# Trigeminal neuralgia secondary to basilar invagination responsive to botulinum toxin type A. Case report

*Neuralgia do trigêmeo secundária à invaginação basilar responsiva a toxina botulínica do tipo A. Relato de caso*

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## ABSTRACT

**BACKGROUND AND OBJECTIVES**: Trigeminal neuralgia (TN) is a headache characterized by paroxysmal episodes of intense pain in the facial region. TN can occur secondary to structural mechanisms, such as vascular compression of the trigeminal nerve root. Basilar invagination (BI) is a malformation of the craniovertebral junction characterized by invagination of the odontoid process of the axis through the foramen magnum into the posterior fossa, and 1% of cases may present associated TN. This article presents a clinical case of TN secondary to BI and vascular compression of the trigeminal nerve root, which responded only to treatment with botulinum toxin type A.
**CASE REPORT**: A 34-year-old patient with a clinical presentation consistent with TN for approximately 12 years. The symptoms were debilitating and impacted the quality of life, culminating in constant insomnia, severe depression, and suicidal thoughts. Treatment with botulinum toxin type A was fundamental in managing this patient's pain.
**CONCLUSION**: The case reported here demonstrated the therapeutic success of treatment with botulinum toxin type A in a complex and refractory case of pain syndrome.
**Keywords**: Basilar invagination, Botulinum toxin A, Trigeminal neuralgia.

## RESUMO

**JUSTIFICATIVA E OBJETIVOS**: Neuralgia do trigêmeo (NT) é uma cefaleia caracterizada por episódios paroxísticos de dores intensas na região da face. A NT pode ocorrer secundariamente a mecanismos estruturais, como a compressão vascular da raiz do nervo trigêmeo. A invaginação basilar (IB) é uma má formação da junção craniovertebral caracterizada por invaginação do processo odontóide do Axis através do forâmen magno na fossa posterior, e 1% dos casos podem apresentar NT associada. Este artigo apresenta um caso clínico de NT secundária a IB e compressão vascular da raiz do nervo trigêmeo, que foi responsiva apenas ao tratamento com toxina botulínica tipo A.
**RELATO DO CASO**: Paciente do sexo masculino, 34 anos de idade com quadro clínico compatível com NT há aproximadamente 12 anos. Os sintomas eram debilitantes e impactavam na qualidade de vida, culminando em insônia constante, depressão grave e pensamentos suicidas. O tratamento com toxina botulínica tipo A foi fundamental no tratamento da dor deste paciente.
**CONCLUSÃO**: O caso reportado evidenciou o sucesso terapêutico do tratamento com toxina botulínica tipo A em um caso complexo e refratário de síndrome dolorosa.
**Descritores**: Invaginação basilar, Neuralgia do trigêmeo, Toxina botulínica do tipo A.

## INTRODUCTION

Basilar invagination (BI) refers to an anomaly at the craniovertebral junction where the odontoid process of the axis protrudes above the foramen magnum into the posterior fossa. Radiographically, measurement of the distance from the odontoid tip to specific reference lines – such as the digastric or bimastoid lines (in the coronal plane), or McRae, Chamberlain, or McGregor

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**HIGHLIGHTS**
- Trigeminal neuralgia (TN) can occur secondary to basilar invagination.
- TN is refractory to medical treatment in many cases.
- Botulinum toxin type A can be used as treatment in complex and refractory cases of TN.

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lines (in the midsagittal plane) – is crucial[1]. This structural abnormality can lead to various clinical manifestations, including chronic headaches, myelopathy, sensory abnormalities, brainstem dysfunction, vascular compromise, and/or lower cranial nerve dysfunction[1,2].

Trigeminal neuralgia (TN) is a severe paroxysmal facial pain resembling electric shocks[3,4]. It occurs in approximately 1% of BI cases, with no definitive consensus on the optimal treatment modality established through randomized studies[5,6]. Classic TN typically arises from neurovascular compression, often involving the superior cerebellar artery pressing on the trigeminal nerve roots[7]. This compression induces demyelination, resulting in abnormal nerve firing. Subsequent changes include demyelination at the trigeminal nerve entry point, alterations in peripheral axons, and damage to Schwann cells and peripheral myelin[8]. The "Ignition Hypothesis" links these structural changes to sudden bursts of pain, suggesting that damaged neurons become overly excitable, prompting nearby neurons to follow suit, leading to heightened electrical activity and intensified pain signals due to proximity and damage to myelin sheaths[9].

