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An overlooked nerve in neuropathies associated with intragluteal injections: the posterior femoral cutaneous nerve

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ABSTRACT

Objective: The aim of this study was to investigate the frequency of posterior femoral cutaneous nerve (PFCN) lesions in patients referred to the electrophysiology laboratory with an initial diagnosis of sciatic nerve lesion following injection, and to create awareness that PFCN lesions can occur following intramuscular injections administered to the gluteal region.

Methods: Fifty-seven patients who were referred to the electrophysiology laboratory because of injection neuropathy were identified from the hospital records. In addition to the routine electrophysiological examination, PFCN sensory conduction study was performed according to the technique of Dumitru and Nelson. The scores of the Hospital Anxiety and Depression Scale (HADS) and the Leeds Assessment of Neuropathic Symptoms and Signs Pain Scale were recorded for all participants.

Results: Of the 21 participants who agreed to participate in the study, 2 patients were diagnosed with PFCN lesions, one of them had isolated complete PFCN lesion, and another had it accompanied by sciatic nerve lesion. Patients with PFCN lesions had a lower body mass index and a higher HADS score than patients with sciatic nerve lesions ($p = 0.01$, $p = 0.04$, respectively)

Conclusions: As correct diagnosis is the priority starting point for successful treatment, clinicians should plan examinations taking into consideration the fact that PFCN lesions can occur following gluteal region injection.

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1. Introduction

Iatrogenic peripheral nerve injuries (IPNI) may cause medico-legal and social problems. IPNI may be caused directly by surgery or surgery-related reasons, also injection neuropathies are an important cause of IPNI in developing countries [1,2]. Although the frequency of injection neuropathies is reduced with the use of correct and safe injection methods, the morbidity associated with injection neuropathies continues to be a topic of judicial processes.

Sciatic nerve lesions are among the most frequent injection-related peripheral nerve injuries, but injuries to other peripheral nerves, such as the radial, axillary, and median nerves, have also been reported [3]. Posterior femoral cutaneous nerve (PFCN) lesions, which can be overlooked due to isolated sensory complaints and lack of adequate awareness of clinicians, are usually reported in the literature as case presentations and can be seen as isolated or with sciatic nerve lesion after injections in the gluteal region [3,4].

Although the anatomic origin of the PFCN, which has the characteristic of being a purely sensory nerve, can include superior or inferior roots, it derives from the anterior and posterior rami of the first three branches of the sacral plexus [5,6]. It passes through the sciatic foramen and follows a course medially adjacent to the sciatic nerve deep in the gluteus maximus muscle under the piriformis muscle, and separates beginning from the lower edge of the gluteus maximus muscle in the pelvis [6]. Although cluneal and perineal branches of the PFCN are shown in traditional anatomical drawings that they originate from a single origin at the level of the tuber ischiadicum, a recent study has shown that the nerve is divided into two main branches, defined as a high division on the tuber ischiadicum, and gives cluneal and perineal branches from these main branches [7]. With these branches, PFCN provides sensory innervation of the posterior surface of the thigh between the posterior lower hip, popliteal fossa, lower buttock, ischial tuberosity, and perineum [7,8].

PFCN lesions may occur due to intramuscular injections administered to the gluteal region or in the form of pressure neuropathies due to long-term cycling, pelvic tumor, venous malformation, collection, etc. [9,10]. In addition, pain with sitting is another clinical condition in which PFCN is triggered [8]. In PFCN lesions, sensory complaints are experienced in the lower buttock and posterior surface of the thigh, sometimes extending to the perineum. Electrophysiological methods are used in diagnosis and differential diagnosis. Although the diagnosis of frequently seen injection neuropathies can be

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made from standard nerve conduction studies and needle electromyography findings, these may not be sufficient in rare neuropathies such as PFCN neuropathy. The sensory conduction study method defined by Dumitru and Nelson [11] is used in the investigation of the presence of PFCN neuropathy. Cases with PFCN neuropathy have been identified in a few electrophysiological studies in literature, and in even fewer with the Dumitru and Nelson's technique, but there are insufficient data about iatrogenic PFCN injuries.

The aim of this study was to investigate the frequency of PFCN lesions in patients referred to the electrophysiology laboratory with an initial diagnosis of sciatic nerve lesion following injection and to create awareness among physicians that PFCN lesions can be caused following intramuscular injections administered to the gluteal region.

