



# Retro-Odontoid Pseudotumor without Radiologic Atlantoaxial Instability: A Systematic Review

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## Key words

- Atlantoaxial instability
- Periodontoid mass
- Retro-odontoid pseudotumor

## Abbreviations and Acronyms

- AA:** Atlantoaxial  
**AAI:** Atlantoaxial instability  
**ADI:** Atlantodental interval  
**CPDD:** Calcium pyrophosphate deposition disease  
**JOA:** Japanese Orthopedic Association  
**MRI:** Magnetic resonance imaging  
**RA:** Rheumatoid arthritis  
**RP:** Retro-odontoid pseudotumor  
**RPWRI:** Retro-odontoid pseudotumor without radiologic instability

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## INTRODUCTION

The increased use of magnetic resonance imaging (MRI) to evaluate the craniovertebral junction has led to more frequent discovery of masses adjacent to the odontoid process. Retro-odontoid pseudotumor (RP) is a condition in which the formation of abnormal tissue occurs around the odontoid process, causing cervicomedullary compression. RP has various terms, including pannus and periodontoid mass. Pannus has been mainly used to describe RP in patients with rheumatoid arthritis (RA). RP can occur secondary to a variety of conditions such as RA,<sup>1</sup> trauma, os odontoideum,<sup>2</sup> long-term hemodialysis,<sup>3</sup> deposition of different substances, amyloidoma, calcium pyrophosphate, tumors,<sup>4-10</sup> and migrated disc herniation.<sup>11</sup> It is postulated that pseudotumor formation is the direct

■ **BACKGROUND:** Retro-odontoid pseudotumor (RP) can be caused by several diseases, especially rheumatoid arthritis, and is usually associated with the presence of atlantoaxial instability. On the other hand, a different group of patients have been identified in whom RP is observed without radiologic findings of atlantoaxial instability. The pathophysiology, clinical characteristics, and prognosis of this latter group of patients are not well described in the literature.

■ **METHODS:** A PubMed and Scopus search adhering to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines was performed to include studies reporting patients with RP without radiologic instability (RPWRI). The data gathered from this review were analyzed to characterize RPWRI.

■ **RESULTS:** The search yielded 36 articles with a total of 62 patients. All studies were case reports and small case series. Different characteristics of RPWRI are described, including causes, pathophysiology, and treatment.

■ **CONCLUSIONS:** The results of this review show that RPWRI has different causes such as hypermobility, deposition of substances, and perhaps disc herniation. Depending on the cause of RPWRI, the pathophysiologic mechanism is different. Treatment should be tailored based on the primary cause of RP and the degree of compression of the cervicomedullary junction. Different degrees of improvement are usually observed after surgical treatment in these patients regardless of the treatment used, but a higher rate of mass regression was observed in those patients in whom the atlantoaxial joint was stabilized.

result of chronic (AA) instability (AAI), especially in cases of RA or trauma. The development of RP in cases of AAI is a clinical entity in which the pathophysiology has been widely described in the medical literature. Different investigators have stated previously that RP is a direct consequence of AAI.<sup>1,12</sup> In these cases, it is considered that instability can cause repeated tears and subsequent hypertrophy of ligaments, leading to RP formation.<sup>13</sup>

Although AAI seems to be the main causative factor of RP, there is a group of patients in whom instability is not shown on imaging studies, thus calling into question if AAI is the only causal factor for the development of RP. In many cases of RPWRI, the cause is not identified; nonetheless, spine ankylosis has been observed at adjacent levels to C1-2 in many patients.<sup>14-20</sup>

In the past 2–3 decades, a transoral approach was considered to be the treatment of choice to remove the retro-odontoid mass and decompress the neural structures; however, several investigators have recently reported a significant RP reduction or regression after posterior C1-C2 fixation.<sup>15-17</sup>

RPWRI is not well described in the literature; for this reason, the aim of this article is to describe the characteristics of this uncommon condition.

## METHODS

### Study Selection

A comprehensive literature search of PubMed and Scopus was performed in accordance with PRISMA (Preferred Reporting Items for Systematic Reviews

and Meta-Analyses) guidelines. The search for publications was undertaken using the following keywords: “retroodontoid pseudotumor,” “retro-odontoid pseudotumor,” “periodontoid mass,” “retro odontoid soft mass,” and “odontoid pannus.” When different terms were found, these were searched further to find more studies. The search extended to all available English language articles from 1960 to March 2018. Cases were included in the final review only if patients had clinical and radiologic characteristics of RPWRI. Further, the references for all search-selected articles were also reviewed for potential cases. The following studies were excluded: literature reviews, animal studies, correspondence or letters, articles not available in full text, articles reporting different diseases from RPWRI, RP associated with RA or other inflammatory disease, RP associated with trauma, articles focusing on surgical techniques or anatomic studies, articles showing AAI on description or imaging, and articles with incomplete clinical information. Titles and abstracts were initially reviewed to identify articles with positive exclusion criteria.

#### Data Extraction

Data were extracted from eligible cases. Specific information was obtained from eligible articles. Collected data included 1) age, 2) presence of associated diseases, 3) presence of associated factors, 4) clinical status, 5) type of treatment, 6) postoperative changes of RP, 7) presence of postoperative instability, 8) time of follow-up, and 9) outcome.

AAI was determined based on the description and radiologic findings shown in the articles. AAI was considered when patients showed an atlantodental interval (ADI) >3 mm in adults and >5 mm in children. When the Japanese Orthopedic Association (JOA) score was used to evaluate the neurologic status, the outcome was assessed and calculated according to the Hirabayashi method: recovery rate (%) = (postoperative JOA – preoperative JOA) / (17 [full score] – preoperative JOA) × 100. Depending on the degree of improvement, the outcome was rated as excellent (75%–100%), good (50%–74%), fair (25%–49%), or poor (0%–24%). When JOA was not used to evaluate the neurologic status, the outcome was

labeled as improvement, unchanged, or worsened in cases of deterioration.

