

Retro-odontoid pseudotumor: a poorly recognized alteration of the craniocervical junction

 Andrew Vinícius de Souza Batista¹
 Guilherme Brasileiro de Aguiar²
 Jefferson Walter Daniel²
 José Carlos Esteves Veiga³

1. Médico residente de Neurocirurgia da Faculdade de Ciências Médicas da Santa Casa de São Paulo, São Paulo, SP, Brasil.
2. Neurocirurgião titular da Sociedade Brasileira de Neurocirurgia; assistente da disciplina de Neurocirurgia da Faculdade de Ciências Médicas da Santa Casa de São Paulo, São Paulo, SP, Brasil.
3. Neurocirurgião titular da Sociedade Brasileira de Neurocirurgia; professor livre-docente e chefe da disciplina de Neurocirurgia da Faculdade de Ciências Médicas da Santa Casa de São Paulo, São Paulo, SP, Brasil.

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SUMMARY

INTRODUCTION: *Retro-odontoid pseudotumor (ROP) is a rare disease that affects the atlantoaxial joint and, in general, is associated with local biomechanical alterations that may or may not cause instability.*

METHODS: *Descriptive study of the literature available in databases MEDLINE/PubMed, LILACS, and Scopus. The research was conducted in April 2019.*

DISCUSSION: *ROP is, possibly, a syndromic designation that encompasses a significant variety of diseases of the atlantoaxial joint. There are different pathophysiological mechanisms implicated in its genesis. The patients, almost in their entirety, present with severe myelopathy, and most of them are treated surgically, with the posterior decompression being the most commonly used method, with or without arthrodesis. Evolution is usually favorable.*

CONCLUSION: *The ROP is still poorly recognized as a differential diagnosis between the diseases of the cranial-cervical junction. The information available in the literature analyzed was based mainly on the study of reports or case series; therefore, it is insufficient to define conducts with a high level of scientific evidence.*

KEYWORDS: *Odontoid process/pathology. Atlanto-axial joint/pathology. Review.*

INTRODUCTION

Retro-odontoid pseudotumors (ROP) are an infrequent disorder that involves the atlantoaxial joint. As a result of population aging (with the consequent appearance of degenerative changes in the cervical spine) and the use of imaging examinations on a

larger scale - particularly of magnetic resonance -, the number of cases identified has increased^{1,2}.

When present, expansive retro-odontoid lesions should draw attention to the possibility of coexisting rheumatopathies involving the atlantoaxial joint,

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CORRESPONDING AUTHOR: Andrew Vinícius de Souza Batista

Rua Dr. Cesário Motta Jr., 112 - Faculdade de Ciências Médicas da Santa Casa de São Paulo, Vila Buarque, SP, Brasil - CEP 01221-020

Tel: +55 11 2176-7000

E-mail: andrewvsb@gmail.com

particularly the subluxation observed in rheumatoid arthritis. Cases of ROP without subluxation or C1-C2 instability are rare^{3,4}.

Over the past decade, there was an increased understanding of the physiopathology of ROP, thus, patients started to be better grouped in order to determine the most appropriate treatment for each case. However, the data currently available in the literature are not sufficiently uniform to ensure the development of strong evidence. From this analysis, we understand that it is fundamental to have an organized presentation and discussion about the disease, its differential diagnoses, and therapeutic modalities to contribute to the clinical practice, particularly of neurosurgeons, orthopedists, and rheumatologists.

METHODS

A descriptive study of the literature available in the Medline/PubMed, Lilacs, and Scopus databases. The search was carried out using the terms “retro-odontoid pseudotumor”, “retro-odontoid mass”, and “cervical *Pannus*”. Other variants and expressions found in articles from the search were included in order to sensitize the method. Works that were duplicated and whose content was not within the context studied were excluded. The search was carried out in April 2019.

DISCUSSION

One of the first descriptions using the term “pseudotumor” in order to refer to a mass in the craniocervical junction was made by Sze et al.⁵ in 1986. This author reported the cases of three patients with expansive lesions of atypical presentation in that area.

However, the lesions involving this segment of cervical spine are classically described as *pannus*, in patients with rheumatoid arthritis. By definition, *pannus* is an inflammatory tissue that causes erosion of the subchondral bone and cartilage in the synovial joints. However, similar lesions in individuals without systemic inflammatory diseases has led to the discovery of a pathological entity characterized by the presence of a non-inflammatory mass composed predominantly of fibrocartilaginous tissue. Joint cysts of degenerative nature are described between pseudotumoral lesions in this region⁶.

