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Radiotherapy-induced tumors of the spine, peripheral nerve, and spinal cord: Case report and literature review

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Abstract

Background: The development of a secondary malignancy in the field of radiation is a rare but well-recognized hazard of cancer treatment. The radiotherapy-induced (RT-I) tumors are even more aggressive and potentially lethal than the primary tumor. To goal of this article is to report a case of RT-I neural tumor located in the peripheral nerve and spinal cord and to perform a literature review of the subject.

Case Reports: Thirty-year male with symptoms of hypoesthesia and dysesthesia of the L5 nerve root distribution and previous treatment of a testicular seminoma 20 years previously. The lumbar magnetic resonance imaging showed the growth of a nerve root tumor. Surgery was performed, and a fusiform tumor was resected with clear margins. The anatomopathological and immunohistochemical studies were compatible with a malignant peripheral nerve sheath tumor. A total of 30 cases were included in the review. The mean age of the patients at diagnosis of the induced tumor was 39.36 (±16.74) years. Most were male (63.3%). The main type of primary disease was neural tumors (30%). The most common type of histology was fibrosarcoma (20.0%). No difference was found in age, gender, and time of diagnosis between neural and nonneural tumors. The mean survival after the diagnosis of the secondary tumor was 10.7 months (±13.27), and neural tumors had a longer survival period ($P = 0.031$).

Conclusion: The current gold standard therapy is complete resection with clear margins, since most tumors do not respond to chemotherapy and RT. The neural type of RT-I tumor presented a longer survival period.

Key Words: Malignant peripheral nerve sheath tumor, radiation-induced tumor, radiotherapy, spine, spine surgery

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INTRODUCTION

The development of a secondary malignancy in the field of radiation is a rare but well-recognized hazard of cancer treatment.[9,38] This type of treatment has been associated with an increased rate of solid tumors, specially after Hodgkin's lymphoma irradiation.[1] The first bone tumor secondary to radiotherapy (RT) was described in 1922 by Beck, who reported three cases of the bone tumor after irradiation for tuberculosis.[6]

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Even though the risk for developing a new tumor is low, varying from 0.9% to 2%,[18] the long survival time may present a considerable risk for the development of a new tumor.[15] Tsang *et al.*[40] reported a relative risk of 1.8/10,000 persons per year. The RT-induced (RT-I) tumors are even more aggressive and potentially lethal than the primary tumor.[19]

Usually, the site of the RT-I tumor is the periphery of the radiation field.[12] In general, the most common type of radiation-induced tumor of the spine is bone and soft tissue sarcoma,[1,21] neural tumors being more unusual. The capacity to induce secondary neural tumors requires the higher doses of radiation, and the mean latency period can reach 10 years.[27]

RT-I tumors have become increasingly important because of the longer life of the general population, even the oncologic patients. The goal of this study is to report a case of neural tumor secondary to RT and to perform a literature review on the cases of RT-I tumors of the spine.

CASE REPORT

A 30-year-old male presented with symptoms of hypoesthesia and dysesthesia of the L5 nerve root distribution, with right positive Lasègue, and normal strength and reflexes for 60 days. The patient presented no comorbidities, except the previous treatment of a testicular seminoma with orchiectomy and adjuvant RT 20 years ago. The radiation dose utilized for the treatment of the seminoma was 30.6 Gy, irradiating the cervical and para-aortic regions. There was no personal or family history of neurofibromatosis. He had undergone coronal, sagittal, and axial T2-weighted contrast-enhanced magnetic resonance imaging (MRI) of the lumbar spine that revealed a contrast enhancement of two nodular formations placed in the L4 nerve root, the first located proximally, measuring 1.1 cm × 0.6 cm, and the second distally in the right lateral recess of the spinal canal, measuring 2.1 cm × 0.9 cm [Figure 1a]. Investigation with a neurophysiologic study of lower limbs, genetic analysis, and brain, cervical, and thoracic MRI was indicated.

The results of the electroneuromyography of lower limbs revealed subacute and chronic right L5 neuropathy without muscle denervation. The genetic analysis was normal. The brain and cervical spine MRI were normal [Figure 2a].