Not all articles provided information for each item; therefore, a comparative analysis was limited by the nature of the source data. Statistical analysis was not conducted for this review because comparative analyses could not be performed.

#### RESULTS

The literature search yielded 630 articles. After removal of duplicates, the title and abstract of 525 articles were screened and based on exclusion criteria, 445 articles were eliminated. After this initial filter, 80 articles were assessed for eligibility, of which 44 were excluded because of the presence of AAI or inadequate information. Thus, 36 studies with a total of 62 patients were eligible for analysis (Figure 1). Table 1 shows the characteristics of these patients that were identified from previous articles.<sup>4-7,10,11,13-42</sup> All studies were case reports or case series.

#### Patient Demographics

The youngest patient was 5 years old and the oldest was 87 years. The average age was 72.6 years. Forty-five percent of all cases occurred among individuals in their eighth decade of life and 67% of patients were male.

#### Causes and Associated Diseases

The most common cause of RPWRI observed in this study was related to hypermobility (28 cases), followed by deposition disease secondary to amyloidosis and calcium pyrophosphate deposition disease (CPDD). Many patients of the hypermobility group showed different grades of ankylosis at either the cephalad or caudal adjacent level to the C1-2 segment. RP associated with hemodialysis was observed in 4 patients. In some cases, the cause of RP could not be identified.

#### Clinical Status

The main clinical presentation was progressive myelopathy, which was observed in 95% of cases, followed by neck pain, which occurred in 10% of cases. Some patients reported unusual symptoms such as C2 radiculopathy and bulbar symptoms.

#### Type of Treatment

The results of this review show that the treatment of RPWRI is not standardized. A variety of surgical techniques are described for the treatment of these patients, including decompressive procedures, which may or may not include resection of the mass (C1 laminectomy or laminoplasty, suboccipital craniectomy and C1 laminectomy, far lateral, and transoral), posterior stabilization procedures (Harms technique, AA transarticular fusion, and occipitocervical fusion), and transoral surgery followed by posterior stabilization.

#### Postoperative Changes of RP

Regardless of the type of treatment, most patients showed a decrease in the size of RP. However, a complete regression of the periodontal mass was more commonly seen in patients who underwent posterior stabilization through any surgical technique.

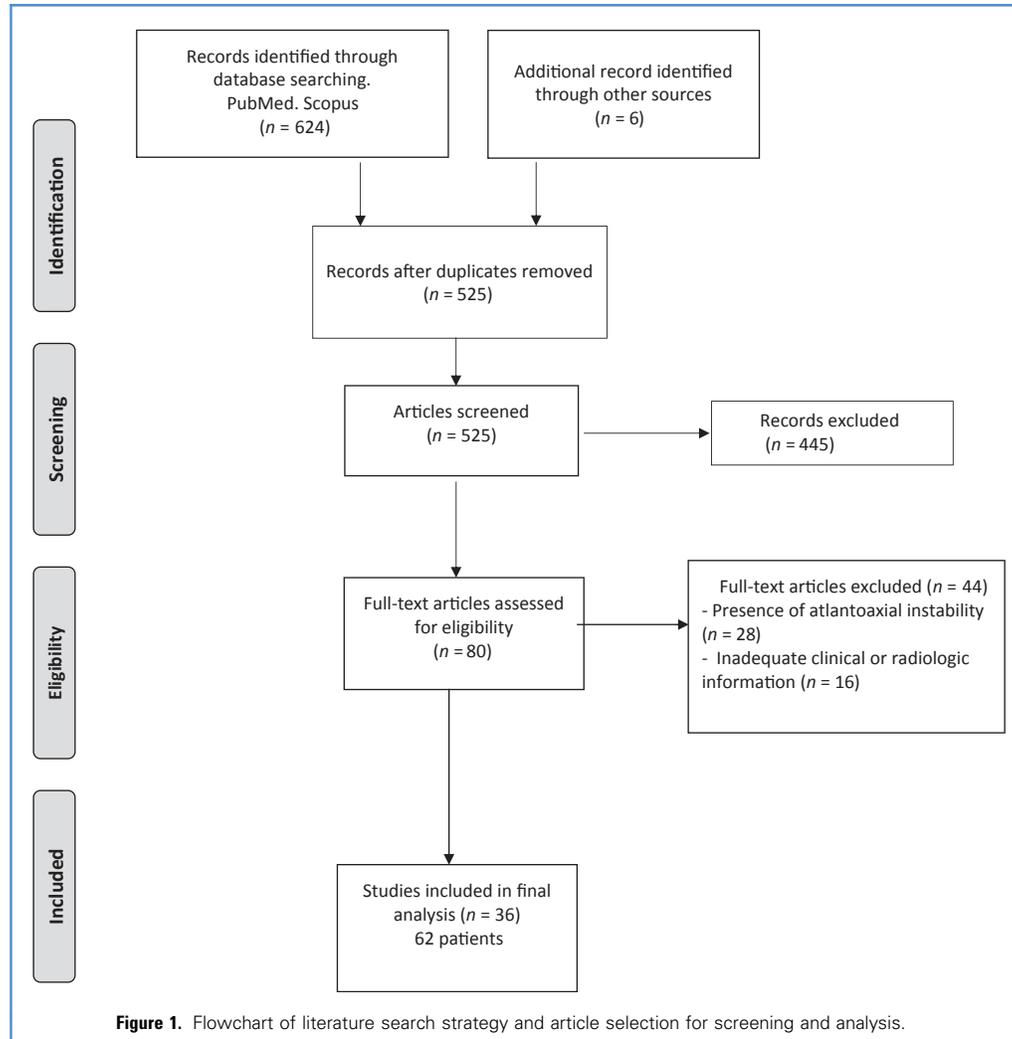
#### Outcome

Clinical outcome using the Hirabayashi method was reported in only 41% of cases, and most patients showed excellent or good improvement. In the remaining cases, the less objective method was used (improvement, unchanged, or worsened), with all patients in this outcome scheme showing improvement.