2. Materials and methods

A total of 57 patients were identified, who were referred to the electrophysiology laboratory of a tertiary care referral hospital within the last 5 years with an initial diagnosis of the sciatic nerve lesion or injection neuropathy, or who had received a report from the Forensic Medicine Polyclinic because of injection neuropathy. Patients were invited to participate in the study by phone or letter. A total of 21 patients agreed to participate in the study and gave a signed informed consent. Approval for the study was granted from the Local Ethics Committee (2020–10-29150). The study was conducted according to the principles of the Declaration of Helsinki.

Sociodemographic data of age, gender, and body mass index (BMI), as well as comorbidities, the reason for intramuscular injection, the time from injection to the onset of neurological symptoms, the duration of symptoms, the medicine used in the injection, current physical examination findings, previous electromyography (EMG) results, and the scores of the Hospital Anxiety and Depression Scale (HADS) and the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) Pain Scale, were recorded for all subjects.

The HADS was used to evaluate the psychological status of the patients. This is a questionnaire of a total of 14 items, evaluating cognitive and emotional aspects of anxiety and depression with 7 items each. Each item is scored on a 4-point Likert scale from 0 to 3, where higher scores indicate more severe anxiety and depression [12]. The levels of anxiety and depression are scored separately as HAD-A and HAD-D. The Turkish version of the scale was found to be valid and reliable [13].

The presence of neuropathic pain in the patients was investigated with the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) Pain Scale [14]. The LANNS Pain Scale is a rapid and practical method based on the analysis of sensory definitions and examination of sensory disturbances. A score of ≥12 points in the LANNS Pain Scale shows a predominance of neuropathic pain. The Turkish version of the scale was found to be valid and reliable [15].

Electrophysiological examinations were performed using a Dantec Keypoint Focus EMG/NCS/EP device. The Bandpass filter was set to 20 Hz-10 kHz for motor conduction studies, 20 Hz-2 kHz for sensory conduction studies, and 10 Hz-10 kHz for Needle EMG. Extremity temperature was maintained at ≥31°C. A surface recording electrode was used for nerve conduction studies, and a single-use 50 mm monopolar concentric needle electrode was employed for Needle EMG. The peroneal and tibial nerve motor conduction studies in the patients' extremities where the injection had been administered were made with the orthodromic method, and sural nerve sensory conduction studies were performed with the antidromic standard method [16]. The PFCN conduction study was applied bilaterally using the technique of Dumitru and Nelson [11] (Figure 1). An active recording electrode was attached to 6 cm proximal of the popliteal fold on the midline on the posterior surface of the thigh of the patient lying in the prone position. The PFCN was stimulated from the midline in the proximal 12 cm of the recording electrode. The motor conduction rate was calculated using initial latency, and the sensory conduction rate was measured using negative peak latency. The peak-to-peak amplitudes of the responses obtained in the motor and sensory conduction studies were also measured.

The vastus lateralis, tibialis anterior, peroneus longus, medial gastrocnemius, the short head of biceps femoris, and semitendinosus muscles were evaluated at rest, in mild contraction and in full contraction using Needle EMG examinations. The L3-S1 paravertebral muscles were evaluated at rest only to investigate the presence of denervation.

2.1 Statistical analysis

Data obtained in the study were analyzed statistically using SPSS v22 software (SPSS Inc., Chicago, IL, USA). Type 1 error level was accepted as 0.05. Conformity of the data to normal distribution was assessed using visual (histogram, probability graphs) and analytical methods (Kolmogorov-Smirnov/Shapiro Wilk). Descriptive statistics were presented as mean ± standard deviation (SD) values for quantitative variables with normal distribution, as median ± interquartile range for quantitative variables with abnormal distribution, and as number (n) and percentage (%) for categorical variables. In the comparisons of patients with sciatic nerve lesions and those with PFCN lesions, the Independent Samples t-test, Mann Whitney U test, or Chi-Square test were used.

3. Results

Twenty-one patients participated in the study, they were between 13 and 72 (39.6 ± 12.8), and 17 (81%) of them were female. The mean BMI of all the patients was 21.9 ± 1.7 (range, 16.4–24.6) and one patient had a cachectic appearance. Twelve participants (57.1%) had received injections from the left gluteal region, and neuropathy had occurred most frequently due to analgesic agents. Complaints of pain, paresthesia, and weakness were seen to have started immediately after the injection in 16 (76.2%) patients, and within the first day in 5 patients (23.8%). The HAD-A score was determined as 5.4 ± 1.8, HAD-D as 7.1 ± 2.3, and LANSS as 12.9 ± 1.3 (Table 1).

