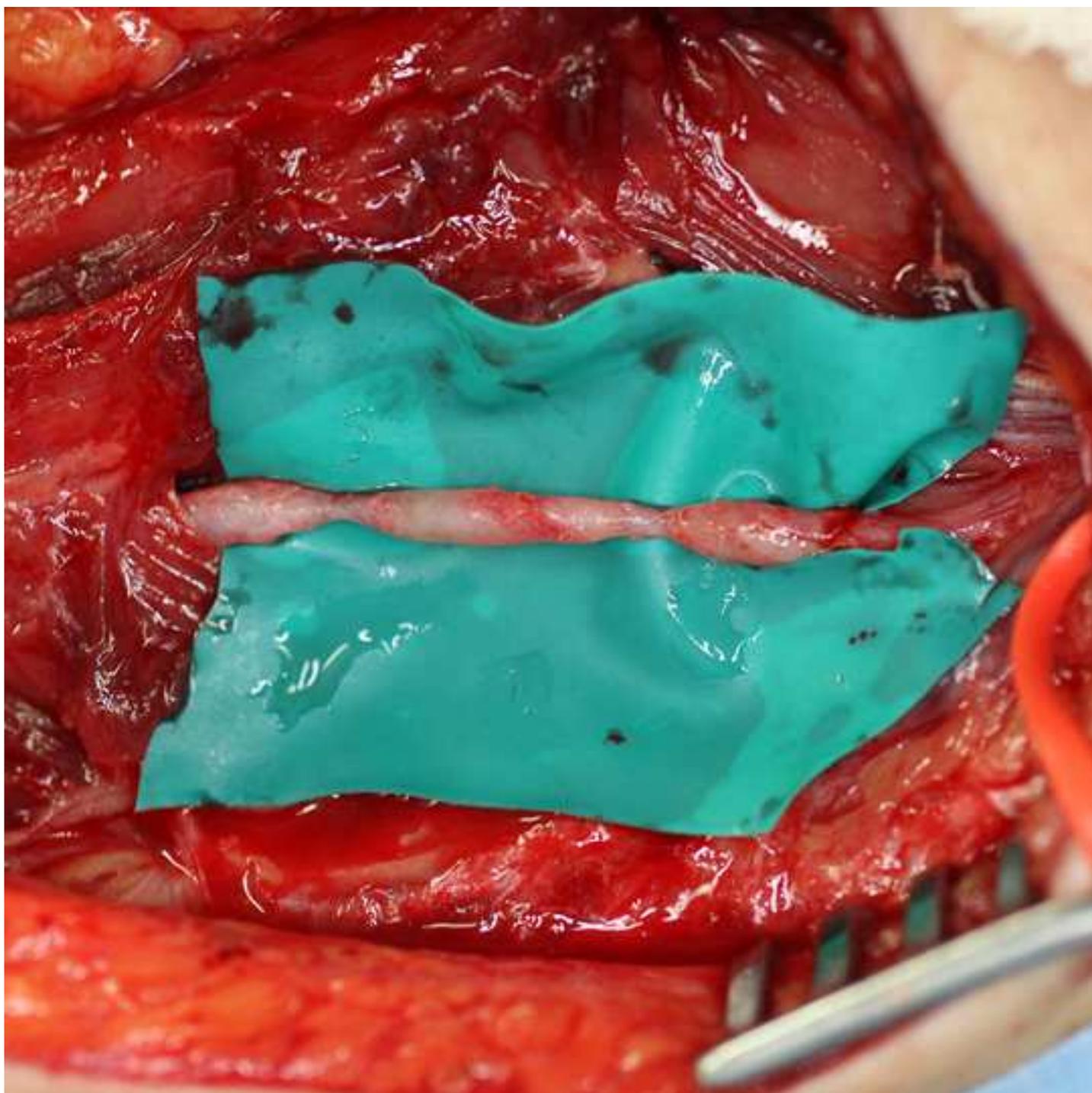
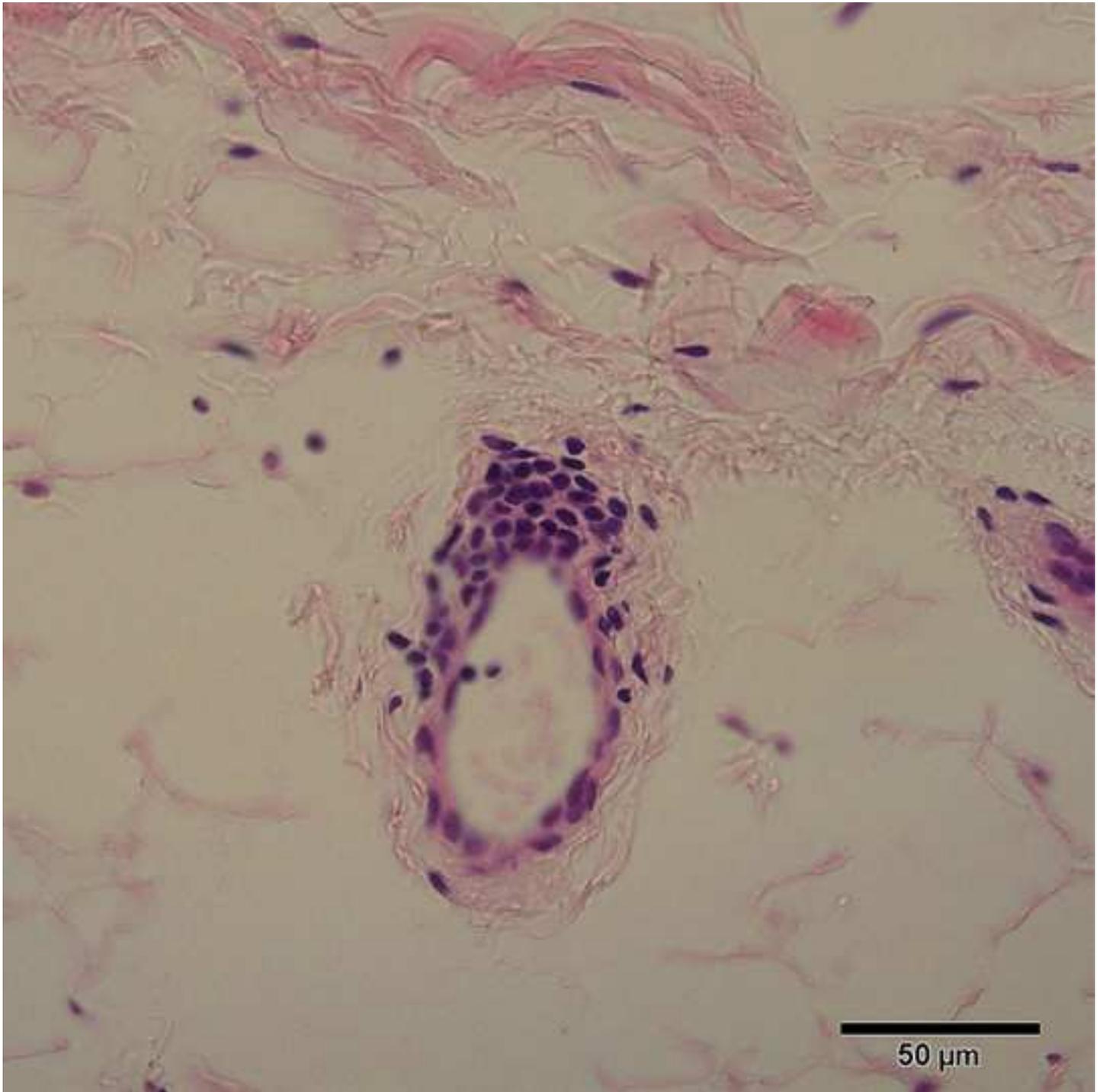


Figure 2. Surgically exposed nerve in the patient from Figure 1. Constriction of the radial nerve is evident immediately proximal to the elbow (proximal to a branch of the extensor carpi radialis longus).

Figure(s)

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**Figure 3.** Pathological examination of the perineurium and epineurium of a distal neuralgic amyotrophy lesion. Hematoxylin and eosin-stained cross-section through a peripheral nerve from a patient with neuralgic amyotrophy, showing perivascular lymphocyte infiltrates.