Combining these 2 outcomes schemes, 98% of patients showed various degrees of improvement regardless of the type of surgery performed.

#### DISCUSSION

Although RP is usually associated with AAI, it may occur in patients without the presence of radiographic instability. The exact pathophysiology of RPWRI is not completely understood, but the results of this review show that RPWRI is basically caused by 2 different mechanisms: C1-C2 hypermobility and deposition disease. In addition, a few patients have been reported with disc herniation as the cause of RP. Atlantoaxial hypermobility is usually secondary to ankylosis of adjacent levels to C1-C2 caused by congenital or degenerative conditions; on the other hand, deposition is usually caused by the deposit of amyloid or calcium pyrophosphate over the periodontoid area.



In patients with symptomatic cord compression, transoral surgery was once considered the standard treatment to remove the odontoid mass and decompress the neural structures. However; in the last 2 decades, different investigators<sup>15-17</sup> have reported that AA fusion and C1 laminectomy usually suffice to improve the patient's condition and observe regression of RP, especially in cases of C1-2 hypermobility. Because the mechanism of RP formation is different depending on the primary cause, each patient should be treated accordingly.

Next, the data obtained from this review and other sources are summarized to describe the characteristics observed in patients with RPWRI.

### RPWRI Secondary to Hypermobility (Adjacent Ankylosis)

**Causes.** As stated earlier, most patients with RP show radiologic instability at C1-C2, especially in cases of RA and trauma. In the group of patients without overt instability, different studies in this review<sup>14-17</sup> reported a high incidence of ankylosis or decrease of range of motion in the subaxial or upper cervical spine. In these patients, ankylosis of the subaxial spine was frequently caused by ossification of the anterior longitudinal ligament,<sup>13,15</sup> ossification of the posterior longitudinal ligament,<sup>13,23</sup> diffuse idiopathic skeletal hyperostosis,<sup>15,19,20</sup> or spondylosis,<sup>14,15,17,18,28</sup> whereas ankylosis in the craniovertebral junction was

frequently associated with congenital malformations such as atlas assimilation.<sup>14,15</sup>

**Pathophysiology.** The hypomobility of adjacent levels can alter the normal biomechanics of C1-2, exposing this level to excessive motion and stress. This excessive stress on the AA segment is greater when both adjacent levels (O-C1 and C2-3) have a low range of motion. This mechanism of hypermobility at C1-C2 is similar to the biomechanical anomaly observed in cases of adjacent segment disease that occurs in different areas of the spine. It has been previously reported<sup>16</sup> that the excessive motion at C1-2 causes greater strain on the atlantoaxial

**Table 1.** Summary of Patients with Retro-Odontoid Pseudotumor without Radiologic Instability in the literature

| Reference                                | Age, Years (Sex) | Associated Disease | Associated Factors                                  | Symptoms        | Treatment                            | Posttreatment Size of RP | Postoperative Instability | Follow-Up (Months) | Outcome     | % Improvement |
|--|------------------|--------------------|---|-----------------|--------------------------------------|--------------------------|---------------------------|--------------------|-------------|---------------|
| Kobayashi et al., 2018 <sup>17</sup>     |                  |                    |   |                 |                                      |                          |                           |                    |             |               |
| Case 2                                   | 67 (M)           | Hemodialysis       | Cervical sp   | Myelopathy      | C1 lam C2-6 lamp                     | Unchanged                | No                        | 12                 | Good        | 71            |
| Sanders et al., 2017 <sup>21</sup>       |                  |                    |   |                 |                                      |                          |                           |                    |             |               |
|  | 5 (M)            | CM                 |   | Bulbar symptoms | Posterior fossa decompression C1 lam | Decreased                | No                        | 18                 | Improvement | NS            |
| Tominaga et al., 2016 <sup>22</sup>      |                  |                    |   |                 |                                      |                          |                           |                    |             |               |
|  | 83 (M)           | No                 |   | Myelopathy      | C1 lam, transdural mass resection    | Decreased                | No                        | 84                 | Good        | 54            |
| Takemoto et al., 2016 <sup>23</sup>      |                  |                    |   |                 |                                      |                          |                           |                    |             |               |
| Case 2                                   | 69 (M)           | No                 | Ossification of the posterior longitudinal ligament | Myelopathy      | C1 lam                               | Decreased                | No                        | 59                 | Improvement | NS            |
| Case 3                                   | 71 (M)           | No                 |   | Myelopathy      | C1 lam                               | Decreased                | No                        | 59                 | Improvement | NS            |
| Case 6                                   | 84 (F)           | No                 | Cervical sp   | Myelopathy      | C1 lam, CLP                          | Unchanged                | No                        | 14                 | Improvement | NS            |
| Case 8                                   | 79 (M)           | No                 | Cervical sp   | Myelopathy      | C1 lam, CLP                          | Decreased                | No                        | 20                 | Improvement | NS            |
| Taschner et al., 2016 <sup>5</sup>       |                  |                    |   |                 |                                      |                          |                           |                    |             |               |
|  | 76 (F)           | Amyloidoma         |   | Neck pain       | TOR                                  | NS                       | No                        | 3                  | Improvement | NS            |
| Wada et al., 2015 <sup>5</sup>           |                  |                    |   |                 |                                      |                          |                           |                    |             |               |
| Case 1                                   | 60 (F)           | Amyloidoma         | Hemodialysis  | Myelopathy      | C1 lam                               | NS                       | No                        | 89                 | Fair        | 33            |
| Case 2                                   | 68 (M)           | Amyloidoma         | Hemodialysis  | Myelopathy      | C1 lam                               | NS                       | No                        | 67                 | Fair        | 27            |
| Fujiwara et al., 2015 <sup>24</sup>      |                  |                    |   |                 |                                      |                          |                           |                    |             |               |
|  | 66 (M)           | No                 |   | Myelopathy      | C1 lam                               | Regression               | No                        | 12                 | Improvement | NS            |
| Ishchenko et al., 2015 <sup>25</sup>     |                  |                    |   |                 |                                      |                          |                           |                    |             |               |
|  | 67 (F)           | SLE                |   | Myelopathy      | Medical, prednisolone                | Decreased                | No                        |                    | Improvement | NS            |
| Castro-Castro et al., 2014 <sup>20</sup> |                  |                    |   |                 |                                      |                          |                           |                    |             |               |
|  | 76 (M)           | DISH               |   | Myelopathy      | O-C fixation                         | Decreased                | No                        |                    | Improvement | NS            |
| Sono et al., 2014 <sup>14</sup>          |                  |                    |   |                 |                                      |                          |                           |                    |             |               |
| Case 6                                   | 68 (F)           |                    | O-C2 and C3-7 decreased ROM                         | Myelopathy      | O-C2 fusion, C1 lam                  | Regression               | No                        | 63                 | Fair        | 32            |
| Case 7                                   | 67 (M)           | Atlas assimilation | O-C1 and C2-6                                       | Myelopathy      | O-C3 fusion                          | Regression               | No                        | 55                 | Fair        | 38            |
| Case 8                                   | 63 (M)           |                    | decreased ROM                                       | NS              | C1-2 lam                             | Regression               | No                        | 12                 | Poor        | 0             |