A surgical indication for diagnosis and treatment as well its complications were discussed with the patient and his family. The patient was afraid of motor deficit complications and decided to control the pain with physiotherapy and oral analgesic medication. The patient was closely observed. The pain was well-controlled with physiotherapy and oral analgesia when necessary during

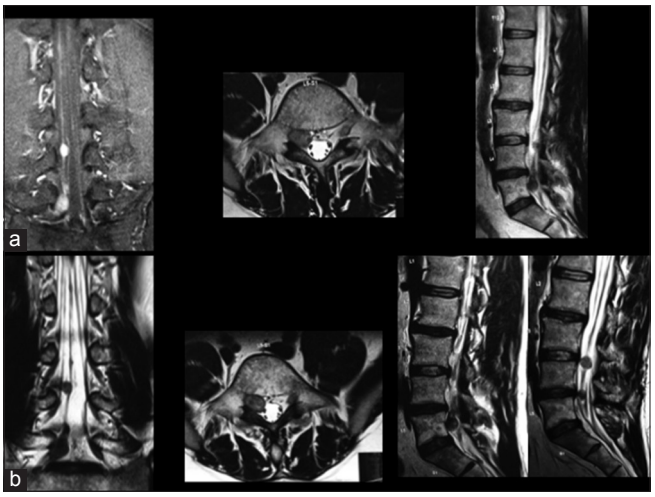

Figure 1: Coronal, sagittal, and axial T2-weighted contrast-enhanced magnetic resonance imaging of the spine that revealed a contrast-enhancement of two nodular formations, one in the L4 nerve root and the second distally in the right lateral recess of the spinal canal (a). After 6 months, the lumbar magnetic resonance imaging showed that a tumor of the nerve root had grown (b)

6 months. After this period, the patient complained of a progressive increase of sciatica, the paresthesia became worse, and the motor strength was quickly and severely reduced with Grade 2 dorsiflexion of the right foot strength. The lumbar MRI showed that a tumor of the nerve root had grown [Figure 1b].

Surgery was indicated and accepted by the patient and his family. The surgical planning was total tumor removal with free margins. A right hemilaminectomy from L3 to S1 was performed. After the incision of the dura mater, a fusiform tumor was visualized adjacent to the L5 foramen and adjacent of the cauda equina nerve roots. The L4 nerve root was individualized and sectioned proximal to the upper margin of the tumor. The distal tumor was dissected, and the nerve root distally to the tumor was individualized and sectioned. The entire segment of L4 nerve root was resected with clear margins [Figure 3]. The dura mater was sutured with 4.0 mononylon. The paravertebral muscle was tightly sutured to avoid cerebrospinal fluid (CSF) leak. The subcutaneous tissue and skin layer were closed in the standard fashion.

The patient was discharged from hospital 3 days after surgery with better resolution of pain, hypoesthesia in the L5 dermatomes, and motor strength Grade 3 of the L5 nerve root. The anatomopathological and immunohistochemical studies showed a hypercellular malignant spindle cell tumor with a high mitotic index and moderate pleomorphism in a nerve root, compatible with a malignant peripheral nerve sheath tumor (MPNST) [Figure 4].

Thirty days later the patient reported somnolence, anisocoria, diplopia, severe Grade 2 paraparesis, neurogenic bowel with flaccid anal sphincter tone, and neurogenic bladder. Sagittal

