Synovial Sarcoma of the Cervical Spine: Case Report

Nuno Oliveira (nunocruzoliveira1@gmail.com)
Hospital de Braga https://orcid.org/0000-0003-2117-6438
Sofia Carvalho
Hospital de Braga
Paulo Cunha
Hospital de Braga
Joni Nunes
Hospital de Braga
Pedro Varanda
Hospital de Braga
Paulo Coutinho
Hospital de Braga
Elso Pereira
Hospital de Braga

Research Article

Keywords: Synovial Sarcoma, Spine Tumour, Neurological Deficits, Cervical Spine

Posted Date: September 27th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-312716/v1

Abstract

Purpose

To describe a very rare case of Synovial Sarcoma affecting cervical spine vertebra.

SS is a rare malignant and aggressive soft tissue tumour arising from mesenchymal cells. Primary bone origin SS is a much rarer entity that affects more commonly long bones.

Ideal therapeutic strategy is yet to be defined due to very small number of cases reported so far.

Case report

A 55-year-old male, construction worker, with no other relevant medical history presented with a progressive tetraparesis after recurring several times during a 4-week period to assistant physician and emergency department complaining about bilateral shoulder pain.

Image studies revealed an osteolytic lesion centred on C4 vertebra with intracanalar and intraforaminal extension, causing neurologic compression.

Patient was submitted to urgent surgical decompression intervention. C3 and C4 corpectomy and excisional biopsy followed by stabilization with C2-C5 arthrodesis.

Outcomes

Neurological deficits did not improve after surgery. Histopathological and immunohistochemical analysis revealed phenotypical characteristics of a biphasic Synovial Sarcoma. Patient died 4 weeks after surgery due to a respiratory tract infection.

Discussion

SS is a malignant rare and aggressive soft tissue tumour that usually affects young adults. Very few cases of primary bone SS affecting the spine are described in literature.

Imaging studies may suggest the diagnosis of synovial sarcoma but definitive diagnosis can only be confirmed by histological and immunohistochemical analysis.

The rarity of these lesions demands high clinical suspicion for the diagnosis and due to the low number of cases reported ideal therapeutic strategy is yet to be defined.

Introduction

Synovial Sarcoma (SS) is a malignant and aggressive soft tissue tumour arising from mesenchymal cells and is responsible for 2,5 to 10,5% of soft tissue tumours. Primary bone origin SS is a much rarer entity that affects more commonly long bones. Femur is the most common, followed by tibia and pelvic bones.

SS can occur in any age, but it is most commonly seen in adolescents and young adults [1–4]. In cases of primary bone SS age distribution seems to be broader and these tumours also seem to be more aggressive than soft tissue SS [1].

Despite its name, SS does not arise from any cell of the *synovium*. It can arise in any anatomic area and in fact it is extremely rare in joints [3–6].

There are no specific symptoms or laboratory tests for the diagnosis of SS, therefore a high clinical suspicion is needed and these tumours can take a long time to be diagnosed. Pain, vertebral body collapse, spine instability and neurologic deficits may occur when these tumours affect the spine [7].

SS radiological aspect is variable but usually appears as a lithic lesion that may have sclerotic areas. Most of times cortical bone is compromised and invasion of local soft tissues is variable [1, 8].

Genetically, SS is characterized by translocation t(X,18) which is present in about 90% of the cases and is immunoreactive to EMA (*Epithelial Membrane Antigen*) and several cytokeratins (CK), namely CK7 e CK19 that usually are not expressed by other sarcomas [1, 2, 4, 8–10].

First line of treatment is complete margin free or compartmental resection of the tumour whenever possible (9). Chemotherapy and radiotherapy can be used both as adjuvant and neoadjuvant strategies but their role is not yet clearly defined. [2, 8].

Authors present a rare case of SS located in the cervical spine.

Case Report

Patient was a 55-year-old male, construction worker, ex-smoker, with controlled hypertension disease and hypercholesterolemia with no other relevant personal or family medical history. Presented several times during a 4-week period to assistant physician and emergency department complaining about bilateral shoulder pain, with progressive intensity. Shoulder radiographs were normal and symptoms were associated with increased physical demand at work. He presented again with a progressive tetraparesis which motivated the transfer to our hospital.

At physical examination patient presented dyspnea, peripheral blood oxygen saturation of 92% without supplementary oxygen, hypoesthesia starting at C4 dermatome, and tetraparesis worse on the left side (muscular strength reported from 0 to 5 using Medical Research Council Manual Muscle Testing scale – Right/Left) C5 2/1; C6 1/0; C7 2/2; C8 3/2; T1 2/1; L2 2/1; L3 3/2; L4 3/2; L5 3/3; S1 3/2. Bilateral extension plantar reflexes were present. Urinary catheterization was needed due to urinary retention. Non-invasive ventilation was needed during night to keep peripheral blood oxygen saturation levels over 90%. Patient was admitted for further investigation, Karnovsky score of 20%.