M, male; Cervical sp, cervical spondylosis; C1 lam, C1 laminectomy; lamp, laminoplasty; CM, Chiari malformation; NS, not specified; F, female; DISH, diffuse idiopathic skeletal hyperostosis; ROM, range of motion; AATF, atlantoaxial transarticular fusion; CPDD, calcium pyrophosphate deposition disease; MIS, minimal invasive surgery; OALL, ossification of the anterior longitudinal ligament; O-C, occipito-cervical.

Continues

Table 1. Continued

| Reference   | Age, Years (Sex) | Associated Disease  | Associated Factors        | Symptoms         | Treatment                            | Posttreatment Size of RP | Postoperative Instability | Follow-Up (Months) | Outcome     | % Improvement |
|---|------------------|---------------------|---------------------------|------------------|--------------------------------------|--------------------------|---------------------------|--------------------|-------------|---------------|
| Case 10   | 49 (F)           |                     | C2-3 decreased ROM        | Myelopathy       | C1-2 Harms                           | Regression               | No                        | 66                 | Excellent   | 89            |
| Case 11   | 75 (M)           |                     | C-5 decreased ROM         | NS               | C1 lam AATF, C3-6 lam AATF           | Regression               | No                        | 6                  | Good        | 54            |
| Werner et al., 2013 <sup>7</sup>                              | 77 (F)           | Amyloidoma          |                           | Myelopathy       | 0-C5 fixation<br>C1-3 lam            | Decreased                | No                        | 24                 | Improvement | NS            |
| Klineberg et al., 2013 <sup>26</sup>                          | 83 (M)           | CPDD                |                           | Myelopathy       | MIS TOR                              | Decreased                | No                        | 6                  | Improvement | NS            |
| Barbagallo et al., 2013 <sup>15</sup> (average age, 65 years) |                  |                     |                           |                  |                                      |                          |                           |                    |             |               |
| Case 1  | NS               | DISH                | Cervical sp               | Myelopathy       | C1-2 Harms                           | Regression               | No                        | 8                  | Improvement | NS            |
| Case 2  | NS               | atlas assimilation  | Cervical sp               | Myelopathy       | C1 lam                               | Regression               | No                        | 13                 | Improvement | NS            |
| Case 3  | NS               | atlas assimilation, | Cervical sp               | Myelopathy       | C1-2 Harms                           | Regression               | No                        | 6                  | Improvement | NS            |
| Case 4  | NS               | platybasia, CM      | Cervical sp               | Myelopathy       | 0-C3 fixation                        |                          | No                        | 14                 | Improvement | NS            |
| Kakutani et al., 2013 <sup>13</sup>                           |                  |                     |                           |                  |                                      |                          |                           |                    |             |               |
| Case 1  | 76 (M)           |                     | Cervical kyphosis         | Myelopathy       | C1 lam                               | Decreased                | No                        | Average 20         | Excellent   | 84.6          |
| Case 2  | 64 (M)           |                     | C3-7 OPPL                 | Axial pain       | C1 lam                               | Decreased                | No                        |                    | Excellent   | 100           |
| Case 3  | 73 (M)           |                     | Kyphosis                  | Myelopathy       | C1 lam                               | Decreased                | No                        |                    | Excellent   | 72.2          |
| Case 4  | 87 (M)           |                     | C3-4 fusion               | Myelopathy       | C3-6 lamp                            | Decreased                | No                        |                    | Good        | 56.5          |
| Case 5  | 70 (M)           |                     | C3-6 OALL                 | Axial pain       | C1 lam                               | Decreased                | No                        |                    | Excellent   | 95.2          |
| Case 6  | 82 (M)           |                     | Kyphosis                  | Myelopathy       | C1 lam                               | Decreased                | No                        |                    | Good        | 48.3          |
| Case 7  | 77 (F)           |                     | C3-6 OALL                 | Myelopathy       | C1 lam                               | Decreased                | No                        |                    | Fair        | 40            |
|   |                  |                     |                           | Myelopathy       | C3-6 lamp                            |                          |                           |                    |             |               |
|   |                  |                     |                           | Myelopathy       | C1 lam                               |                          |                           |                    |             |               |
|   |                  |                     |                           | Axial pain       | C3-6 lamp                            |                          |                           |                    |             |               |
| Takeshima et al., 2012 <sup>27</sup>                          | 51 (F)           | Amyloidoma          | Hemodialysis for 29 years | C2 radiculopathy | C1-2 hemilaminectomy. Mass resection | Decreased                | No                        | 10                 | Improvement | NS            |
| Tanaka et al., 2010 <sup>28</sup>                             | 72 (M)           |                     | C2-7 decreased ROM        | Myelopathy       | AATF<br>C1-2 lam                     | Decreased                | No                        | 6                  | Improvement | NS            |

