

Coexistence of Crowned Dens Sign and Calcification of Ligamentum Flavum in the cervical Spine: coincidence or association?

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Research Article

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Abstract

Background: Calcification of the cervical ligamentum flavum (CLF) and odontoid calcification are two rare diseases in the orthopaedic clinic. Only few reports have described these coexisting conditions.

Objectives: We present our cases of cervical radiculomyelopathy caused by CLF combined with or without odontoid calcification, and the relationship between the two clinical conditions are briefly discussed on the review of data of the literature.

Methods: We retrospectively reviewed 33 patients with CLF. In our case series, the clinical and radiological characteristics of patients are described and analyzed. The calcification surrounding the dens is termed as crowned dens sign (CDSign) in our study. And the relationship between the two conditions of CLF and CDSign are discussed.

Results: There were 28 women and 5 men aged between 56 and 86 years. Neurological symptoms and neck pain were presented in most patients. Calcification sites on axial CT images were described in 33 cases with 81 levels, C4-5 and C5-6 were attacked most frequently, and multiple- rather than single-level involvement could be observed in our series. CDSign was identified in 26 cases, and the prevalence were 79%. Following evaluation, 23 patients received posterior surgery, and 8 patients underwent anterior cervical surgery.

Conclusions: The coexistence of CDSign and CLF is an uncommon phenomenon. The association of these two diseases is stronger than a coincidence. It is possible that the coexistence of CLF with CDSign may be a rare form of the cervical manifestation of calcium pyrophosphate dihydrate (CPPD) deposition disease.

Introduction

Ligamentum flavum, known as the yellow ligament because of its richness in yellow elastin, forms part of the posterior wall of the spinal canal, which plays an important role in the protection against spinal cord damage. Degenerative changes of the ligamentum flavum is common in an aging or degenerative spine. The ligamentum flavum may undergo various pathologic changes including hypertrophy, calcification, ossification, and cyst formation^[1]. Ossification or calcification of the ligamentum flavum mainly occurs in the thoracic spine, and is relatively rare in the cervical region^[2]. A large number of histologic studies have confirmed that calcification of the ligamentum flavum may be related to crystal deposition, especially in the patients with CPPD disease^[3].

Odontoid calcification is an under-recognized entity, which is usually discovered incidentally by computed tomography (CT) of the cervical spine. And it has been reported that odontoid calcification due to CPPD disease can result in inflammation and acute neck pain^[4]. In this study, we report a case series of cervical radiculomyelopathy due to calcification of the ligamentum flavum combined with or

without periodontoid calcification/CDSig radiologically. The probability of an association between these two conditions will be discussed.

Methods

This was a retrospective study with the institutional review board of our hospital (Shanghai Changzheng Hospital Clinical Research Ethics committee) approval. This program was conducted on the basis of the informed consent by the participants. Electronic medical record search was performed from September 2020 to January 2021, identifying patients were diagnosis of ossification and/or calcification of the ligamentum flavum of the cervical spine. Using these records, the disease-related data were extracted and summarized, such as: demographic characteristics (sex, age), clinical characteristics (inflammatory index, chief complaint, disease duration), radiological characteristics (lesion segment, contiguous/ non-contiguous involvement, concomitant periodontoid calcification, associated degenerative changes), and treatment. The data of histological examination of calcified lesions were reviewed if data was available. The calcification surrounding the dens is termed crowned dens sign (CDSig) in our study. During the study period, this search yielded 42 patients, 9 patients were excluded due to incomplete imaging and poor image quality. Thus, the total number of subjects were 33 for the study purpose.

Statistical analyses

A statistical analysis was performed using t test and Fisher's exact sign and a value of $P < 0.05$ was considered to be significant. All statistical analyses were conducted using the Statistical Package for the Social Sciences software program version 21.0 (SPSS).

Results

33 cases were recorded and the basic clinical data are summarized in Table 1. Most of the patients affected were women (28 women and 5 men), and were aged over 60 on average (median 70.6 years, range: 56 ~ 86 years). The average age of the patients was 69.9 years in females and 74.6 years in males (Table 1).

Clinical Characteristics and Radiological Assessment

Neurological symptoms occurred in most patients, 11 patients had radiculopathy, 19 had myelopathy, and 2 cases presented with acute cervical spinal cord injury after a minor trauma, whereas one patient had no complaint. Among these patients with CLF, 22 patients had intractable neck pain. The average duration of symptoms before diagnosis was 8.5 months (range, 2 days ~ 50 months) (Table 1). In available data of blood examinations, there was no significant difference in the level of serum uric acid and electrolytes.

Cervical CT scans that performed in all patients revealed oval or round-shaped calcifications located ventrally to the lamina. Calcification sites on axial CT images were described in 33 cases with 81 levels (Table 2). A total of 25 cases involved multiple segments, while 8 cases involved single segments. Affected segments of calcification included C2-3 in 2 cases, C3-4 in 10 cases, C4-5 in 27 cases, C5-6 in 25 cases, C6-7 in 13 cases, and C7-T1 in 4 cases. The segment most frequently affected by calcification was C4-5, then C5-6 (Fig. 1).

Also, degenerative spondylolisthesis were noted in 21 patients, and spondylolisthesis tends to occur at the same or neighboring segment of the CLF margin. In addition, two patients were accompanied by cervical ossification of posterior longitudinal ligament (Table 2).

Prevalence of the Crowned Dens Sign and Patient Characteristics

The curvilinear calcifications around the odontoid of the axis on CT images was identified in 26 cases (Table 2), which was defined as CDSign. The cohort of 26 cases with the coexistence of CDSign and CLF was analyzed as a separate group with the prevalence of 79%.