Cervical radiograph revealed a C4 fracture with vertebral body collapse that motivated a cervical spine computed tomography scan (CT). CT revealed an osteolytic lesion of apparent neoplastic origin, centred

on C4 vertebra with extension to posterior elements of C3 and C4, with intracanalar and intraforaminal extension, causing medullar and nerve root compression (Fig. 1). Gadolinium enhanced Magnetic Resonance (MR) showed a pathological fracture of C4 vertebra with a neoplastic formation centred at C4, extending from C2 to C5. Hyposignal on T1-weighted acquisitions, hypersignal on T2-STIR weighted images. Severe cervical canal stenosis with medullar hypersignal between C3 to C5. C3-C4 foramina were also compromised bilaterally. Tumour extended from zones 2 to 11 and layers A trough D according to the Weinstein-Boriani-Biagini System.

Bone scintigraphy and a thoracic, abdominal and pelvic CT excluded lesions elsewhere. Cervical angiotomography excluded invasion of vertebral arteries.

Under general anaesthesia, supine position, patient was submitted to urgent surgical decompression intervention. C3 and C4 corpectomy and C2-C5 arthrodesis with expandable cage and anterior C2-C5 plate and screw fixation. An enlarged submandibular lymph node was also removed.

There was no improvement in neurological deficits after surgery.

Histopathological analysis revealed intralesional excision of the tumour with histological and phenotypical characteristics of SS. Biphasic synovial sarcoma with well-formed glandular structures and spindle cells arranged in a fascicular pattern was observed. Numerous mitotic figures were present. The excised lymph node was invaded by the tumour (Fig. 3).

Immunohistochemical studies revealed diffuse expression in the epithelial component and focal expression in the spindle-cell component of CK18, CK19 and EMA and diffuse membranous expression of CD99 (Fig. 4).

Post operatory CT scan showed a good central decompression but it also revealed signs of incomplete resection of the tumour (Fig. 5).

Due to severe cardiorespiratory debilitation, our multidisciplinary oncology team decided not to consider immediate adjuvant therapy.

Four weeks after surgical intervention, patient acquired a nosocomial pneumonia that lead to severe cardiorespiratory dysfunction and death.

Discussion

SS are rare and aggressive soft tissue tumors that usually affects adolescents and young adults. It rarely presents in the spine and primary bone origin is even rarer with sparse cases reported in the literature. Therefore, there are no specific studies on primary bone origin SS and therapeutic approach is extrapolated from studies involving other types of SS and other aggressive types of sarcoma.

It is widely accepted that the most effective treatment is a complete margin free, block excision. Adjuvant radiotherapy seems to decrease local recurrence and seems beneficial both in patients with complete resections and marginal resections [2, 8, 13].

In our case, due to the fast progressive clinical deterioration, a decompressive intervention was performed by C3 and C4 corpectomy, piecemeal resection of identifiable intracanalar tumor mass and anterior cervical fusion from C2 to C5.

Chemotherapy schemes based on anthracycline, alone or combined with ifosfamide can be used in advanced disease [2, 8]. Despite most of the studies not showing statistical differences in the global survival rate in patients with aggressive sarcomas treated with adjuvant chemotherapy [15–18], Ferrari A. et al [2], in a retrospective study that included 271 SS patients, showed that patients treated with adjuvant chemotherapy had a longer metastasis free survival rate compared to patients submitted to surgical treatment only, suggesting it may have a role in the prevention of metastatic disease.

Chemotherapy and radiotherapy may also have a role in tumor size reduction in the preoperative period for unresectable SS. Radiotherapy has a well-established role in improving local control, especially after less-than-compartmental resection. [7]

SS survival rates are best in young patients and those in whom a complete margin free resection is achievable. Worse prognosis is associated with no margin free resection, advanced age (> 25 years), tumor dimension greater than 5cm, tumor necrosis, vascular invasion, lower cellular differentiation, and high mitotic index [8, 11, 13].

Histologically, SS is composed mainly by two different cell types, epithelial and spindle cells. Depending on the proportion of each of the components and the degree of differentiation of them, SS can be categorized into biphasic, which comprise the two cell types in varying proportions, or monophasic, most of which consist of spindle cells. A third undifferentiated round cell type has been described (can comprise up to 20% of the cases) which represents a form of tumor progression that can occur in both single-phase and biphasic tumors and has a more aggressive behavior [1, 2, 8].