|                                       |        |                 |                   |            |                        |            |    |    |             |      |
|---------------------------------------|--------|-----------------|-------------------|------------|------------------------|------------|----|----|-------------|------|
| Brent and Hartley, 2010 <sup>10</sup> | 82 (M) | CPDD            | Fusion C2-5       | Myelopathy | Partial odontoidectomy | NS         | NS | 4  | Improvement | NS   |
| Chikuda et al., 2009 <sup>16</sup>    |        |                 |                   |            |                        |            |    |    |             |      |
| Case 6                                | 81 (M) |                 | OALL C2-7         | Myelopathy | O-C2 fusion            | Regression | No | 12 | Fair        | 33   |
| Case 7                                | 73 (F) |                 | OALL C3-7         | Myelopathy | C1 lam                 | Regression | No | 12 | Excellent   | 100  |
| Case 8                                | 73 (M) |                 |                   | Myelopathy | C3-7 lam               | Regression | No | 12 | Excellent   | 100  |
| Case 9                                | 71 (F) |                 |                   | Myelopathy | O-C2 fusion            | Regression | No | 12 | Excellent   | 100  |
| Case 10                               | 64 (M) |                 |                   | Myelopathy | C3-7 lam               | Regression | No | 12 | Excellent   | 75   |
|                                       |        |                 |                   |            | O-C2 fusion            |            |    |    |             |      |
|                                       |        |                 |                   |            | C1 lam                 |            |    |    |             |      |
|                                       |        |                 |                   |            | O-C2 fusion            |            |    |    |             |      |
|                                       |        |                 |                   |            | C2 lam                 |            |    |    |             |      |
|                                       |        |                 |                   |            | O-C4 fusion            |            |    |    |             |      |
|                                       |        |                 |                   |            | C1-2 lam               |            |    |    |             |      |
| Storch et al 2008 <sup>19</sup>       | 69 (M) | DISH            |                   | Myelopathy | Mass resection         | NS         | No | NS | Improvement | NS   |
|                                       |        |                 |                   |            | C1 hemilam             |            |    |    |             |      |
|                                       |        |                 |                   |            | O-C4 fusion            |            |    |    |             |      |
| Doita et al 2007 <sup>29</sup>        | 75 (M) | CPDD            |                   | Myelopathy | C1 lam, C2 hemilam     | NS         | No | 6  | Improvement | NS   |
| Lin et al., 2006 <sup>30</sup>        | 74 (F) | CPDD            |                   | Myelopathy | C1 lam                 | NS         | No | NS | Improvement | NS   |
| Matsumoto et al., 2006 <sup>31</sup>  | 76 (M) |                 | Previous lam C3-6 | Myelopathy | C1 lam                 | Regression | No | 12 | Good        | 69   |
|                                       |        |                 |                   |            | O-C6 fusion            |            |    |    |             |      |
| Yamaguchi et al., 2006 <sup>32</sup>  |        |                 |                   |            |                        |            |    |    |             |      |
| Case 3                                | 75 (M) |                 |                   | Myelopathy | C1 lam                 | Regression |    | 14 | Good        | 66.6 |
|                                       |        |                 |                   |            | O-C3 fusion            |            |    |    |             |      |
| Suetsuna et al., 2006 <sup>33</sup>   |        |                 |                   |            |                        |            |    |    |             |      |
| Case 1                                | 75 (M) |                 |                   | Myelopathy | C1 lam                 | Regression | No | 10 | Excellent   | 76   |
| Case 3                                | 76 (M) |                 |                   | Myelopathy | C1 lam                 | Regression | No | 24 | Excellent   | 90   |
| Matsuno et al., 2004 <sup>34</sup>    | 77 (M) | Disc herniation |                   | Myelopathy | Far lateral            | Decreased  | NS | 1  | Improvement | NS   |
| Mulleman et al., 2004 <sup>35</sup>   | 79(F)  | Amyloidoma      |                   | Myelopathy | TOR                    | NS         | No | 12 | Improvement | NS   |
|                                       |        |                 |                   | Neck pain  | AATF                   |            |    |    |             |      |
| Jun et al., 2002 <sup>36</sup>        | 74 (M) | DISH            |                   | Myelopathy | TOR                    | NS         | No | NS | Improvement | NS   |
|                                       |        |                 |                   |            | AATF                   |            |    |    |             |      |

M, male; Cervical sp, cervical spondylosis; C1 lam, C1 laminectomy; lam, laminoplasty; CM, Chiari malformation; NS, not specified; F, female; DISH, diffuse idiopathic skeletal hyperostosis; ROM, range of motion; AATF, atlantoaxial transarticular fusion; CPDD, calcium pyrophosphate deposition disease; MIS, minimal invasive surgery; OALL, ossification of the anterior longitudinal ligament; O-C, occipito-cervical.

