

## Radiation-Induced Brachial Plexopathy. Two Case Revision

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Received: November 17, 2020

Published: December 10, 2020

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### Abstract

**Introduction:** The brachial plexus is a complex anatomical structure formed by the lower cervical and upper thoracic nerve roots. In case of suspected brachial plexopathy, nerve conduction and electromyography studies are often used to locate the lesion and assess its severity.

**Clinical Case:** There are two clinical cases, the first of a 70-year-old male patient with a history of a squamous oropharynx adenocarcinoma with cervical lymph node metastasis, treated by surgery, chemotherapy and radiotherapy, and the second case, a 70-year-old woman undergoing a radical right mastectomy following breast cancer, treated with chemotherapy, radiotherapy and hormone therapy. In both cases, patients developed a late-onset brachial plexopathy in relation to the treatment. Radiotherapy-induced brachial plexopathy has been described as a rare complication. It is usually debuted with paresthesias rather than pain and usually associates amyotrophy. Radiation-induced plexopathies appear to affect the upper and middle trunk of the brachial plexus in greater proportion, being unusual to affect the lower trunk.

**Keywords:** Carcinoma; Electroneurography; Electromyography; Neoplasm; Plexopathy; Radiotherapy

### Abbreviation

RIBPN: Radiation-Induced Brachial Plexus Neuropathy

### Introduction

The brachial plexus is a complex anatomical structure formed by the lower cervical and upper thoracic nerve roots. Radiotherapy-induced brachial plexopathy is a fairly rare compilation, with few cases described in the revised current literature, and in which it is also unusual to affect the lower trunk.

### Clinical Case I

A 70-year-old male patient with a history of high blood pressure, benign prostate hyperplasia, mild renal failure, bilateral ca-

rotid atheromatosis (60 - 50%) and squamous adenocarcinoma of oropharynx T3N2MX, intervened by left extended tonsillectomy with left modified radical emptying and right functional emptying plus chemotherapy and adjuvant radiation therapy at age 64. Among other surgical backgrounds, cervical arthrodesis C5-C6, C6-C7 at age 55 stands out for this case. Chronically taken tamsulosin 0.4 mg, dutasteride 0.5 mg and candesartan 8 mg.

The patient consulted for progressive and disabling dull pain at the level of the shoulder, scapula, medial face of the arm and left forearm, which increases with the supine decubitus, but not with the active or passive mobilization of the limb. In a few weeks the pain reached an intensity level of 8 according to the analog visual

scale (VAS). He associated paresthesia on the 4<sup>th</sup> and 5<sup>th</sup> finger of the left hand a year before the onset of pain and amyotrophy at the level of the intrinsic musculature of the same hand. He was treated by the pain unit under the suspicion of possible cervical radiculopathy and an associated left ulnar neuropathy, with 150 mg of pregabalin every 8 hours and 25 mg of tapentadol once a day and a cervical magnetic resonance imaging was requested, in which a central focal protrusion of C4-C5 disc was evident, highlighting nothing else.

After not presenting clinical improvement after two months of evolution, a neurophysiological assessment was performed by electroneurographic and electromyographic study, which con-

cludes: 1) Generalized involvement in upper and lower limbs, compatible with mild symmetrical polyneuropathy. 2) Chronic neurogenic pattern in the root-dependent muscles C5-C6-C7 left compatible with a root involvement established at these levels and 3) Acute-subacute neurogenic pattern in C8-T1 root-dependent muscles, compatible with lower trunk plexopathy.

Due to the findings in neurophysiological exploration, it was decided to expand the study by performing a bilateral tractography of brachial plexus, in which changes in signal strength were evident at the level of the middle and lower primary trunk of the left brachial plexus and the middle and posterior ipsilateral scalene muscles.

Left Upper Limb Electromyography: Clinical Case I									
Muscle Pattern	Spontaneous activity			Voluntary motor unit action potentials					
	Insertion activity	Fibrillations	Fasciculations	Activation	Recruitment	Duration	Amplitude	Polyphasic	Maximum effort pattern
Deltoid	NL	0	0	NL	↓	↑	↑	↑	Intermediate-submaximal
Left biceps	NL	0	0	NL	↓	↑	↑	↑	Intermediate-submaximal
Brachioradialis	NL	0	0	NL	↓	↑	↑	↑	Intermediate-submaximal
Triceps	NL	0	0	NL	↓	↑	↑	↑	Intermediate-submaximal
FCR	NL	+	0	NL	↓	↑	↑*	↑	Intermediate-submaximal
EIP	NL	++	0	NL	↓	↑	↑*	↑	Simple
FDI	NL	++	0	NL	↓	↑	↑*	↑	Simple
APB	NL	++	0	NL	↓	↑	↑*	↑	Simple
ABD DM	NL	++	0	NL	↓	↑	↑*	↑	Simple

↑: Increased; ↑\*: Increased, presence of late potentials; ↓: Reduced; NL: Normal; FCR: Flexor Carpi Radialis; EIP: Extensor Indicis Proprius; FDI: First Dorsal Interosseus I; APB: Abductor Pollicis Brevis; ABD DM: Abductor Digiti Minimi.