As a result of the electrophysiological examinations, sciatic nerve lesion was determined in 15 patients where the peroneal nerve was more significantly affected, and in 3 patients where the tibial nerve was more evidently affected. In one patient where there was a more evident effect on the peroneal

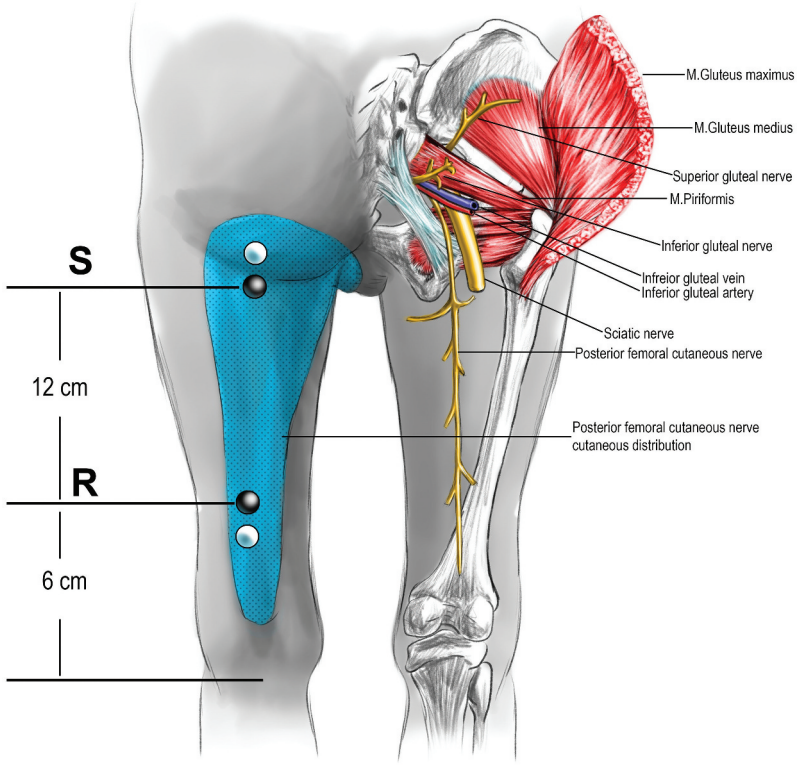

Figure 1. Posterior femoral cutaneus nerve anatomy (left side of figure) and electrode locations in sensory conduction study according to Dimitru and Nelson technique (right side of figure).

nerve, a complete PFCN lesion accompanying a sciatic nerve lesion was observed. An isolated complete PFCN lesion was determined in one patient (Table 2).

When compared with the previous EMG examinations, it was seen that evaluations for PFCN had not been made in the previous examinations, sciatic nerve effects were the same, and in one patient with a normal current EMG examination, there was a sciatic nerve lesion, affecting the peroneal nerve more evidently at a mild level. When the demographic and clinical data of the patients with sciatic nerve lesions and those with PFCN were compared, the BMI values of patients diagnosed with PFCN were determined to be lower ($p = 0.01$) and the HADS-A score was higher ($p = 0.04$) (Table 3).

4. Discussion

The aim of this study was to determine whether or not there was an overlooked PFCN lesion in patients referred to the electrophysiological laboratory with an initial diagnosis of sciatic nerve lesion following an injection to the gluteal region. The results showed that PFCN lesion was determined in 2 of the 21 patients involved in the study. One of the patients was determined to have an isolated PFCN lesion, and in the other, it was accompanied by a sciatic nerve lesion. The patients with PFCN lesions were found to have lower BMI and a higher HAD-A score.

Intramuscular injections are preferred especially in developed countries for reasons such as the rapid reduction of pain and fever, and the societal belief that treatments administered with injection provide better results [17–20]. However, peripheral nerve injuries may be seen to be associated with intramuscular injection, which is an important phenomenon due to the neurological sequelae and judicial processes resulting from these injuries [21,22]. The sciatic nerve is the most frequently injured peripheral nerve associated with injections [23].

PFCN, which is located in close proximity to the sciatic nerve below the gluteus maximus muscle, can be influenced as isolated or together with the sciatic nerve following injections administered to the gluteal region [4,24,25]. As the PFCN is smaller than the sciatic nerve and has a more medial localization, it is affected at a lower rate by intraneural injection-related neuropathies [3]. But it is not protected from the chemical effect of the injected medicines. The fact that the effect of the nerve does not cause motor weakness since it is a pure sensory nerve, and associating patients' sensory complaint with sciatic nerve lesion, as well as not examining them in routine nerve conduction studies, can cause a lack of diagnosis.