Continues

Table 1. Continued

| Reference                            | Age, Years (Sex) | Associated Disease | Associated Factors | Symptoms   | Treatment                | Posttreatment Size of RP | Postoperative Instability | Follow-Up (Months) | Outcome     | % Improvement |
|--------------------------------------|------------------|--------------------|--------------------|------------|--------------------------|--------------------------|---------------------------|--------------------|-------------|---------------|
| Assaker et al., 2001 <sup>37</sup>   |                  |                    |                    |            |                          |                          |                           |                    |             |               |
| Case 1                               | 77 (M)           | CPDD               |                    | Myelopathy | TOR                      | Decreased                | No                        | 12                 | Improvement | NS            |
| Case 2                               | 83 (F)           | CPPD               |                    | Myelopathy | TOR                      | NS                       | No                        | 3                  | Improvement | NS            |
| Cai et al., 2001 <sup>38</sup>       |                  |                    |                    |            |                          |                          |                           |                    |             |               |
| Case 1                               | 71 (F)           |                    | Cervical sp        | Myelopathy | TOR                      | NS                       | No                        | 12                 | Improvement | NS            |
| Case 2                               | 74 (M)           |                    |                    | Myelopathy | Posterior C1-2 fusion    | NS                       | No                        | 3                  | Improvement | NS            |
|                                      |                  |                    |                    |            | TOR                      |                          |                           |                    |             |               |
|                                      |                  |                    |                    |            | Posterior C1-2 fusion    |                          |                           |                    |             |               |
| Hasegawa et al., 2000 <sup>4</sup>   | 84 (M)           | CPDD               | OALL               | Myelopathy | C1-2 hemilaminectomy     | Regression               | No                        | 12                 | Improvement | NS            |
|                                      |                  |                    |                    |            | transdural               |                          |                           |                    |             |               |
| Moonis et al., 1999 <sup>39</sup>    | 79 (M)           | Amyloidoma         |                    | Myelopathy | TOR                      | NS                       | NS                        | NS                 | NS          | NS            |
|                                      |                  |                    |                    | Neck pain  | O-C3 fusion              |                          |                           |                    |             |               |
| Chen and Lui, 1997 <sup>40</sup>     | 63 (F)           |                    |                    | Myelopathy | TOR                      | NS                       | No                        | 24                 | Improvement | NS            |
|                                      |                  |                    |                    |            | Halifax stabilization    |                          |                           |                    |             |               |
| Nishizawa et al., 1996 <sup>41</sup> | 82 (M)           | Disc herniation    | Cervical sp        | Myelopathy | Suboccipital craniectomy | Regression               | No                        | 2                  | Improvement | NS            |
|                                      |                  |                    |                    |            | C1-3 lam                 |                          |                           |                    |             |               |
| Crockard et al., 1991 <sup>18</sup>  |                  |                    |                    |            |                          |                          |                           |                    |             |               |
| Case 2                               | 83 (M)           |                    | Cervical sp        | Myelopathy | TOR                      | NS                       | NS                        | NS                 | Improvement | NS            |
| Case 3                               | 79 (M)           |                    | Cervical sp        | Myelopathy | TOR                      | NS                       | NS                        | NS                 | Improvement | NS            |
| Rosenberg et al., 1991 <sup>11</sup> |                  |                    |                    |            |                          |                          |                           |                    |             |               |
| Case 1                               | 74 (F)           | Disc herniation    | Cervical sp        | Myelopathy | Suboccipital craniectomy | Regression               | No                        | 36                 | Improvement | NS            |
| Case 2                               | 82 (F)           | Disc herniation    |                    | Myelopathy | C1-2 lam                 | Regression               | No                        | 3                  | Improvement | NS            |
|                                      |                  |                    |                    | Neck pain  | Suboccipital craniectomy |                          |                           |                    |             |               |
|                                      |                  |                    |                    |            | C1-3 lam                 |                          |                           |                    |             |               |
| Ciricillo and Weinstein, 1989        | 84 (F)           | CPDD               |                    | Myelopathy | TOR                      | Decreased                | No                        | 3                  | Improvement | NS            |

M, male; Cervical sp, cervical spondylosis; C1 lam, C1 laminectomy; lam, laminoplasty; CM, Chiari malformation; NS, not specified; F, female; DISH, diffuse idiopathic skeletal hyperostosis; ROM, range of motion; AATF, atlantoaxial transarticular fusion; CPDD, calcium pyrophosphate deposition disease; MIS, minimal invasive surgery; OALL, ossification of the anterior longitudinal ligament; O-C, occipito-cervical.

ligaments, especially the transverse ligament. This scenario causes repetitive ligament injury and a subsequent reparative process with reactive hypertrophy that leads to pseudotumor formation.<sup>14,18</sup> Thus, RP is not necessarily associated with overt AAI in these cases, because hypermobility of C1-2 is the prime biomechanical disorder causing the mass formation.<sup>16</sup> In these patients, if the hypermobility does not stop either spontaneously or by means of surgery, very likely, this excessive movement progresses to overt radiologic instability. These hypotheses are supported by the fact that in many of these patients the RP regresses once the AA joint is stabilized.

**Treatment and Outcome. C1-2 Stabilization.** In recent years, a direct relationship has been identified between hypermobility of the AA segment and the presence of RP. This development has led to the application of fusion principles to the C1-2 segment in the treatment of patients with RPWRI. Different stabilization methods have been reported in the treatment of these patients, including occipitocervical fusion, C1-2 Harms technique, and AA transarticular fusion.<sup>14,17</sup> In many of these patients, C1 laminectomy is also performed as an adjunct treatment to decompress the spinal canal.<sup>14,16</sup> Patients in whom a stabilization procedure was performed showed a higher rate of complete regression of the RP.<sup>14,15,17</sup>

Kobayashi et al.<sup>17</sup> reported 100% regression of the RP in cases treated with stabilization, and they also reported that patients with gadolinium enhancement of RP on MRI have higher chances of mass regression after fusion. Barbagallo et al.<sup>15</sup> showed that a posterior stabilization procedure of C1-2 is sufficient to achieve a good outcome and regression of the retro-odontoid mass; furthermore, they believe that transoral surgery is not required in these cases. Other investigators<sup>14,16</sup> have reported the same findings of clinical improvement and a high rate of RP regression after fusion of the AA joint. The period for mass regression after surgery is variable, but there are even investigators<sup>43,44</sup> who report the disappearance of RP in the immediate postoperative period. These latter patients had RP secondary to AAI associated with RA.