## Clinical Case II

The second case is a 70-year-old woman with a history of high blood pressure, hypothyroidism and reversed atrial fibrillation, right radical mastectomy as a result of breast cancer at 31 years, treated with chemotherapy, radiotherapy and hormone therapy, who has relapsed after 20 years of being free of tumor, so radiotherapy and hormone therapy are prescribed. Takes bisoprolol 2.5 mg and levothyroxine 88 mcg daily.

In this case the patient consulted the neurology service, presenting paresthesias in the right hand with a year of evolution and loss of strength at that level in the last 3 months. Cervical magnetic resonance imaging was performed in which degenerative osteo-articular and discal changes and moderate anterior spinal canal stenosis were observed at levels C5-C6, C6-C7 without signs of myelopathy.

The study is broadened by a neurophysiological assessment (electroneurography and electromyography) in which it is concluded: 1) Very proximal localization root involvement, which affects the root-dependent musculature C5-C6 and C7-C8 to a greater extent with spontaneous activity in extensor indicis proprius. These findings are consistent with a possible injury involving the three primary trunks of the brachial plexus.

Similarly in this case due to the findings of the neurophysiological evaluation, it was decided to expand the study of the patient through the realization of a bilateral tractography of brachial plexus, which reflex significant axonal damage at the level of the three primary trunks of the right brachial plexus and ruled out the presence of fibrosis.

Right Upper Limb Electromyography: Clinical Case II									
Muscle Pattern	Spontaneous activity			Voluntary motor unit action potentials					
	Insertion activity	Fibrillations	Fasciculations	Activation	Recruitment	Duration	Amplitude	Polyphasic	Maximum effort pattern
Deltoid	NL	0	0	NL	↓	↑	↑	↑	Intermediate-submaximal
Biceps	NL	0	0	NL	↓	↑	↑	↑	Intermediate-submaximal
Brachioradialis	NL	0	0	NL	↓	↑	↑	↑	Intermediate-submaximal
Triceps	NL	0	0	NL	↓	↑↑	↑↑*	↑↑	Intermediate-submaximal
EDC	NL	0	0	NL	↓	↑↑	↑↑	↑↑	Intermediate-submaximal
FCR	NL	+	0	NL	↓	↑	↑↑*	↑	Intermediate-submaximal
EIP	NL	++	++	NL	↓	↑↑	↑↑*	↑↑	Simple
FDI	NL	++	0	NL	↓	↑	↑*	↑	Simple

↑= Increased; ↑\*: Increased, presence of potentials; ↓: Reduced; NL: Normal; EDC: Extensor Digitorum Communis; FCR: Flexor Carpi Radialis; EIP: Extensor Indicis Propius; FDI: First Dorsal Interosseus.

## Discussion

Radiation-induced brachial plexopathy is a rather rare complication. Although this pathology has been documented in patients with neck, mediastinum, breast, lung and lymph nodes neoplasms, there is little information in the literature [1,2]. It has been described as a rare complication and should be proposed as a differential diagnosis to neoplastic plexopathy and fibrosis compression, in case there is a previous history of a neoplasm treated with radiation therapy in which radiation windows involve the brachial plexus [3]. Clinical, electromyographic and radiological data help its diagnosis [4].

Brachial plexopathy of neoplastic origin, can be triggered by tumor invasion or compression, lymphomas, breast cancer and lung cancer are the most common for these mechanisms; it can also be generated by primary nerve sheath tumors such as schwannomas, neurofibromas or neurofibrosarcomas in a lower frequency [5]. Palatine amygdala tumors have, according to different series, a frequency of 1 to 3% of all tumors in the body, 10% of all head and neck tumors [6-8]; Tumor relapses occur at 90% in the first two years. On the other hand, invasive breast cancer is the most common cancer in the female sex, accounting for 22% of all cancers and in the case of relapses these are usually late, giving even in decades [9].