Treatments

Following evaluation, twenty-three patients received posterior cervical decompression surgery with instrumentation (Fig. 3), and eight patients underwent anterior cervical surgery (Fig. 2). The surgery went well with a satisfactory result. All but two patients received conservative treatment (Table 1). A total of 6 patients had post-operative histopathological findings, which showed degenerated ligamentum flavum with dark blue calcifications.

Discussion

Ossification of the spinal ligaments is a group of disease, characterized by heterotopic ossification or calcification in the tissues of the spinal ligaments. Among them, ossification of the ligamentum flavum (OLF) is rarely observed, particularly in the cervical spine. Liang et al.^[5] reviewed the CT data for 2000 patients with the whole-spine images and reported that the prevalence of OLF in the cervical spine was 0.25%. And the condition is more likely to affect the East Asians, especially in Japanese and Chinese population.

In clinical practice, CLF and OLF are often confused because of inadequate histological examination. CLF and OLF are rare entities that have similarities in their clinical features and treatments, but the two conditions of calcification and ossification significantly differ in pathological mechanism and neuroradiologic appearances^[3]. Calcification is characterized by deposition of calcium or salt-related compounds in soft tissue, while ossification refers to the abnormal formation of mature trabecular bone. Radiologically, CLF is usually demonstrated on cervical CT as a non-contiguous, oval-shaped mass,

located at the posterolateral part of the lamina, which is involved in crystal deposits. Unlike calcification, ossified lesion is more irregular, and usually shows V-shaped high density masses along the lamina^[6]. In addition, previous reports have identified that CLF occurs predominantly in the lower part of the cervical spine, whereas OLF was usually distributed in the upper or lower thoracic region^[6]. Cervical CT scan was performed on all patients of our study, the lesion was oval in shape, non-contiguous, adhered ventrally to the lamina. The pathological results of six cases revealed degenerative ligamentum flavum with dark blue calcifications, which were consistent with those of CPPD diseases.

In 1976, Nanko et al.^[7] reported the first case of symptomatic calcification of the ligamentum flavum in the cervical spine. In 1980, Kawano et al.^[8] reported one case with cervical radiculomyelopathy due to CPPD in the ligamenta flava. Since then, many reports of this condition followed. The exact pathophysiology of CLF is largely unknown; however, it involves accumulation of calcium pyrophosphate dehydrate crystals^[9]. CPPD, also known as pyrophosphate arthropathy or pseudogout, is defined by the accumulation of CPPD crystal in articular and periarticular tissues. The disease predominantly affects the peripheral joints, but may also concern spine^[10]. The cervical region is the most commonly affected site within the spine followed by the thoracic and lumbar spine. Aging is a major risk factor for the development of CPPD crystal-associated arthritis, and CLF predominantly affects elderly women^[3, 6, 10]. Baba, et al.^[11] published a 8 cases series along with a review of 91 reports of CLF. Of all, 85% were female with an average age of 64.8 years. In our study, the male: female ratio was 1:6 and the mean age was 70.6 years, which is consistent with previous reports. It has been postulated that decreased estrogen levels at old age may be partially responsible for higher incidence of CLF in females compared to male.

Periodontoid calcification is a radiological signs defined by the radiographic calcifications in a crown-like configuration around the odontoid process, which is usually detected by CT scans. Calcification can develop anywhere around the odontoid process, whereas it tended to be usually located in the transverse ligament of the atlas (TLA)^[12]. Calcified lesion around the odontoid process caused by CPPD disease is a cause of acute inflammatory neck pain and stiffness, which is typically known as the crowned dens syndrome^[13] (CDSyn). However, calcification is not always symptomatic. Sano et al.^[14] reported that the prevalence of CDSyn in patients with periodontoid calcification was 12.5% (11/88). Based on the analysis of our own experience and of the published literature, the calcifications surrounding the odontoid process without clinical symptoms were defined as crowned dens sign (CDSign) in our study. In 2016, Kobayashi et al.^[15] reported one patient with acute neck pain caused by calcified cervical yellow ligament combined with periodontoid calcification. Later, Chang et al.^[16] and Lee et al.^[17] reported the cases of cervical myelopathy caused by calcification of the ligamentum flavum of the cervical spine with asymptomatic CDSyn, respectively. The coexistence of CLF and CDSign is an extremely rare event, only three similar cases have been reported in the English-language literature. It seems that either association of CDSign and CLF is a rare entity or it is a coincidence. In our study, twenty-six patients with both CLF and CDSign were the main focus of this study, and the CDSign was identified in 79% (26 of 33) of the patients with CLF. Lu et al.^[6] reported that 72%(13/18) of patients had periodontoid calcifications in

patients with calcifications of cervical ligamentum flavum due to CPPD deposition. Thus, the coexistence of two diseases is unlikely to be fortuitous. We found that it is more than half of cases with CLF and concurrent CDSign overlap syndrome in our study, it mightly suggest the association of these two conditions is stronger than a coincidence. On the basis of literature review, Muthukumar et al.^[18] found two types of CPPD crystal deposition in the cervical spine: calcifications of the ligamenta flava in the subaxial cervical spine (Type 1) and periodontoid calcifications in the upper cervical spine (Type 2). The exact relation between these entities is not known, but the relatively frequent association among these rare diseases suggests that there may be a pathophysiological relationship among them and not only a simple coincidence. In our opinion, CLF combined with CDSign may be a rare form of the cervical manifestation of CPPD disease, rather than a coincidence.