**Decompression Only.** A group of patients were found in this review who were treated only with decompression without any stabilization procedure.<sup>13,23,33</sup> These patients did not show preoperative radiologic instability of the craniocervical area; however, a mild increase of the ADI was observed in some of these cases. The most common decompressive procedure was C1 laminectomy, which was performed in 34% of cases, followed by C1 laminoplasty. Average follow-up time was 29 months. In some patients, the ADI increased postoperatively, but no clinical consequences were observed.<sup>13</sup> Postoperative imaging showed that in 50% of cases the size of RP did not change; however, 100% of patients achieved neurologic improvement after surgery. Although the average postoperative follow-up was almost 2 years, there is no way to know if some of these cases showed delayed instability and subsequent clinical deterioration. The investigators of these studies considered that decompression as a single treatment in cases of RP is an acceptable surgical strategy for elderly patients in whom a low-risk procedure is desirable.

#### RPWRI Caused by Deposition

**Deposition by Calcium Pyrophosphate (Pseudogout).** CPDD occurs when crystals form deposits in the joints and surrounding tissues; this condition is also known as pseudogout. The deposition of these crystals in joints and bursae leads to subsequent articular inflammatory reaction and pain, and it is most commonly observed in the knee or wrist.<sup>10</sup> CPDD is a rare cause of retro-odontoid mass in the elderly. In the spine, crystal deposition occurs in the small joints and intervertebral discs and it is reported that a high incidence of subclinical periodontoid involvement occurs in cases of CPDD.<sup>8</sup> The most common clinical manifestations are neck pain and myelopathy. Radiologic studies in patients with CPDD show some characteristics that could help in the preoperative diagnosis of this condition. On computed tomography scan, the presence of periodontoid calcifications is a frequent finding. In addition, the most common radiologic findings observed on MRI are an isointense mass on T1 and hypointensity of the lesion on T2. Histologic analysis shows birefringent

crystals with rectangular and rhomboid shapes in fibrocartilage tissue.<sup>8,29</sup>

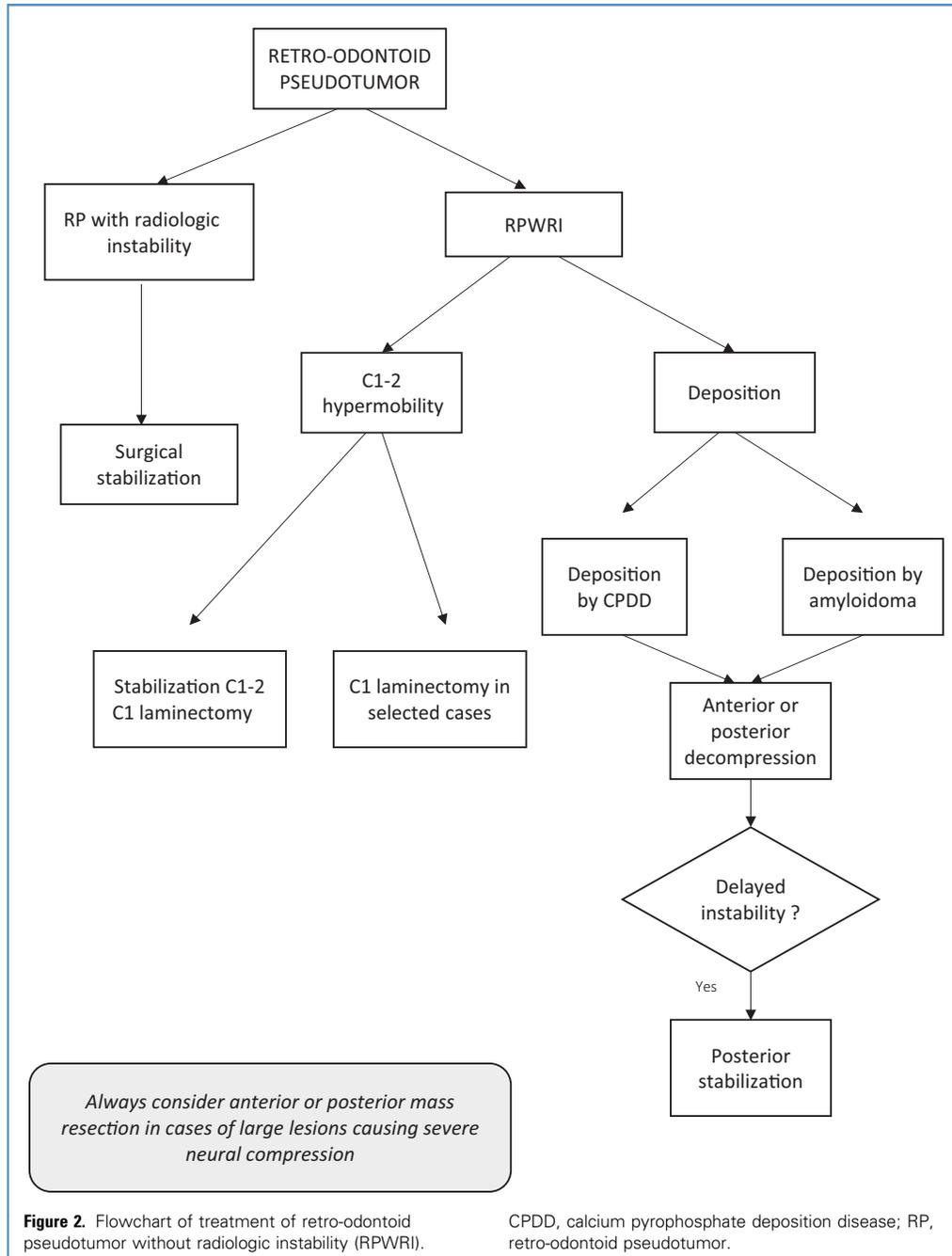
Different surgical treatment strategies have been reported in the management of RP caused by CPDD. Some investigators<sup>8,9</sup> have reported aggressive treatment that includes a transoral approach followed by posterior stabilization, whereas others have reported a less invasive treatment such as decompression and RP resection without stabilization. These less invasive surgical techniques include minimally invasive transoral resection,<sup>26</sup> partial odontoid resection without posterior fixation,<sup>10,42</sup> C1 laminectomy, and mass resection.<sup>4,29,30</sup> In several patients treated with C1 laminectomy, resection of the mass was performed through a transoral approach.<sup>4,22,24</sup> In these latter patients, the follow-up period ranged from 3 to 12 months, and for this reason, it is difficult to know how many of these patients developed delayed instability and required posterior stabilization.