Moreover, compression from the odontoid process in the cervicobulbar region can trigger symptoms such as paresis, spasticity, vertigo, gait ataxia, appendicular abnormalities, and altered sensation, albeit rarely in conjunction with TN[6-10]. Managing these symptoms necessitates a comprehensive approach encompassing pharmacotherapy, surgical interventions, and rehabilitation strategies aimed at alleviating pain and optimizing compromised neurological function[4,11].

This article presents a challenging clinical scenario involving a patient with TN secondary to basilar invagination and vascular compression on the trigeminal nerve root, refractory to optimized oral drugs, thereby precluding surgical intervention. Highlighting the inherent complexities of therapeutic decision-making, it is emphasized the pivotal role of Botulinum toxin type A therapy in pain management for this patient.

## CASE REPORT

Male patient, 34-year-old, presented to the outpatient neurology clinic with clinical symptoms consistent with trigeminal neuralgia (paroxysmal shock-like pains in the territory innervated by the right V2 and V3) persisting for approximately the last 12 years. Neuroimaging revealed basilar invagination and neurovascular conflict of the trigeminal nerve (Figure 1). During regular medical follow-up, attempts were made to optimize drug treatment, including some combinations of duloxetine (maximum dose achieved 120 mg/day), carbamazepine (1,200 mg/day), valproate (1,500 mg/day), lamotrigine (200 mg/day), and a recent trial of cannabidiol, without significant improvement. Surgical intervention was deemed inappropriate by a neurosurgeon. This debilitating condition severely impacted the patient's quality of life, leading to suicidal ideation, severe depression, constant insomnia, and cessation of employment.

Upon initial assessment at the botulinum toxin outpatient clinic, a physical examination revealed a short neck, allodynia, hyperalgesia in the territories of the right V2 and V3, and signs of poor self-care. Treatment with botulinum toxin type A (Botox®) (BoNT/A) was initiated at a dose of 30 units, distributed subcutaneously along the territory of V2 and V3, according to figure 2, with a 2 cm distance between each point of application[12]. Remarkably, the patient experienced an 80% improvement in pain intensity (Visual Analogue Scale from 10/10 to 2/10) and frequency (from constant to few attacks in the day) following the first dose.

Furthermore, significant improvements were observed in quality of life (assessed by the Quality Of Life Scale from the American Chronic Pain Association), from 0 - meaning that the patient stays in bed all day and feels hopeless and helpless about

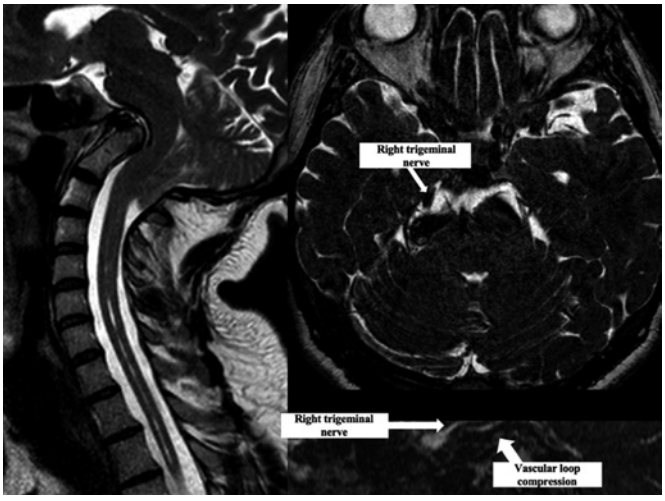


**Figure 1**. Basilar invagination and neurovascular conflict in a patient with trigeminal neuralgia refractory to optimized oral drugs over 12 years, who responded to botulinum toxin type A therapy.
Chiari malformation and syringomyelia can be observed.