Clinical manifestations of patients with CLF are diverse, most cases presented with radiculomyelopathy, some patients can be completely asymptomatic. The primary symptoms of CDSyn are acute inflammatory neck pain and neck stiffness. In our study, 22 patients reported axial neck pain, 11 patients had radicular symptoms, 19 patients had myelopathy. Coexistent CDSign was observed in 26 patients, however, which may not affect clinical outcome in the treatment of CLF. In addition, there is a high incidence of cervical spondylosis among the patients with CLF of our study. Posterior cervical spine surgery is a common surgical technique used to treat a variety of cervical spine disorders. Yang J et al.^[19] reported 15 cases of cervical myelopathy caused by OLF, all patients underwent bilateral laminectomy, and achieved satisfactory clinical results. Finally, in our study, 23 patients underwent posterior surgery, 8 patients received anterior surgery, and 2 patients received conservative treatment. The surgery went well with a satisfactory result. In our opinion, anterior decompression surgery is effective in the treatment of patients with severe disc herniation and CLF.

Conclusions

Calcification of the ligamentum flavum is a rare disease. The coexistence of CDSign and CLF is an uncommon phenomenon. However, our data demonstrated that there is a relatively high incidence of coexisting CDSign in patients with CLF of the cervical spine, the increase in the number of reported patients who have a coexistence of these two diseases might suggest that the association of these two diseases is stronger than a coincidence. It is possible that the coexistence of CLF with CDSign may be a rare form of the cervical manifestation of CPPD disease.

Abbreviations

CLF Calcification of the cervical ligamentum flavum

CDSign Crowned dens sign

CPPD Calcium pyrophosphate dehydrate deposition disease

CT Computed tomography

OLF Ossification of the ligamentum flavum

CDSyn Crowned dens syndrome

Declarations

Ethics approval and consent to participate

The study was approved by Shanghai Changzheng Hospital Clinical Research Ethics committee. Informed consent was obtained from patients included in the study. All procedures were performed following the ethical standards of our institutional and national research committees and within the bounds of the 1964 Helsinki declaration and its later amendments.

Availability of data and materials

All data generated or analysed during this study are included in this published article.

Competing interests

The authors declare no competing commercial or financial conflicts of interest.

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Authors' contributions

Yake Meng drafted the manuscript and facilitated study steering group discussions. The study was conceived by Yake Meng and co-designed by all authors (who also form the study steering group). The study steering group members also contributed to the design and piloting of the survey questionnaires, and survey distribution. In addition, all contributed to the writing, editing and final approval of this manuscript.

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References

1. Zaki SM. Study of the human ligamentum flavum in old age: a histological and morphometric study. *Folia Morphol (Warsz)*. 2014;73(4):492–9. 10.5603/FM.2014.0074.
2. Guo JJ, Luk KDK, Karppinen J, Yang H, Cheung KMC. Prevalence, distribution, and morphology of ossification of the ligamentum flavum: a population study of one thousand seven hundred thirty-six

- magnetic resonance imaging scans. *Spine*. (Phila Pa 1976). 2010;35(1):51–6. 10.1097/BRS.0b013e3181b3f779.
3. Takahashi T, Hanakita J, Minami M. Pathophysiology of Calcification and Ossification of the Ligamentum Flavum in the Cervical Spine. *Neurosurg Clin N Am*. 2018;29(1):47–54. 10.1016/j.nec.2017.09.016.
 4. Lu PL, Niu ZF, Qiu CW, Hu XY. Odontoid calcification and crowned dens syndrome: data from a Chinese center. *Neurol Res*. 2020;42(11):930–5. 10.1080/01616412.2020.1792700.
 5. Liang Haifeng L, Guobing Lu, Shunyi, et al. Epidemiology of ossification of the spinal ligaments and associated factors in the Chinese population: a cross-sectional study of 2000 consecutive individuals. *BMC Musculoskelet Disord*. 2019;20(1):253. 10.1186/s12891-019-2569-1.
 6. Lu Y-H, Hsi-Hsien L, Hsuan-Ying C et al. Multilevel calcium pyrophosphate dihydrate deposition in cervical ligamentum flavum: clinical characteristics and imaging features. *BMC Musculoskelet Disord*. 2021;22(1):929. DOI: 10.1186/s12891-021-04812-6.
 7. Nanko S, Takagi A, Mannen T, et al. A case of cervical radiculo-myelopathy due to calcification of the ligamentum flavum. *Neurol Med*. 1976;4:205–10. [in Japanese].
 8. Kawano N, Yoshida S, Ohwada T, Yada K, Sasaki K, Matsuno T. Cervical radiculomyelopathy caused by deposition of calcium pyrophosphate dihydrate crystals in the ligamenta flava. *J Neurosurg*. 1980;52(2):279–83. 10.3171/jns.1980.52.2.0279.
 9. Mwaka ES, Yayama T, Uchida K, et al. Calcium pyrophosphate dihydrate crystal deposition in the ligamentum flavum of the cervical spine: histopathological and immunohistochemical findings. *Clin Exp Rheumatol*. 2009;27(3):430–8.
 10. Ann K, Rosenthal LM, Ryan. Calcium Pyrophosphate Deposition Disease. *N Engl J Med*. 2016;374:2575–84. 10.1056/NEJMra1511117.
 11. Baba H, Maezawa Y, Kawahara N, Tomita K, Furusawa N, Imura S. Calcium crystal deposition in the ligamentum flavum of the cervical spine. *Spine*. (Phila Pa 1976). 1993;18(15):2174–81. 10.1097/00007632-199311000-00005.
 12. Anno M, Oshima Y, Taniguchi Y, et al. Prevalence and Natural Course of Transverse Ligament of the Atlas Calcification in Asymptomatic Healthy Individuals. *Spine* (Phila Pa 1976). 2018;43(24):E1469–73. 10.1097/BRS.0000000000002744.
 13. Goto S, Umehara J, Aizawa T, Kokubun S. Crowned Dens syndrome. *J Bone Joint Surg Am*. 2007;89(12):2732–6. 10.2106/JBJS.F.01322.
 14. Sano M, Yamashita S, Aiba T. The prevalence of calcification around odontoid process and the incidence of crowned dens syndrome in the neurosurgical ward: A single institution's analysis. *Mod Rheumatol*. 2018;28(1):182–7. 10.1080/14397595.2017.1316461.
 15. Kobayashi T, Miyakoshi N, Abe T, et al. Acute neck pain caused by pseudogout attack of calcified cervical yellow ligament: a case report. *J Med Case Rep*. 2016;10(1):133. 10.1186/s13256-016-0928-1.