SS immunophenotypic examination is usually positive pro EMA and several cytokeratins, in particular CK7 and CK19 whose expression is not observed in other sarcomas. The expression of these three markers is intense and diffuse in the epithelial and focal component and dispersed in the spindle-cell component and in the poorly differentiated type. SS also shows positivity for CD99, bcl-2 and TLE1. In about 30% of cases, focal positivity is observed for the S100 protein and very rarely in the spindle component, CD34 expression is observed [2, 8]

Genetically, SS is characterized by the translocation t(X,18) that merges the SS18 gene (also known as SYT) with the SSX1 (the most common variant), SSX2 or SSX4 genes, on the X chromosome. The sensitivity and specificity for the diagnosis of SS is well established [8, 13]. In up to 5% of the cases, SS

have the typical clinical and morphological characteristics but does not carry any of the SS18-SSX fusion gene [8].

In our case, the histological examination showed histological characteristics compatible with the diagnosis of biphasic synovial sarcoma, as well as an immunophenotype described in the literature as more frequent in this type of tumor, namely positivity for EMA, CK19 and CD99. The cytogenetic testing was negative for the translocation t(X,18).

Patient age (55 years), delay in the diagnosis, histological analysis with tumor necrosis, high mitotic index, marginal resection and distant disease (involvement of submandibular ganglia) culminated in a very poor prognosis case. Despite evidence showing potential beneficial effects of both chemo and radiotherapy in incomplete resections and with distant disease, our multidisciplinary oncology team decided not to immediately initiate adjuvant therapy due to patient cardiorespiratory debilitation.

Additionally, tumor location on high cervical spine, with spinal cord compression and consequent ventilatory mechanics impairment that led to the need of an emergent decompression surgery, greatly contributed to aggravate the already poor prognosis.

Yang M et al [7], reported the largest series of spine SS to our knowledge, with 16 cases in a period of 10 years practice. Only in four cases they achieved a block resection of the tumour, demonstrating that this can be very challenging in the spine due to the complex vertebral anatomy and surrounding structures.

Recently, new therapeutic strategies are emerging [8, 19]. Pazopanib (a multitarget tyrosine kinase inhibitor) has been approved for the treatment of adult patients with advanced soft tissue sarcomas including SS. Other potential targets are the SS18-SSX fusion and New York esophageal squamous cell carcinoma 1 (NY-ESO-1), that is expressed by several tumors and is present in nearly 60% of SS [20]. New studies on these and new potential targets are ongoing.

A high suspicion level is essential for the diagnosis of these lesions to identify them early in order to allow multidisciplinary treatment planning and improve prognosis.

Conclusion

The rarity of these lesions demands high clinical suspicion for the diagnosis and due to the low number of cases reported ideal therapeutic strategy is yet to be defined. Complete surgical resection seems to be the most unanimous goal strategy. Controversy still exists in regard of chemotherapy and radiotherapy as adjuvant and neoadjuvant treatments. New immunotherapeutic strategies are emerging, that can change prognosis especially in cases of advanced and relapsed disease. Multicentre prospective studies are needed.

Declarations

i. Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

ii. Conflicts of interest

The authors have no conflicts of interest to declare that are relevant to the content of this article.

iii. Ethics approval

Not applicable.

iv. Consent to participate

Obtained.

v. Consent for publication

Obtained.

vi. Availability of data and material

Not applicable.

vii. Code availability

Not applicable.

viii. Authors' contributions

Nuno Oliveira – gathered data, literature review and article conception.

Sofia Carvalho – pathological anatomy, histological and immunohistochemical analysis.

Paulo Cunha – literature review, manuscript revision.

Joni Nunes – surgical team member, manuscript revision.

Pedro Varanda – head spine unit, manuscript revision

Paulo Coutinho – surgical team member, manuscript revision.

Elso Pereira – surgical team leader, manuscript revision.