Each of our patients had a bilateral brachial plexus tractography. In the first clinical case changes in signal strength were found at the level of the middle and lower primary trunk of the left brachial

plexus and the middle and posterior ipsilateral scalene muscles. In the second clinical case the tractography reflex significant axonal damage at the level of the three primary trunks of the right brachial plexus. In both cases the tractography allowed to rule out the presence of fibrosis, as this could cause compression of the plexus and tumor etiology. While it is true in the first case that a possible C8-T1 root involvement was not possible at the level of EMG, we found that the electromyographic findings functionally coincided with the alteration of the signal found in tractography at the level of the primary middle and lower trunks of the left brachial plexus.

In a retrospective study of 31 patients (62 plexuses) with a history of nasopharyngeal carcinoma, who were diagnosed with radiation plexopathy, the interval of onset of symptoms ranges from 6 months to 12 years with an average of 4 years and 2 months [3]. The main symptom (90%) was the paresthesia in C5-C6 territory frequently involving the first and according to the finger. The second most common symptom was persistent neck, shoulder and arm pain (54%). Symptoms with late onset were weakness, amyotrophy and twitching. In our first clinical case the patient debuted with paresthesias on the fourth and fifth finger of the left hand, with an evolution time of 6 years after surgery, and twelve months later, presented the painful symptomatology already described. In the second clinical case the time from the second radiation to the onset of symptoms was 16 years; the patient presented paresthesias in the right hand and loss of strength at that level after seven months of evolution, without becoming associated with pain. A case of lumbosacral plexopathy has been reported 15 years af-

ter radiotherapy for cervical carcinoma in which the patient had slowly progressive loss of force in the lower left limb, with no associated pain [4]. Postradiotherapy plexopathy can be painful only in half of patients [10].

Pain can help differentiate between the two entities, this is an early and more pronounced finding in direct neoplastic invasion. Similarly, the presence of Horner syndrome is much more common in neoplastic invasion [3]. In contrast, sensitive symptoms such as paresthesia and numbness appear more commonly and earlier in cases of radiation damage. In addition, patients with radiation-induced plexopathy are usually asymptomatic for much longer, often many years, before requiring medical attention.

In electrophysiological exploration, the presence of myochemical discharges and twitching are especially useful for differentiating radiation-induced plexopathy from neoplastic, being unusual in the latter [3]. In our second case at the electromyographic level spontaneous activity (myochemical) was found in muscle extensor indicis proprius.

In the above study, EMG/ENG most often found upper and middle trunk-level involvement, with little lower trunk involvement, and a statistically significant difference ( $< 0.005$ ) was found between patients with metastases to lower cervical lymph nodes and the dose of radiation therapy used (-50 Gy) [3]. Our first patient received a total dose of 46 Gy, multiple formed fields, with fractionation of 2Gy/day 5 times/week. In the second clinical case we do not have the radiation dose, however, it should be noted that the brachial plexus was exposed to it in two different periods, during the diagnosis of breast cancer and after relapse 20 years later. While it is true, in the first clinical case the dose of 50 Gy is not exceeded. As a described risk value for radiation plexopathy, if we consider the basic characteristics of our patient, we can say that there is greater nervous lability globally, due to polyneuropathy of probable toxic-metabolic origin in relation to chemotherapy and the antecedent of chronic renal failure, which could have decreased the level of radiation tolerance and therefore the safety margin for this particular case. In our second case with high probability there was a greater lability of the brachial plexus, since this was exposed twice to the radiation.

Taking into account the factors described above, clinical, electromyographic and radiological data allow us to consider that brachial plexopathy was radiation induced in both patients, with few

cases described in the literature, let alone with lower trunk involvement.

First-line treatment for neuropathic pain includes tricyclic antidepressants, antiepileptics and opioids making individualized adjustments based on each patient's response, requiring monitoring and control in most cases by units of pain [11]. Immunotherapy has been described as a therapeutic option [12,13]. Surgical intervention is unnecessary to treat radiation plexopathy in most cases, due to a relative rarity of radiation-induced fibrosis surrounding the plexus, however, surgical examination also allows the nerve to be released from fibrotic tissue [11]. Periscapular amputation is an aggressive treatment, which could be considered as a treatment option when radiation plexopathy has progressed to severe nerve injury [14,15].

## Conclusion

In the event of a previous history of a neoplasm treated with radiation therapy, whose radiation windows involve the brachial plexus, and a slowly progressive lesion develops, the radiotherapeutic origin between differential diagnoses should be considered.

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