16. Chang DG, Park JB, Jung HY, Seo KJ. Cervical myelopathy due to subaxial calcium pyrophosphate dihydrate (CPPD) deposition with simultaneous asymptomatic crowned dens syndrome:two case reports. BMC Musculoskelet Disord. 2020;21(1):713. 10.1186/s12891-020-03736-x.
17. Lee J, Lee S, Bae J. Calcium Pyrophosphate Dihydrate Crystal Deposition Disease Involving the Ligamentum Flavum of the Cervical Spine with Intense Enhancement on MRI: A Case Report. J Korean Soc Radiol. 2020;81(5):1234. 10.3348/jksr.2019.0068.
18. Muthukumar N, Karuppaswamy U, TUMORAL CALCIUM PYROPHOSPHATE DIHYDRATE DEPOSITION DISEASE OF THE LIGAMENTUM. FLAVUM Neurosurg. 2003;53(1):103–8. 10.1227/01.neu.0000068861.47199.a8. discussion 108-9.
19. Yang J, Ni B, Xie N, Guo Q, Wang L. Surgical Treatments of Myelopathy Caused by Cervical Ligamentum Flavum Ossification. World Neurosurg. 2011;75(3–4):546–50. 10.1016/j.wneu.2010.10.041.

Tables

Tables 1 to 2 are available in the Supplementary Files section

Figures

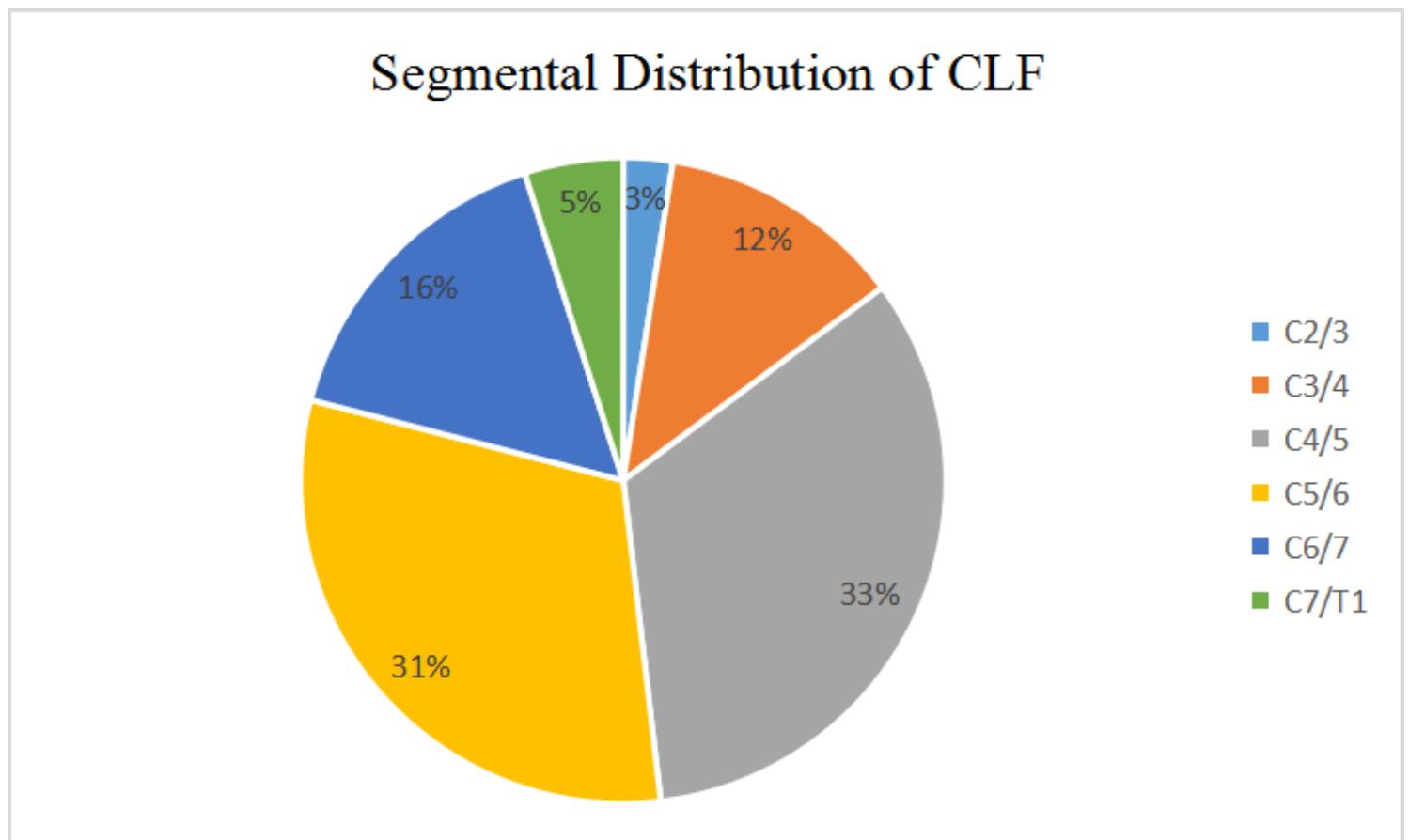


Figure 1

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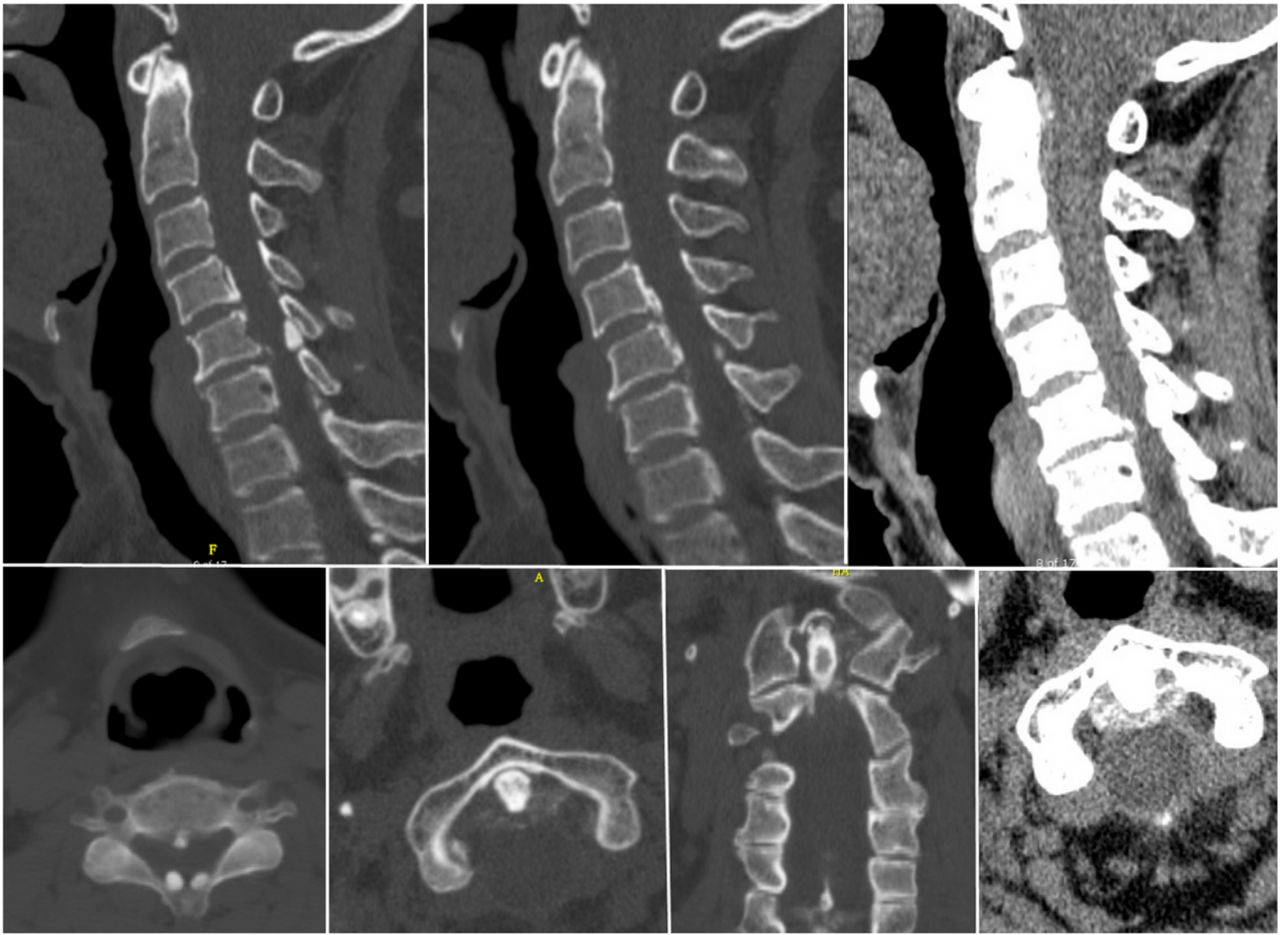
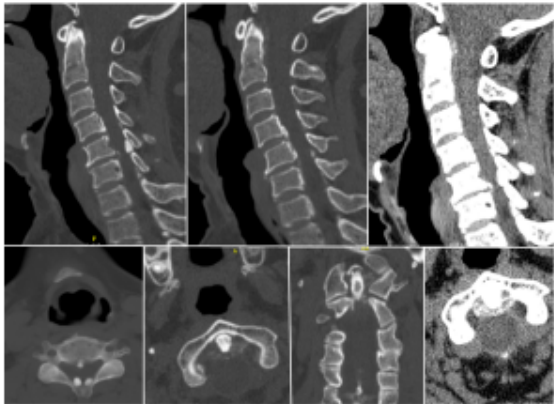
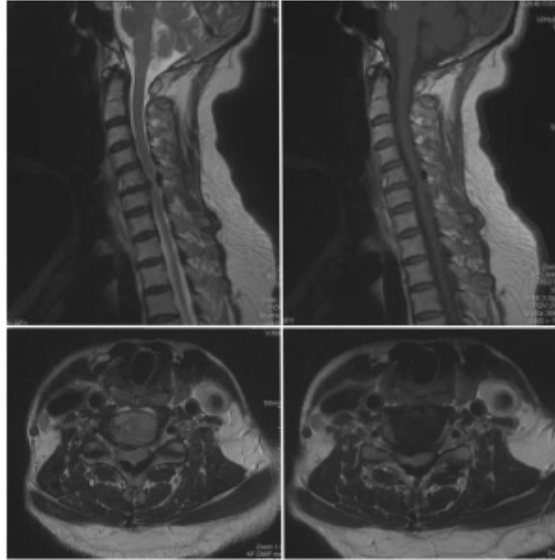