References

1. Sbaraglia M, Righi A, Gambarotti M, Vanel D, Picci P, Dei Tos AP. Soft Tissue Tumors Rarely Presenting Primary in Bone; Diagnostic Pitfalls. Surg Pathol Clin. 2017;10(3):705–30.
2. Ferrari A, Gronchi A, Casanova M, Meazza C, Gandola L, Collini P, et al. Synovial sarcoma: a retrospective analysis of 271 patients of all ages treated at a single institution. Cancer. 2004;101(3):627–34.
3. Zulkarnaen M, Pan K, Shanmugam P, Ibrahim Z, Chan W. Intraosseous synovial sarcoma of the proximal femur: Case report. Malays Orthop J. 2012;6(1):49–52.
4. Kim KW, Park SY, Won KY, Jin W, Kim SM, Park JS, et al. Synovial sarcoma of primary bone origin arising from the cervical spine. Skeletal Radiol. 2013;42(2):303–8.
5. Kim J, Lee SH, Choi YL, Bae GE, Kim ES, Eoh W. Synovial sarcoma of the spine: a case involving paraspinal muscle with extensive calcification and the surgical consideration in treatment. Eur Spine J. 2014;23(1):27–31.
6. So IT, Cho KB, Lee JY, Kim SJ, Jung HI, Choi JH, et al. A primary gastric synovial sarcoma: A case report and literature review. Med (Baltim). 2017;96(49):e8904.
7. Yang M, Zhong N, Zhao C, Xu W, He S, Zhao J, et al. Surgical management and outcome of synovial sarcoma in the spine. World J Surg Oncol. 2018;16(1):175.
8. El Beaino M, Araujo DM, Lazar AJ, Lin PP. Synovial Sarcoma: Advances in Diagnosis and Treatment Identification of New Biologic Targets to Improve Multimodal Therapy. Ann Surg Oncol. 2017;24(8):2145–54.
9. O'Sullivan PJ, Harris AC, Munk PL. Radiological features of synovial cell sarcoma. Br J Radiol. 2008;81(964):346–56.
10. de Ribaupierre S, Vernet O, Beck-Popovic M, Meagher-Villemure K, Rilliet B. Cervical nerve root synovial sarcoma in a child with chromosomal (X;18) translocation. Case report and review of the literature. Pediatr Neurosurg. 2007;43(5):382–5.
11. Bergh P, Meis-Kindblom JM, Gherlinzoni F, et al. Synovial sarcoma: identification of low and high risk groups. Cancer. 1999;85:2596–607.
12. Lewis JJ, Antonescu CR, Leung DH, et al. Synovial sarcoma:a multivariate analysis of prognostic factors in 112 patients with primary localized tumors of the extremity. J Clin Oncol. 2000;18:2087–94.
13. Guillou L, Coindre J, Gallagher G, et al. Detection of the synovial sarcoma translocation t(X;18)(SYT;SSX) in paraffin embedded tissues using reverse transcriptase-polymerase chain reaction: a

reliable and powerful diagnostic tool for pathologists. A molecular analysis of 221 mesenchymal tumors fixed in different fixatives. Hum Pathol. 2001;32(1):105–12.

14. Kaloostian PE, Gokaslan ZL. Surgical management of primary tumors of the cervical spine: surgical considerations and avoidance of complications. Neurol Res. 2014;36(6):557–65.
15. Antman K, Crowley J, Balcerzak SP, Rivkin SE, Weiss GR, Elias A, et al. An intergroup phase III randomized study of doxorubicin and dacarbazine with or without ifosfamide and mesna in advanced soft tissue and bone sarcomas. J Clin Oncol. 1993;11(7):1276–85.
16. Bramwell V, Rouesse J, Steward W, Santoro A, Schraffordt-Koops H, Buesa J, et al. Adjuvant CYVADIC chemotherapy for adult soft tissue sarcoma–reduced local recurrence but no improvement in survival: a study of the European Organization for Research and Treatment of Cancer Soft Tissue and Bone Sarcoma Group. J Clin Oncol. 1994;12(6):1137–49.
17. Edmonson JH, Ryan LM, Blum RH, Brooks JS, Shiraki M, Frytak S, et al. Randomized comparison of doxorubicin alone versus ifosfamide plus doxorubicin or mitomycin, doxorubicin, and cisplatin against advanced soft tissue sarcomas. J Clin Oncol. 1993;11(7):1269–75.
18. Italiano A, Penel N, Robin YM, Bui B, Le Cesne A, Piperno-Neumann S, Tubiana-Hulin M, Bompas E, Chevreau C, Isambert N, et al. Neo/adjuvant chemotherapy does not improve outcome in resected primary synovial sarcoma: a study of the French Sarcoma Group. Ann Oncol. 2009;20:425–30.
19. Baldi GG, Orbach D, Bertulli R, Magni C, Sironi G, Casanova M, et al. Standard treatment and emerging drugs for managing synovial sarcoma: adult's and pediatric oncologist perspective. Expert Opin Emerg Drugs. 2019;24(1):43–53.
20. Kakimoto T, Matsumine A, Kageyama S, Asanuma K, Matsubara T, Nakamura T, et al. Immunohistochemical expression and clinicopathological assessment of the cancer testis antigens NY-ESO-1 and MAGE-A4 in high-grade soft-tissue sarcoma. Oncol Lett. 2019;17(4):3937–43.