Most studies found in the literature consists of case reports or case series. Thus, it is not possible to

properly determine the prevalence and incidence of ROP in the population.

It is known, however, that patients with rheumatoid arthritis comprise the subgroup of higher risk for the disease. They may have their cervical spine affected as a consequence of the disease activity in more than 40% of the cases, and anterior atlantoaxial subluxation is the most common form of involvement⁷. On the other hand, most of these patients do not develop ROP⁸. Thus, the disease is unusual^{1,8}, especially if not associated with atlantoaxial instability⁹.

In addition to inflammatory rheumatopathies, other conditions that may be related include long-term hemodialysis, mucoid degeneration of the transverse ligament of the atlas¹⁰, trauma, *os odontoideum*¹¹, deposition of crystals, and disc herniation¹².

There is no clear physiopathological mechanism for ROP. In rheumatoid arthritis, the formation of the *pannus* is usually attributed to the release of proteases, which destroys the extracellular matrix of the cartilage, and the proliferation of fibroblast-like cells. It is possible that the genesis of tissue deposition in the retro-odontoid space in ROP - especially in the topography of the cruciate ligament band¹³ - holds some similarity to these phenomena.

Classically, the element that triggers the process is chronic instability in the atlantoaxial joint. Goel⁹ suggests that the origin of the lesion is related to an instability that begins in the facets and that involves excessive arching of the posterior longitudinal ligament (which predisposes its detachment), with a consequent periosteal reaction and formation of osteophytes.

On the other hand, cases of ROP without demonstrated atlantoaxial instability have been described³. A prospective study with 201 rheumatoid arthritis patients found an inverse relationship between the size of the mass and the atlantodental interval (which expresses the integrity of the transverse ligament and, therefore, the stability of the joint)⁸.

One theory suggests that the change in the amplitude of movement between the occipital condyles and C3 interferes in the process. Chikuda et al.¹ argued that the biomechanical change that occurs, for example, in the calcification of the anterior and posterior longitudinal ligaments and in ankylosis, can determine increased stress on the atlantoaxial complex due to the reduction of movement amplitude below that level. As a consequence, a process of damage and repair is initiated, resulting in the deposition of fibrocartilaginous

material with ligament hypertrophy, involving mainly the transverse ligament. This theory explains the occurrence of ROP on subaxial spondylosis. In this process, the formation of a pseudotumor and the emergence of atlantoaxial instability can be simultaneous or not. Therefore, the hypothesis that patients with an expansive retro-odontoid lesion become symptomatic due to medullary compression before there are radiological signs of residual subluxation in C1-C2 is plausible.

Acknowledging the existence of distinct physiopathologies, Tanaka et al.¹⁴ classified ROP into three types, differentiating them primarily by etiology and findings on magnetic resonance imaging, and type 1 (secondary to atlantoaxial subluxation) is the most prevalent. Table 1 summarizes the author's classification, whose analysis allows us to discuss the theoretical limitations in its construction. In it, for example, are not included cases such as crowned dens syndrome, which cannot be objectively categorized using the basic mechanisms singled out by Tanaka et al.¹⁴.

The clinical presentation is variable, and the most common form is compressive cervical myelopathy, present in up to 100% of the cases of a series¹⁵. In the patients with ROP without atlantoaxial instability evaluated in a systematic review, 95% evolved with progressive myelopathy¹⁶. There can also be mechanical neck pain, bulbar symptoms, and radiculopathy.

Among the differential diagnoses are neoplastic lesions and crowned dens syndrome. The latter is characterized by the presence of a significant inflammatory reaction (usually with increased acute-phase proteins), followed by the calcification of the ligaments around the odontoid process thanks to the deposition of hydroxyapatite or calcium pyrophosphate dihydrate. It usually responds to treatment with anti-inflammatory steroidal and non-steroidal drugs¹⁷. Some authors include crowned dens syndrome as one of the presentations of ROP¹⁶.

Clinical suspicion must be raised primarily for patients with inflammatory reumatopathy and signs of involvement of the cervical spine. Nevertheless, it should also be considered as a differential diagnosis for cervical myelopathy among the elderly.

The diagnosis is aided by imaging methods. Magnetic resonance imaging (MRI) is the main examination method because it provides more detailed information about the lesion (the radiological characteristics of ROP in MRI are described in Table 1 and shown in Figure 1), as well as the degree of involvement of adjacent structures, in particular, the spinal cord.

Computed tomography can contribute to a in-depth study of osseous components and is very useful for identifying calcifications in crowned dens syndrome.

Dynamic radiographs of the cervical spine are relevant because they determine the presence or absence of atlantoaxial instability through measures such as the atlantodental interval (ADI) and changes in the range of motion.