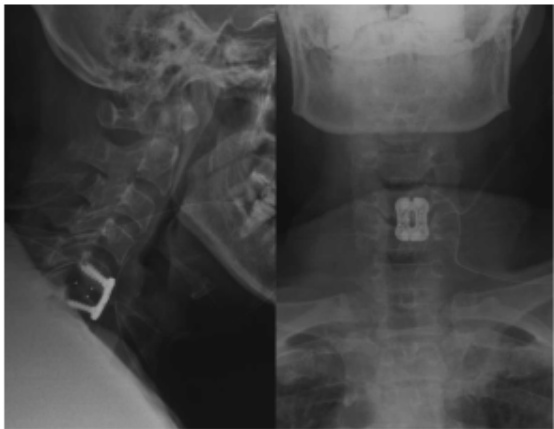
Figure 2



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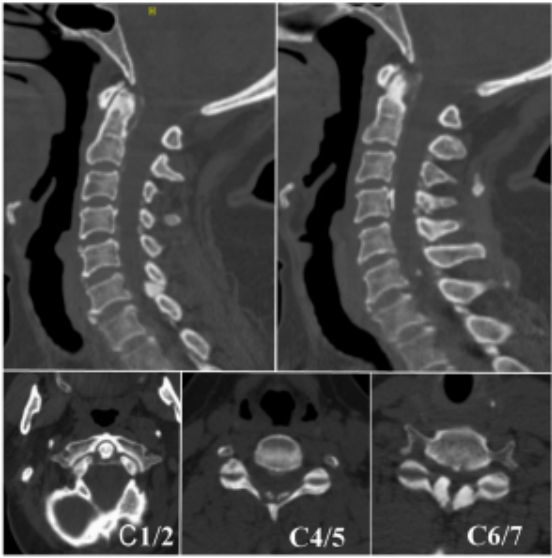
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Figure 2

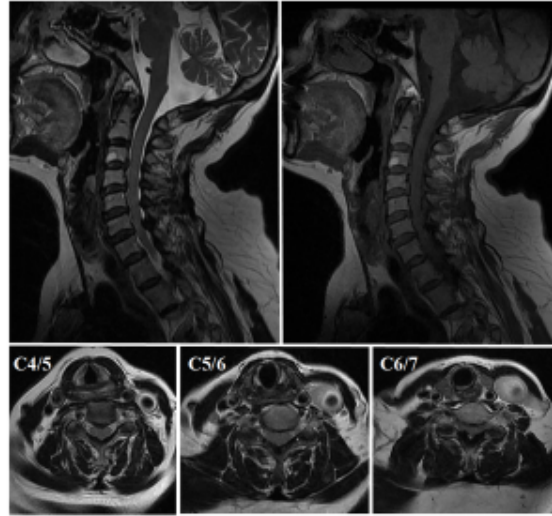
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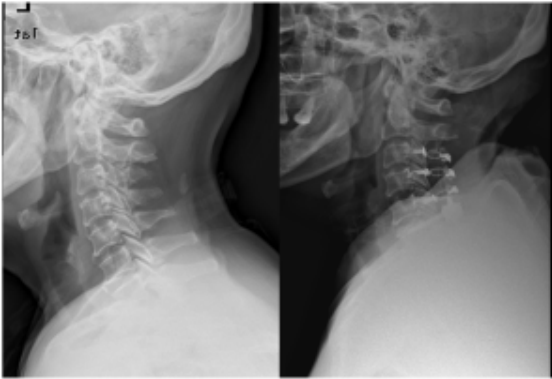
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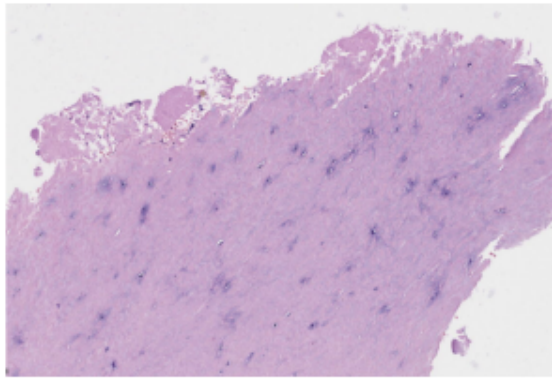
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Figure 3