Figures

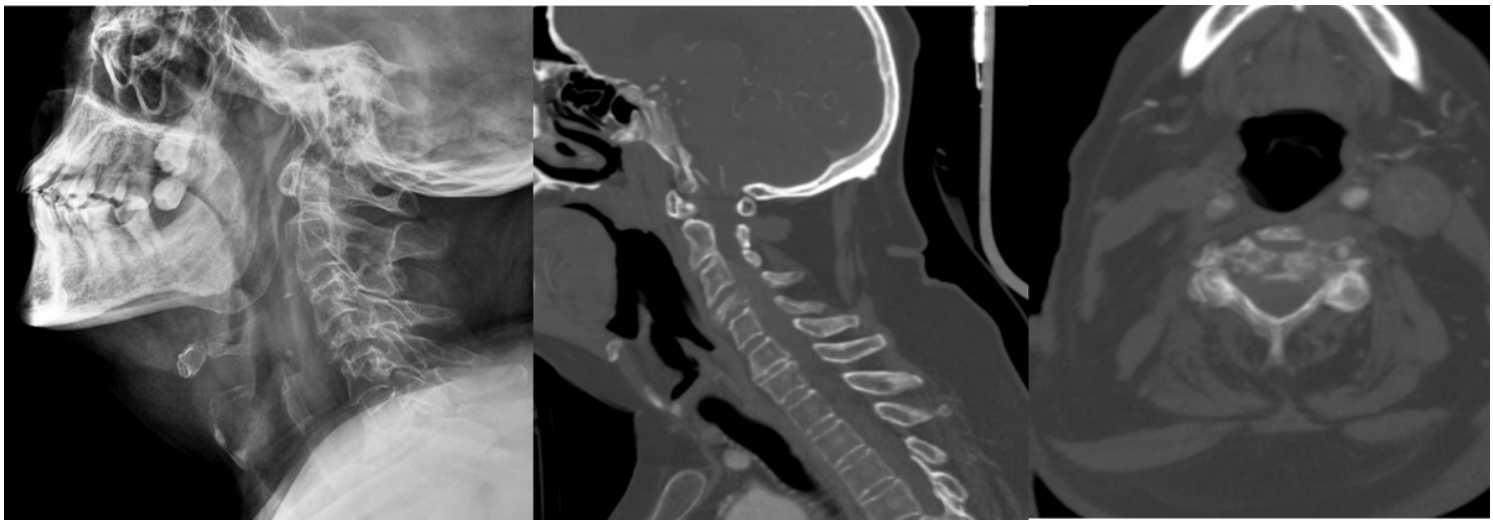

Figure 1

Cervical radiograph revealing a C4 fracture with vertebral body collapse (left). CT scan (middle and right) revealed an osteolytic lesion centred on C4 vertebra with extension to posterior elements of C3 and C4, with intracanalar and intraforaminal extension.