There are limited data in the literature related to the frequency of PFCN injection-related injury; From these, Stohr reported it to be 4.3% of all injection neuropathies, and Iyer and Shields reported a rate of 1% [3,26]. Injection injuries involving the PFCN together with the sciatic nerve were defined as infrapiriformis foramen syndrome by Obach et al. [25]. Injection-related neuropathies may occur related to one or more mechanisms such as direct mechanical injury,

Table 1. Patients' characteristics.

Parameters	Patients
Age, Year (mean min-max)	39.6 (13–72)
Sex	**n(%)**
Female	17 (%80.9)
Male	4(%19.1)
BMI, kg/cm^2 (mean,min-max)	21.9 (16.4–24.6)
Onset of neurologic deficit	**n(%)**
Immediate	16(%76.2)
Late	5(%23.8)
Injected Medicine	**n(%)**
Diclofenac	7(%33.3)
Fenyramidol	1(%4.7)
Methimazole	2(%9.5)
Diclofenac +Thiocolchicoside	3(%14.2)
Ranitidine	1(%4.7)
Clindamycin	2(%9.5)
Metoclopramide	2(%9.5)
Ampicillin	2(%9.5)
Hyoscine butylbromide	1(%4.7)
Affected lower extremity	**n(%)**
Left	12(%57.1)
Right	9(%42.8)
Indication of injection	**n(%)**
Myalgia	4(%19.1)
Back Pain	9(%42.8)
Dental Infection	1(%4.7)
Respiratory Tract Infection	3(%14.2)
Renal Colic	1(%4.7)
Headache	3(%14.2)
Duration, month, (mean, min-max)	13.5 (3–41)
LANSS pain score (mean ± SD)	12.9 ± 1.8
HADS-A Score (mean ± SD)	5.4 ± 1.8
HADS-D Score (mean ± SD)	7.1 ± 2.3

Abbreviations: min: minimum, max: maximum, cm: centimeter, kg: kilogram, m^2:square meter, SD: Standard Deviation, BMI: Body Mass Index, LANSS: The Leeds Assessment Of Neuropathic Symptoms and Signs, HADS-A: Hospital Anxiety and Depression Scale- Anxiety, HADS-D: Hospital Anxiety and Depression Scale- Depression

chemical effect, compression, ischemia, an impaired level of permeability in the blood-nerve barrier, pressure ischemia, vasoconstriction, and increased endoneurial fluid pressure [27]. The position of the needle at the time of injection is the most important determinant of the severity of nerve damage that may occur. The worst-case scenario is injections directly into the nerve [28]. Physical and chemical properties of the medicine are other factors that affect the severity of nerve damage, the formation of axonal or myelin damage in intraneuronal or near-nerve injections. The perineural accumulation creates compression-related nerve damage in high-volume injections, while chemical neuritis is more prominent in neurotoxic medicines [28,29] Vascular causes should be considered in the formation of nerve damage in injections far from the nerve. Ischemic nerve damage may occur due to vasotoxic effects of the medicines which sometimes cause also thrombus [30]. In cases where the PFCN is affected together with the sciatic nerve, chemical neuritis is thought to be more prominent than mechanical injury [25]. As in one of our current cases, patients with cachectic appearance are exposed to increased risk of nerve damage due to weakness of gluteus maximus muscle and lack of fat tissue, which makes peripheral nerves sensitive [10].

Moreover, in the current study, the BMI was found to be lower in patients with PFCN lesions. In addition, as considered in piriformis syndrome, vasotoxicity, and perivascular edema due to injection in the inferior gluteal vein located in the near proximity of both nerves in the piriformis muscle inferior can contribute to the process of neuritis in both nerves [18]. The late onset of neurological deficits and presence of axonal damage in the current study patients with PFCN lesions suggest that there could be chemical and vascular neuritis rather than direct nerve injury.

Symptoms such as pain and numbness in the inferior buttock and posterior thigh, which are typical symptoms of PFCN neuropathy after intragluteal injection, and the detection of sensory impairment in the inferior buttock and posterior thigh in physical examination suggest clinically PFCN lesion [7,8]. As

Table 2. Clinical data of patients with posterior femoral cutaneous nerve lesion.