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Figure 5

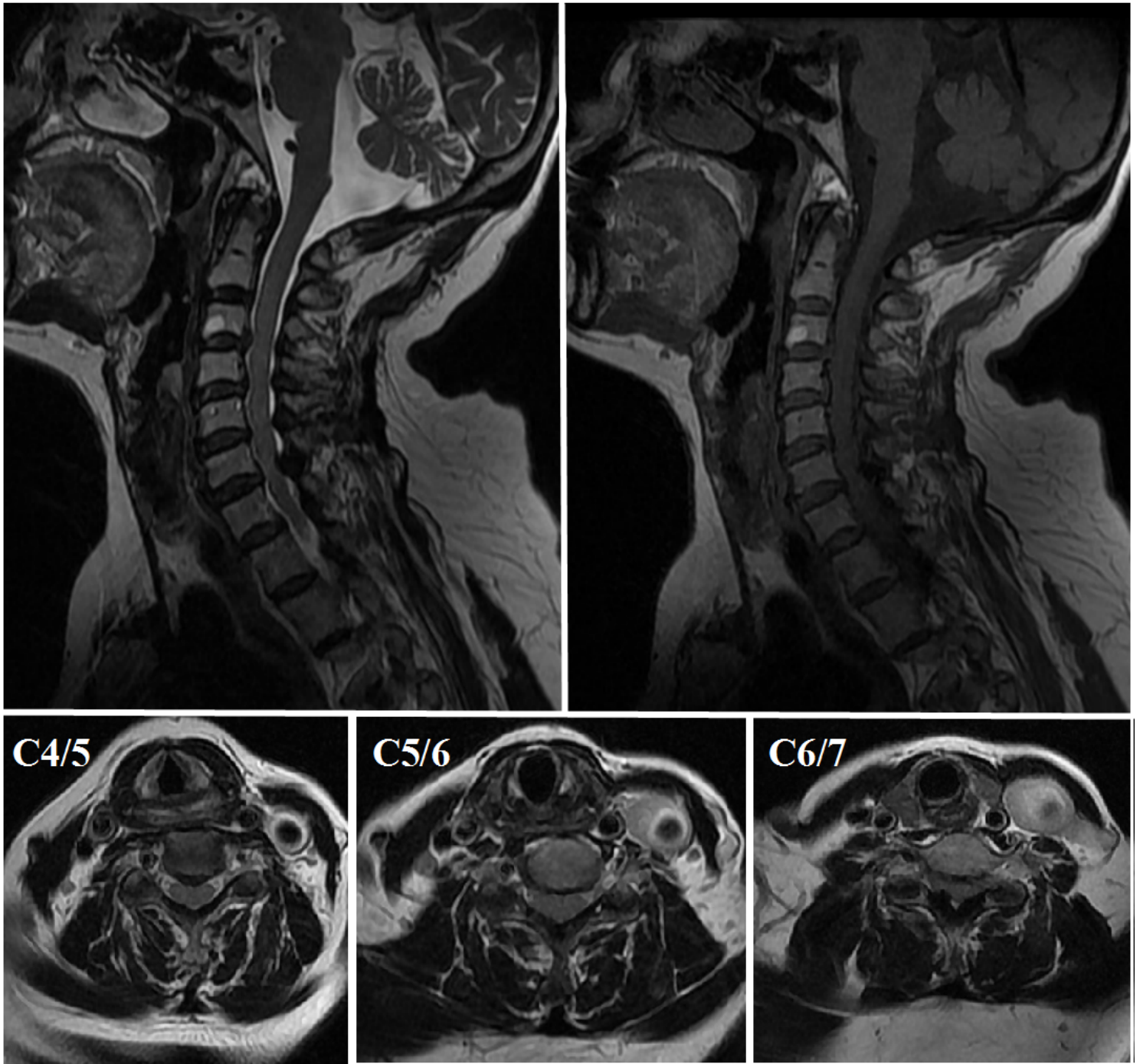


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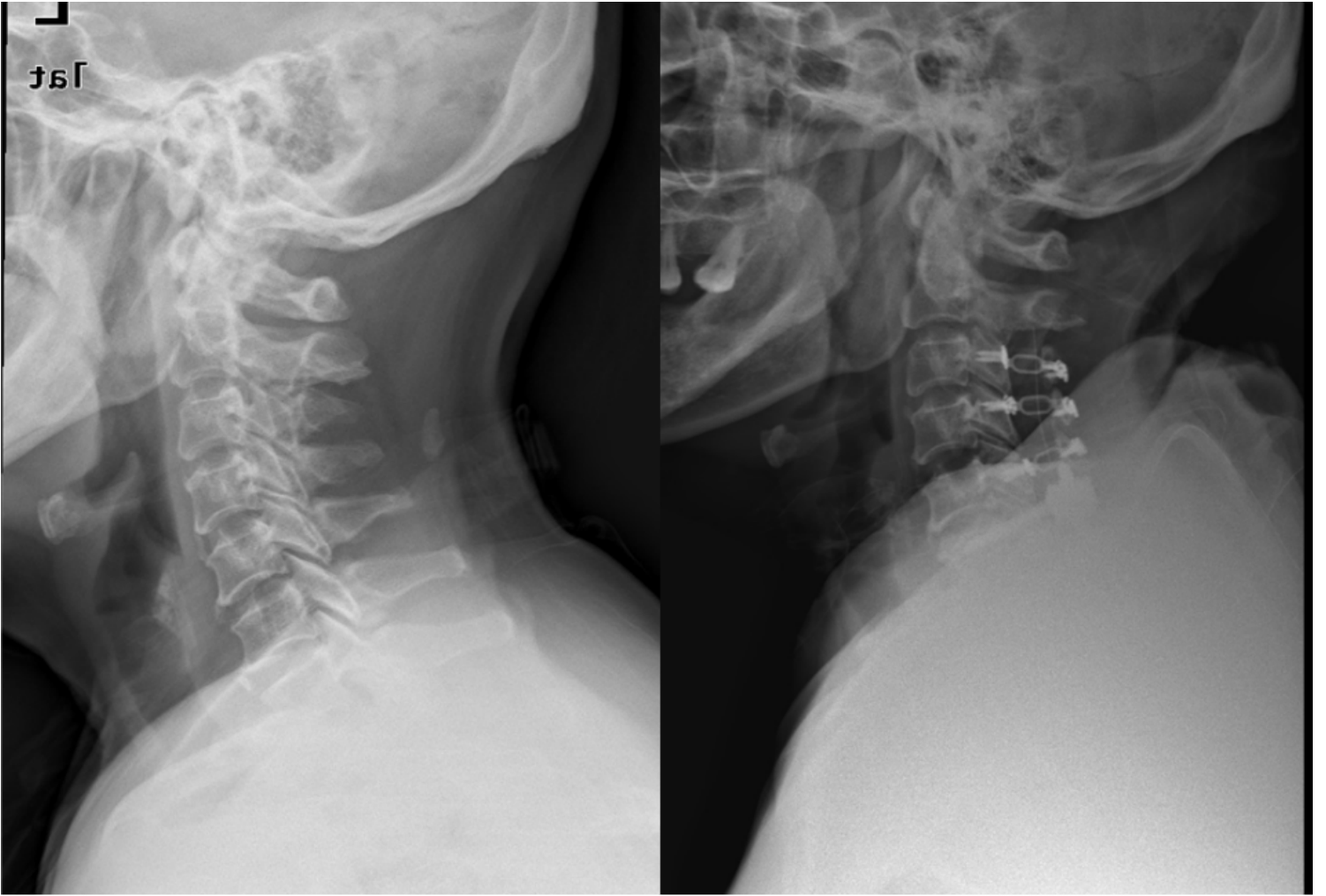