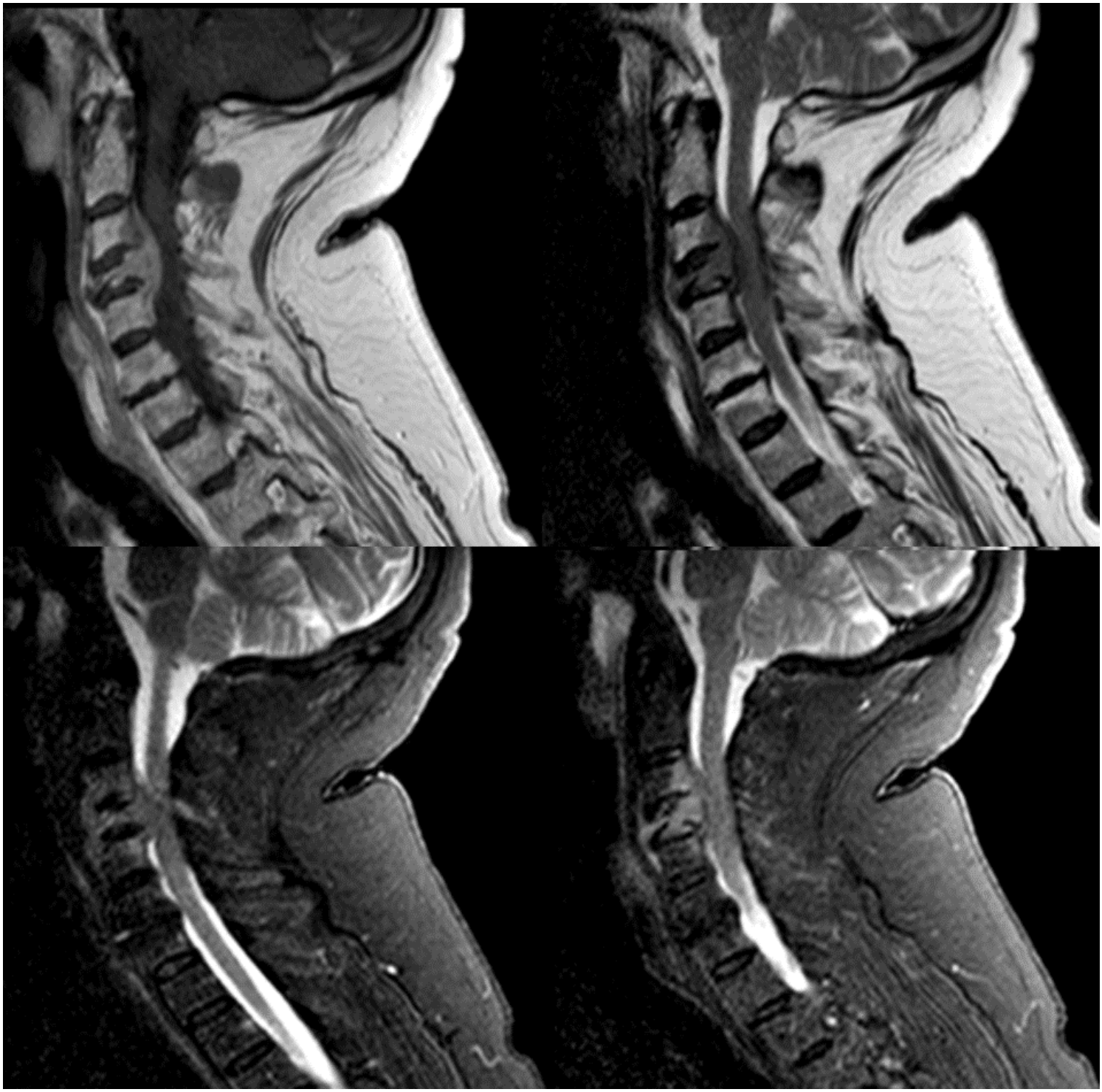

Figure 2

Gadolinium enhanced Magnetic Resonance: pathological fracture of C4 vertebra with a neoplastic formation centred at C4, extending from C2 to C5. Hyposignal on T1-weighted acquisitions, hypersignal on T2-STIR weighted images. Severe cervical canal stenosis with medullar hypersignal between C3 to C5