Patients	Age (years)/ Sex	BMI (kg/ cm^2)	Affected lower extremity	Duration (months)	The Injected Medicine	Indication of injection	Symptoms	Physical Examination	LANSS pain score	HADS-A Score/ HADS-D Score
1	54/ Male	21.8	Left	13	Diclofenac	Headache	Numbness and dysesthesia in his left buttock and posterior thigh	Decreased sensation in the left buttock and posterior thigh	13	6/9
2	22/ Female	16.4	Left	8	Diclofenac+ Thiocolchicoside	Low Back Pain	Weakness in the left foot, global numbness and dysesthesia in the left lower extremity	Ankle Dorsiflexion 2/5, Hallux Dorsiflexion 2/5, Ankle Plantarflexion 3/5, Knee Flexio 4/5, Hypoesthesia and dysesthesia in left sural, tibial, peroneal and PFKS sensory areas	15	10/10

Abbreviations: cm: centimeter, kg: kilogram, m^2:square meter, SD: Standard Deviation, BMI: Body Mass Index, LANSS: The Leeds assessment of neuropathic symptoms and signs, HADS-A: Hospital Anxiety and Depression Scale- Anxiety, HADS-D: Hospital Anxiety and Depression Scale- Depression

Table 3. Compression of patients characteristics.

Parameters	Sciatic nerve Injury	PFCN Injury	p
Age, Year (mean,SD)	39.78 (12.4)	38(22.6)	0.85
BMI, kg/cm^2 (mean,SD)	22.2(1.2)	19.1(3.8)	0.01*
Duration, month, (mean,SD)	13.6(9)	10.5(3.5)	0.60
LANSS pain score (mean ± SD)	12.8(1.3)	14(1.41)	0.24
HADS-A Score (mean ± SD)	5.2(1.6)	8(2.8)	0.04*
HADS-D Score (mean ± SD)	6.9(2.29)	9.5(0.7)	0.14

*p < 0 .05

Abbreviations: cm: centimeter, kg: kilogram, m^2:square meter, SD: Standard Deviation, BMI: Body Mass Index, LANSS: The Leeds assessment of neuropathic symptoms and signs, HADS-A: Hospital Anxiety and Depression Scale- Anxiety, HADS-D: Hospital Anxiety and Depression Scale- Depression, PFCN: Posterior Femoral Cutaneous Nerve

in the diagnosis of other peripheral nerve lesions, electrophysiological examinations are more sensitive than physical examination and are often used in the correct diagnosis and follow-up of patients. Routine nerve conduction studies and needle EMG examinations are not sufficient in the diagnosis of PFCN lesions, and there is a need for additional examinations. Electrophysiological examination of PFCN is a special examination, and it should be considered that PFCN may be affected in gluteal region injection for this examination to be carried out. Although there are different methods in the electrophysiological examination of PFCN, we chose the Dimitru and Nelson technique for stimulation and recording electrodes in our study because there are standardized, easily identifiable landmarks that are not affected by anatomical variations [4,11]. Failure to consider PFCN injection-related injury in differential diagnosis will result in incomplete or incorrect diagnosis for the patient, failure of planning appropriate treatment, and ultimately failure of management of the patient with complications. It is obvious that this situation will bring with it medicolegal problems.

In addition to the importance of electrophysiological examination in diagnosis, it also has a role in influencing the choice of treatment by making partial or complete distinctions of injury, as well as in the follow-up of nerve healing after serial electrophysiological examinations. Surgical resection of PFCN through a recently published technique can be considered in patients without clinical and electrophysiological improvement despite conservative rehabilitation practices that provide desensitization, such as in-water exercise [7,8]. However, this technique should not be overlooked as being used in patients with sitting pain, achieving successful results. Studies investigating the impact of injection-associated PFCN injuries are needed.

Many studies have shown a relationship between neuropathic pain and cognitive disorders, mood disorders, and reduced appetite and motivation [31,32]. The presence of neuropathic pain is related to higher rates of depression and anxiety [33,34]. In addition, a missed diagnosis of patients with PFCN lesions may be associated with their higher anxiety score.

There were some limitations of this study. Primarily, there was not a wide duration beginning from the injection. In this period, patients with a mild partial PFCN lesion may have recovered. Moreover, the relatively high rate of PFCN frequency may have been due to the limited number of subjects included in the study. As there was a statistically low number of cases with PFCN lesion accompanying sciatic nerve lesion, it was not possible to compare the emotional status of these patients with that of patients with isolated nerve damage.

5. Conclusion

In conclusion, the PFCN can be damaged as isolated or together with the sciatic nerve following injection administered to the gluteal region. It should be taken into consideration that diagnosis cannot be made with routine electrophysiological examinations because it will not cause motor weakness since it is a pure sensory nerve, that the sensory area is the back of the thigh and gluteal region, unlike the sciatic nerve, and that it cannot be diagnosed with routine electrophysiological examinations. As correct diagnosis is the priority starting point for successful treatment, clinicians should plan examinations taking into consideration the fact that PFCN lesion can occur following gluteal region injection. Careful anamnesis, physical examination, and the selection of the right electrophysiological technique will prevent the PFCN lesion from being overlooked and the medicolegal problems that this situation will create.

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