The greatest series describing patients with RP secondary to CPDD was reported by Fenoy et al.<sup>8</sup> Most of these patients were treated by transoral-transpalatopharyngeal resection, and a subsequent posterior occipitocervical fusion was also performed in 84% of these cases. The mean follow-up period was 15 months and 86% of patients had improvement or resolution of symptoms after surgery.

Most patients with RP secondary to CPDD are elderly or debilitated individuals; therefore, this situation must be considered when deciding the type of surgery to be performed in each particular case.

Based on the results of the surgical treatment in this group of patients, it seems appropriate to initially treat these cases with anterior or posterior decompression and mass excision and consider a posterior fixation only in those patients who show postoperative instability.

**Deposition of Amyloid.** Localized amyloidomas are rare and often occur secondary to or in association with an underlying condition such as multiple myeloma, plasmacytoma, chronic infections, inflammatory disease, or long-term hemodialysis.<sup>5</sup> On the other hand, there is a group of patients in whom amyloidomas may occur with no evidence of generalized amyloidosis or associated



with other conditions such as those mentioned earlier. The term primary solitary amyloidosis (primary amyloidoma) is used to name these cases.

The occurrence of an amyloidoma in the spine is a rare scenario and typically affects the thoracic spine.<sup>7</sup> In this review, several patients presented with primary amyloidoma,<sup>5,7,35,39</sup> and in some patients, the periodontoid amyloidoma was

associated with kidney dialysis.<sup>6,27</sup> It is reported in the literature that dialysis-related amyloidosis affecting the upper cervical spine may manifest as RP or destructive spondyloarthropathy,<sup>6</sup> although it is also reported that 20%–30% of patients with long-term dialysis may have asymptomatic RPs.<sup>3</sup>

Preoperative radiologic diagnosis of periodontoid amyloidoma is difficult; in

most cases in this review, the diagnosis was performed after histologic analysis. On imaging, computed tomography shows a high frequency of dens or C2 body erosion, and on MRI, the most constant finding was hypointensity of the RP in T2 sequence. The histopathologic study shows amyloid deposits and green birefringence to polarized light after Congo red staining.<sup>7</sup>

A wide variety of surgical methods have been reported in the treatment of RP caused by amyloidoma. In this review, some patients were treated with anterior or posterior decompression and mass resection with no stabilization,<sup>6,24,27</sup> whereas other patients were treated with posterior stabilization associated with transoral or posterior decompression.<sup>7,35,39</sup> Regardless of the type of treatment, most patients showed postoperative clinical improvement on follow-up.

### RPWRI Secondary to Disc Herniation

Several patients have been reported with a retro-odontoid mass secondary to disc herniation.<sup>11,34,41</sup> These patients were treated with posterior decompression (suboccipital craniectomy and C1 laminectomy, far lateral approach) and mass resection with no stabilization. All experienced clinical improvement and decrease of the RP size in postoperative imaging. The characteristics of these patients are similar to those observed in patients with RP associated with hypermobility found in this review. The range of age was 77 to 82 years and the patients clinically manifested with progressive myelopathy; in addition, imaging showed spondylotic changes in the subaxial spine. It is difficult to believe how such a large mass in the retro-odontoid region extending to the basion can be caused by a disk fragment. Furthermore, the presence of ankylosis in the subaxial spine could suggest the presence of hypermobility in the C1-2 segment. Although the histopathologic report in these cases showed findings consistent with disc material, Crockard et al.<sup>18</sup> had previously noted that the material obtained from patients with RP was histologically similar to disc material obtained from lumbar discectomies. Thus, because the materials obtained from RP and disc fragments are similar, this could be the reason why these investigators may mistakenly have diagnosed a disc herniation when the mass was caused by RP associated with hypermobility.

### Treatment Strategy for RPWRI

The first step after the diagnosis of a periodontoid tumor is to establish the presence of risk factors for the development of AAI, such as trauma, inflammatory arthritis, and os odontoideum. The

next step is to confirm the existence of radiologic instability. When the patient presents with instability on imaging studies, the main treatment should be focused on AA stabilization and decompression if considered necessary. If the radiographic studies do not show AAI, we should investigate the presence of ankylosis at supra-adjacent or infra-adjacent levels to C1-2. Special attention should be paid to look for every known cause of cervical fusion, such as atlanto-occipital congenital malformations, or diseases with tendency to the formation of spontaneous fusion in the subaxial cervical spine, such as ossification of the posterior longitudinal ligament, ossification of the anterior longitudinal ligament, or diffuse idiopathic skeletal hyperostosis. In cases of RPWRI secondary to hypermobility, a C1-2 fusion procedure must be selected as the first option, although a simpler procedure such as C1 laminectomy can be considered in special cases such as those of debilitated patients. If AA hypermobility is not observed, a deposition disease should be ruled out (**Figure 2**). Regardless of the surgical treatment selected, a transoral or posterior pseudotumor resection must be performed in cases of large masses causing severe compression of the cervicomedullary junction.

### Limitations

Although this study shows important information about RPWRI, it has some limitations. All these patients were extracted from case reports or small case series, and therefore, they are subject to reporting and description bias. In addition, only English language articles were included for revision, and we may have excluded articles published in a different language. We also believe that RPWRI is underreported, especially historically, because diagnostic techniques were not available to detect this condition.

### CONCLUSIONS

RPWRI is an uncommon disease caused by different conditions, mainly C1-2 hypermobility and deposition disease. Depending on the cause and size of the retro-odontoid mass, the treatment plan must be individualized. Improvement is usually observed after surgery regardless of the type of the procedure that is

performed. Patients who showed a higher rate of RP regression are those in whom stabilization of the C1-2 segment was performed.

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