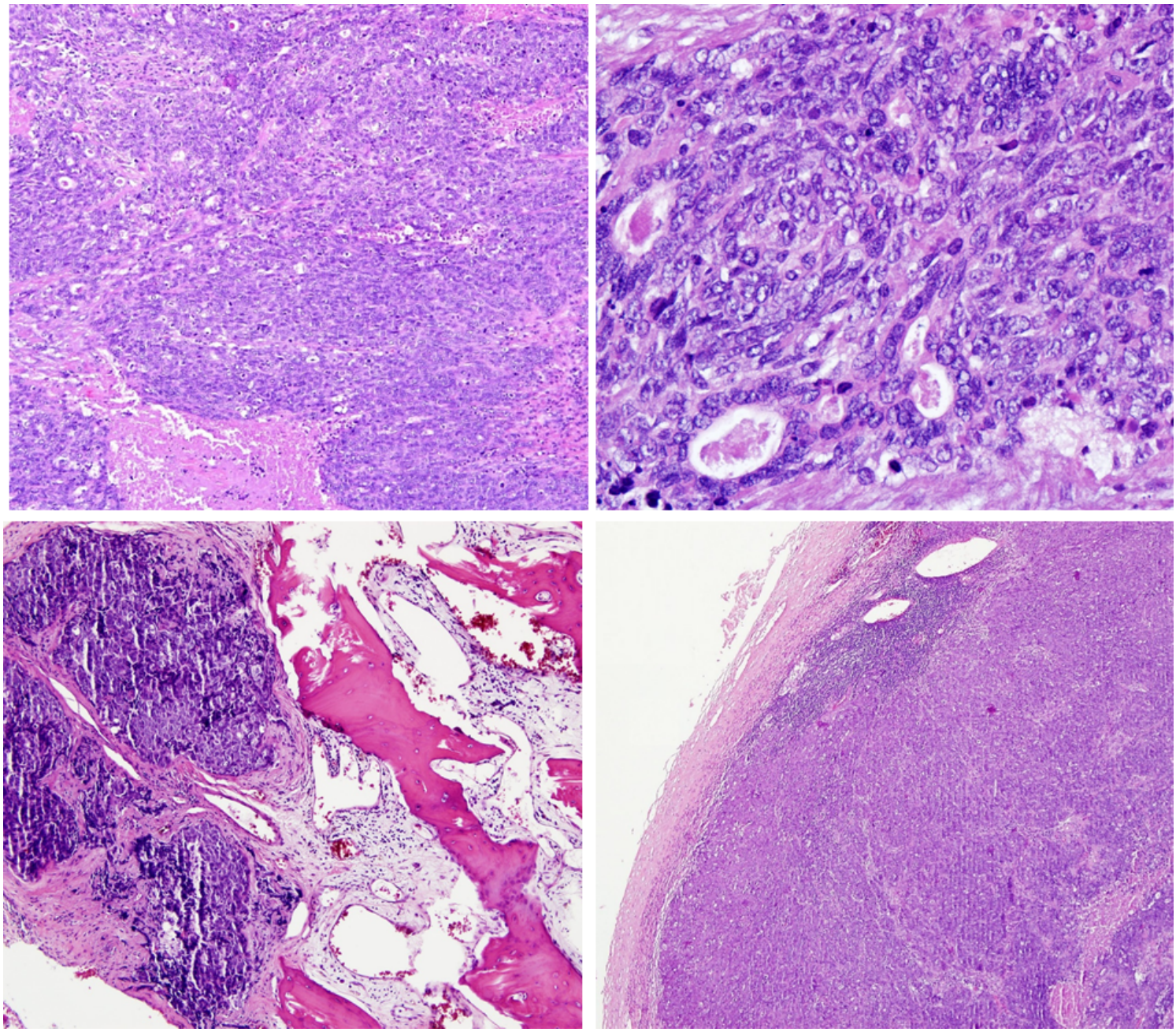

Figure 3

Histopathological analysis. Superior left: Biphasic synovial sarcoma with well-formed glandular structures and spindle cells arranged in a fascicular pattern (H&E, 100x); Superior right: Ovoid vesicular nuclei in both components. Moderately abundant eosinophilic cytoplasm in the epithelial component and scarse basophilic cytoplasm in the spindle-cell component. Numerous mitoses are observed (H&E, 400x); Inferior: Bone (left) and lymph node (right) envolvement, respectively (H&E, 100x).

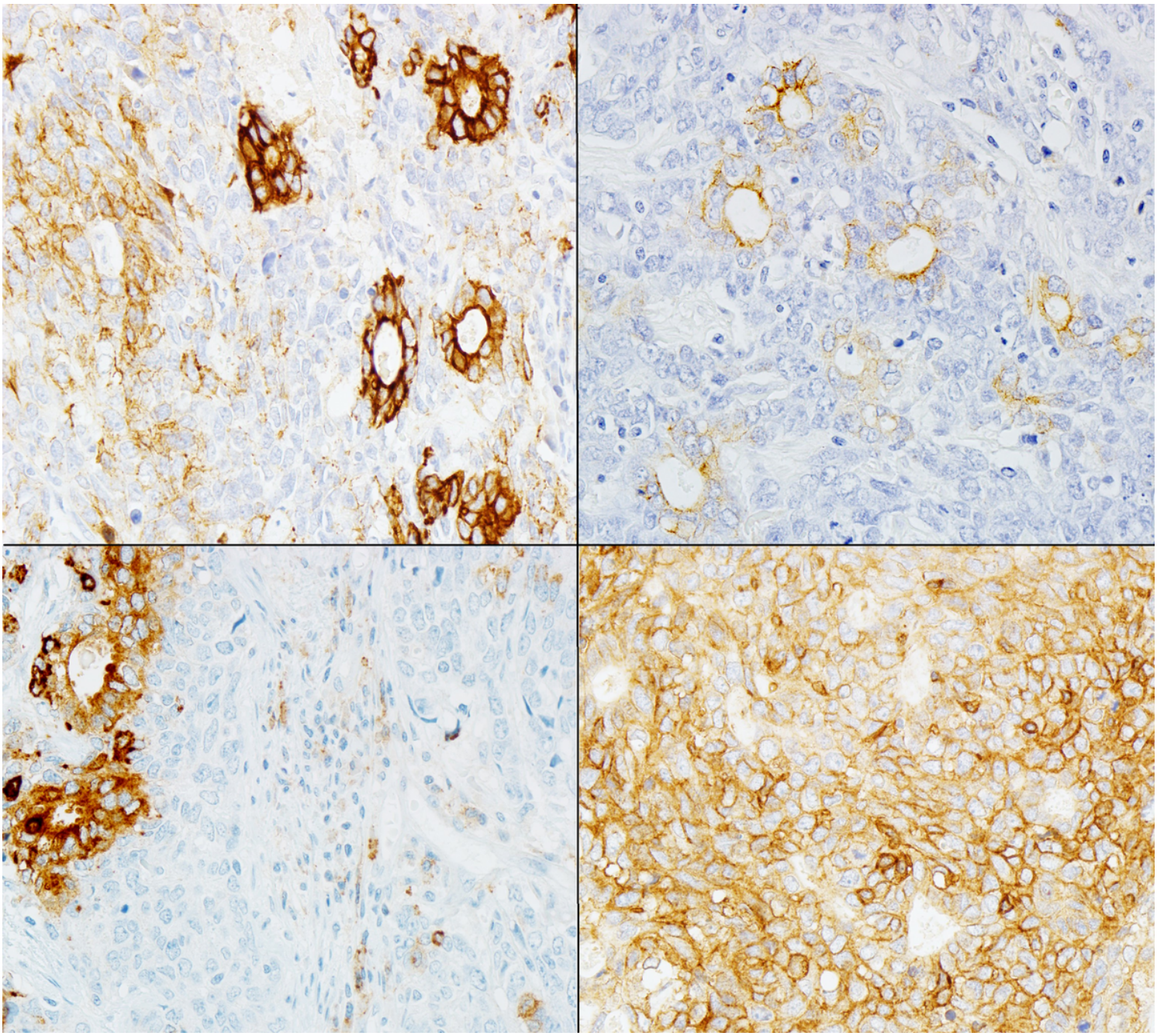

Figure 4

Immunohistochemical study. Diffuse expression in the epithelial component and focal expression in the spindle-cell component of CK18 (superior left), CK19 (superior right) and EMA (inferior left). Diffuse membranous expression of CD99 (inferior right)