In cases in which there is still doubt as to the nature of the retro-odontoid lesion, a biopsy can be carried out to conduct an anatomopathological study. Upon analysis, ROP is composed of predominantly necrotic degenerated fibrocartilaginous tissue¹⁸, which may contain a focal proliferation of blood vessels⁴.

Regarding treatment, in general, the surgical approach is used, consisting of the direct excision of the lesion or spinal cord decompression with or without arthrodesis¹⁹. Direct resection can be done via the transoral route or by posterior laminectomy (epidural or transdural).

Based on the pathophysiological aspects of ROP, it has been established that treatment with decompression and fixation (C1-C2 or occipital-cervical) is associated with better clinical and radiological evolution,

TABLE 1. CLASSIFICATION OF RETRO-ODONTOID PSEUDOTUMOR ACCORDING TO TANAKA

	Type 1	Type 2	Type 3
Incidence	Frequent*	Rare	Rare
Etiology	Atlantoaxial subluxation	Spondylosis Ankylosis OALL	Disc herniation
Finding in MRI	T1: hypo- or isointense T2: heterogeneous (hyper- and hypointense areas)	Same as in type 1	T1: hypo- or isointense T2: Hypointense Herniated C2-C3 disc, contiguous with retro-odontoid space

OALL: ossification of the anterior longitudinal ligament ; MRI: magnetic resonance imaging. *Among the cases diagnosed. Adapted from "Tanaka S, Nakada M, Hayashi Y, Mohri M, Uchiyama N, Hamada J. Retro-odontoid pseudotumor without atlantoaxial subluxation. J Clin Neurosci. 2010 May;17(5):651".

particularly in cases where there is already documented pre-operative atlantoaxial instability. Some authors advocate simple decompression, without arthrodesis, for treating patients with ROP without atlantoaxial subluxation.

In our search, we found no well-controlled randomized clinical trials evaluating the effectiveness of one technique over the other. Kobayashi et al.²⁰ compared, in a series of cases, two groups of patients treated by the posterior route (with and without fusion), and no statistical difference was found between them in relation to functional recovery measured by the JOA (Japanese Orthopaedic Association) score²¹. On the other hand, the groups were statistically different regarding the regression of the lesion on magnetic resonance imaging; it was greater among patients treated with arthrodesis. Other three series of cases comparing fusion and no fusion did not have the same results^{1,22,23}.

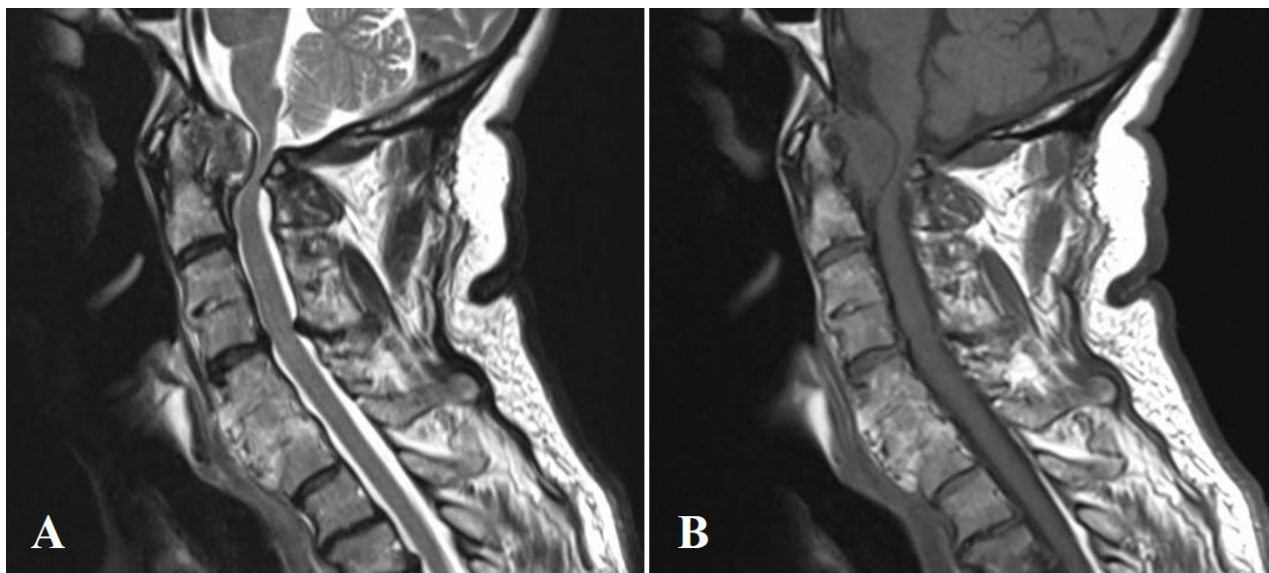
A systematic review performed by Robles & Mundis¹⁶ summarized a strategy for defining the treatment method for these cases from their pathophysiological mechanism, establishing surgery (with or without stabilization) as the standard treatment. However, oligosymptomatic cases and those without focal neurological deficits were not discussed. Special attention should be paid to the fact that about one-third of the patients previously described presented subaxial spondylosis¹⁴. Based on this, the reduction of excessive mechanical demand and of the range of