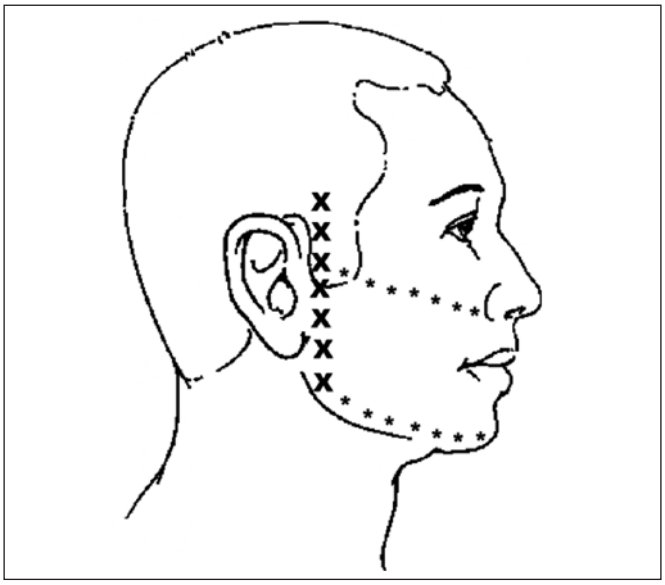

**Figure 2**. Schematic representation of the distribution of 30 units of botulinum toxin type A across the right V2 and V3 territories, with each injection spaced approximately 1-2 cm apart.
X = 2 units; * = 1 unit.

life; going to 10 - meaning a normal quality of life), sleep (assessed subjectively), and mood (evaluated by the Beck Depression Inventory, going from 36 – severe depression, to 2 – normal), with the absence of suicidal ideation and resumption of employment. The results were observed since the 3rd day after the injections, and sustained benefits of BoNT/A therapy were achieved without adverse effects. Reapplications are conducted every three months, and the patient has already undergone three reapplications in total[13]. The patient continues to follow up with good clinical control, with each injection effect lasting approximately three months.

## DISCUSSION

In the management of TN, conventional drugs like carbamazepine and gabapentin are often employed at high doses. However, resistance or adverse effects frequently necessitate alternative treatment modalities, including cannabinoids, oral lacosamide, intranasal lidocaine, botulinum toxin, radiofrequency thermal lesioning, and gamma knife radiosurgery[14-16]. In this case, optimized pharmacotherapy failed to achieve significant pain control, underscoring the refractory nature of certain TN cases[17,18].

Despite previous drugs interventions, treatment with BoNT/A demonstrated excellent efficacy, providing substantial pain relief and improving patient well-being, quality of life, and mood. This highlights the importance of considering unconventional approaches when standard treatments prove ineffective[19]. Recent studies have shown BoNT/A to effectively reduce pain by more than 50% in a significant proportion of TN patients at the 1- and 3-month follow-ups[20].

Additionally, systematic review and meta-analysis of randomized controlled trials support the effectiveness and safety of BoNT/A in TN management[21]. Moreover, surgical interventions can occasionally lead to severe and often untreatable complications that might be even worse than the primary condition[22]. Furthermore, a study reported a recurrence of pain in about half of the patients within 2 years of percutaneous radiofrequency rhizotomy[23].

While the exact mechanism of BoNT/A pain modulation remains elusive, several potential pathways include inhibition of neurotransmitter release such as substance P, glutamate, and calcitonin gene-related peptide, thus impeding protein extravasation and reducing pain sensitivity[24-26]. Botulinum toxin administration also interferes with the fusion process of synaptic vesicles and the cell membrane, affecting the transportation of various receptors, including those responsible for pain perception such as TRPV1 and TRPA1[27,28].

Additionally, BoNT/A also can influence neurons in the dorsal root ganglia and spinal cord, thereby attenuating neuropathic pain and altering neuropeptide expression[29]. BoNT/A may indirectly affect central nervous system pain processing pathways through retrograde transport, inhibiting purinergic transmission and reducing early gene expression in neurons[30-32]. Finally, the interaction between BoNT/A and non-neuronal cells like satellite glial cells suggests an additional analgesic mechanism by inhibiting glutamate release and inflammatory signaling pathways[33,34]. Though the precise mechanisms are not fully understood, BoNT's multifaceted approach offers promising avenues for pain relief in various conditions[35].

## CONCLUSION

This case highlights the necessity for personalized therapeutic approaches to manage trigeminal neuralgia. The success of BoNT/A therapy in treating refractory pain syndromes underscores its potential as a valuable therapeutic alternative in TN management.

## AUTHORS' CONTRIBUTIONS

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Data Collection, Conceptualisation, Project Management, Research, Methodology, Writing - Preparation of the original, Writing - Review and Editing, Supervision, Validation, Visualisation

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