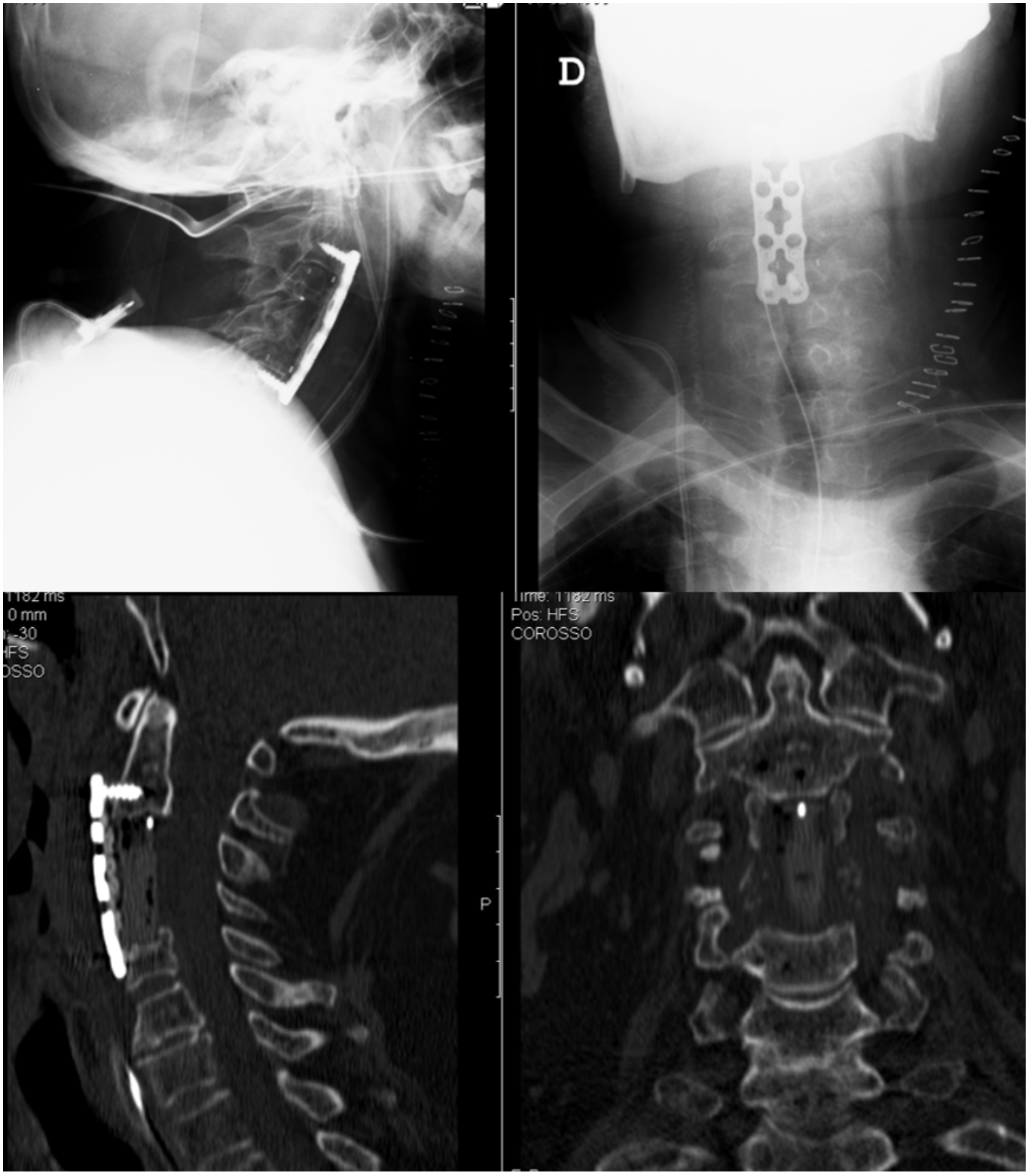

Figure 5

Post operatory radiography and tomography. Post operatory CT scan showed a good central decompression but it also showed signs of incomplete resection of the tumour.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- CAREchecklist.pdf