Figure 7

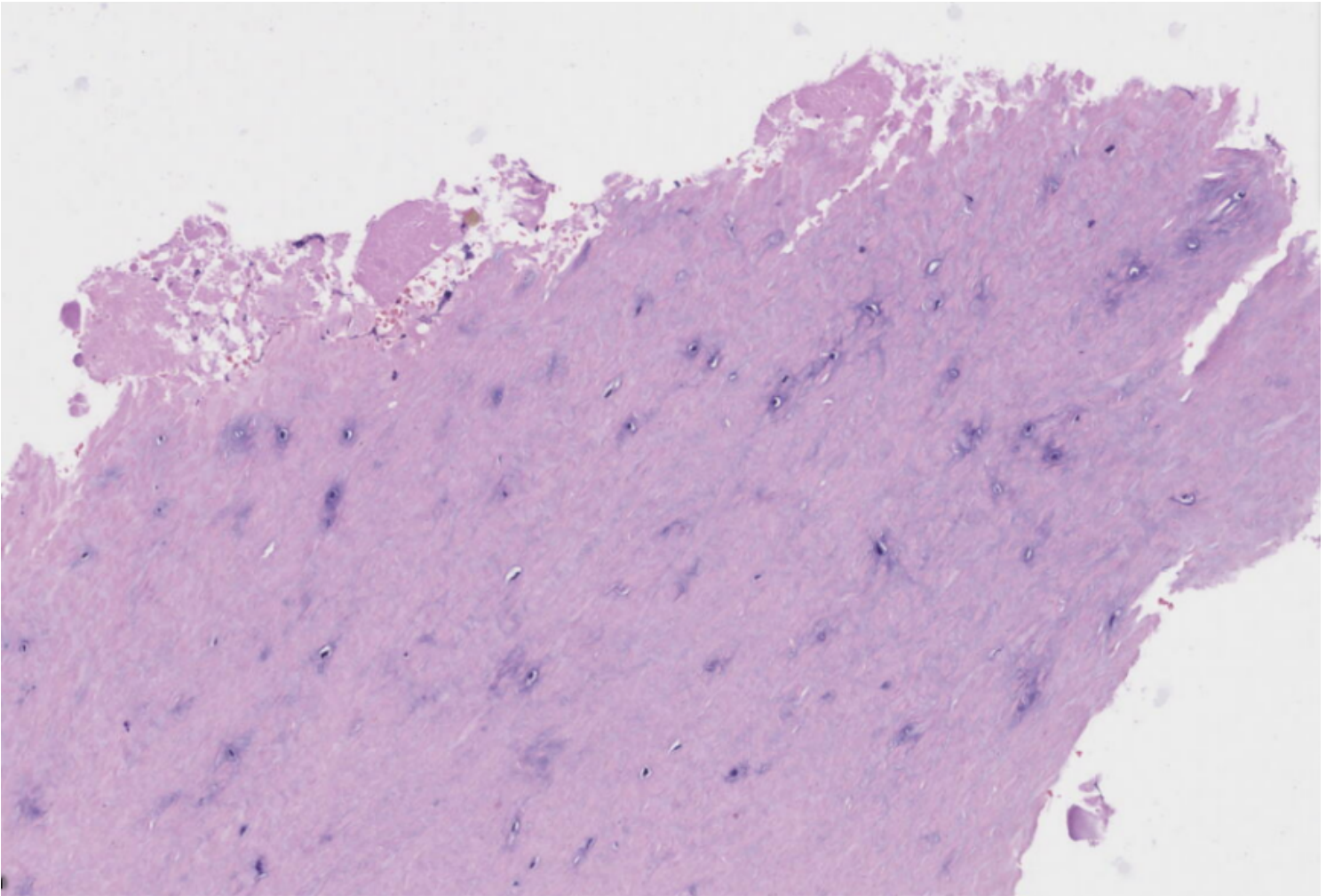


Figure 8

Supplementary Files

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