motion of the atlantoaxial joint may contribute, at least partially, to the local progression of ROP. Thus, and taking into account that elderly patients have higher surgical risk, in patients with no documented instability and milder clinical presentations, without signs of compressive myelopathy, a cervical collar can be used. There are reports of the use of this strategy even for patients with atlantoaxial instability²⁴, with a consequent reduction of ROP observed during follow-up by imaging exams. It is important to emphasize that the conservative approach needs to be followed-up periodically and re-discussed in case of changes in the course of the disease.

CONCLUSION

ROP is a rare disease usually associated with atlantoaxial subluxation, but its pathophysiological mechanisms are not yet fully understood. Its diagnosis is based on clinical, epidemiological, and imaging exams. In general, the treatment is surgical, which is the choice when there is C1-C2 instability. Currently, there is no evidence that the surgical treatment for ROP cases without instability in oligosymptomatic patients presents a greater benefit than the clinical follow-up. Well-controlled prospective, randomized studies can provide new data and conclusions in this regard, in order to guide the best approach for the management of these patients.

FIGURE 1. MAGNETIC RESONANCE SAGITTAL SECTIONS OF THE CERVICAL SPINE SHOWING EXPANSIVE LESION LOCATED POSTERIOR TO THE ODONTOID PROCESS, CHARACTERIZED BY THE PRESENCE OF HETEROGENEOUS SIGNAL IN T2 WEIGHTED IMAGE (A) AND ISO/ HYPOSIGNAL IN T1 (B). IN THIS CASE, SUBAXIAL SPONDYLOSIS IS NOTED, PREDOMINANTLY AFFECTING THE C5-C6-C7 SEGMENT, A FINDING THAT IS OBSERVED IN THE TANAKA TYPE 2 ROP. SOURCE: PERSONAL COLLECTION.



Author's contributions

1. Conception and design of the methodology: Andrew Vinícius de Souza Batista, Guilherme Brasileiro de Aguiar, José Carlos Esteves Veiga. 2. Literature search and selection of articles for review: Andrew Vinícius de Souza Batista, Guilherme Brasileiro de Aguiar, Jefferson Walter Daniel. 3. Analysis and

interpretation of the selected articles: Andrew Vinícius de Souza Batista, Guilherme Brasileiro de Aguiar, Jefferson Walter Daniel. 4. Writing of the manuscript and standardization according to the requirements of the periodical: Andrew Vinícius de Souza Batista, Guilherme Brasileiro de Aguiar. 5. Critical review of the text: Jefferson Walter Daniel, José Carlos Esteves Veiga

RESUMO

INTRODUÇÃO: O pseudotumor retro-odontoide (PRO) é uma patologia rara que acomete a articulação atlantoaxial e, em geral, está associada a alterações biomecânicas locais que podem ou não causar instabilidade.

METODOLOGIA: Estudo descritivo da literatura disponível nas bases de dados Medline/PubMed, Lilacs e Scopus. A pesquisa foi realizada em abril de 2019.

DISCUSSÃO: O PRO é, possivelmente, uma designação sindrômica que abrange uma variedade significativa de doenças da articulação atlantoaxial. Existem diferentes mecanismos fisiopatológicos implicados em sua gênese. Os pacientes, quase em sua totalidade, apresentam quadro de mielopatia grave e a maioria deles é tratada cirurgicamente, sendo a descompressão posterior o método mais utilizado, com ou sem artrodesse. A evolução costuma ser favorável.

CONCLUSÃO: O PRO ainda é pouco reconhecido como diagnóstico diferencial entre as doenças da junção crânio-cervical. As informações disponíveis na literatura analisada foram baseadas principalmente no estudo de relatos ou séries de casos, sendo, portanto, insuficientes para definir condutas com alto nível de evidência científica.

PALAVRAS-CHAVE: Processo odontoide/patologia. Articulação atlantoaxial/patologia. Revisão.

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