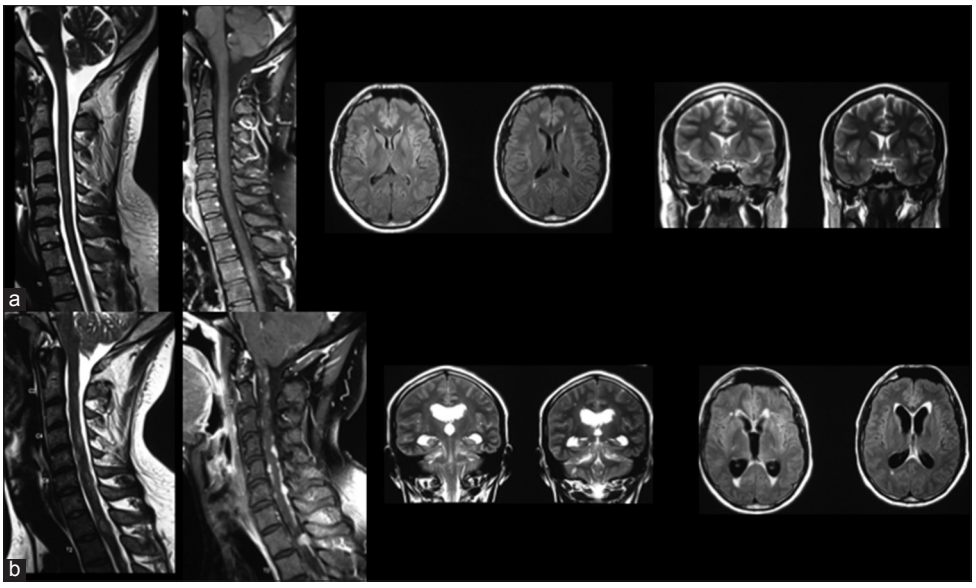

Figure 2: The brain and cervical spine magnetic resonance imaging were normal at the first investigation (a). After 7 months sagittal T1-weighted contrast-enhanced magnetic resonance imaging of brain and spine demonstrated a hypertensive hydrocephalus, leptomeningeal enhancement, and contrast-enhanced masses throughout the cervicothoracic spinal cord surfaces (b)

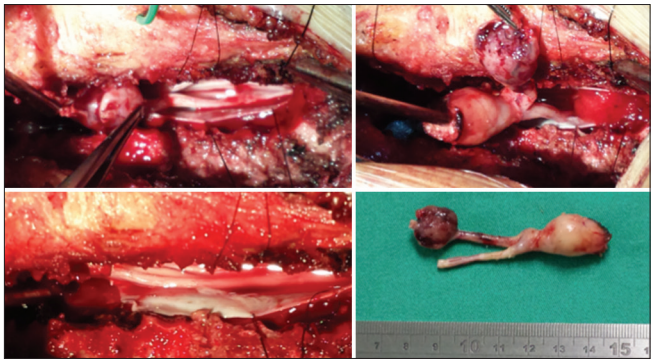

Figure 3: After the incision of the dura mater, a fusiform tumor was visualized adjacent to the L5 foramen and resected with clear margins

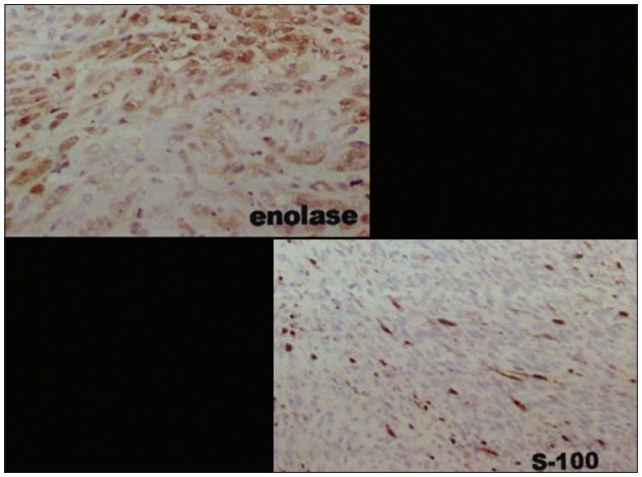

Figure 4: The anatomopathological and immunohistochemical study showed a hypercellular malignant spindle cell tumor with a high mitotic index and moderate pleomorphism in a nerve root, compatible with a malignant peripheral nerve sheath tumor

T1-weighted contrast-enhanced MRI of brain and spine demonstrated a hypertensive hydrocephalus, leptomeningeal enhancement, and contrast-enhanced masses throughout the cervicothoracic spinal cord surfaces [Figure 2b]. The patient underwent urgent cervical decompression via C7-T2 laminectomy with partial resection of the fibrous tumor and a ventricular catheter to monitor intracranial pressure and CSF drainage. Biopsy staining with hematoxylin and eosin revealed features characteristic of the malignant peripheral nerve sheath.

The patient died from acute respiratory failure 48 h after the second surgery. The patient's total time of survival from the time of MPNST diagnosis was 9 months.

DISCUSSION

Cahan and Woodard.[7] proposed that the following criteria should be fulfilled for a sarcoma to be considered as radiation-induced: (1) The sarcoma should begin in the area subjected to irradiation, (2) a latent period (in years) must exist between the time of irradiation and the development of the sarcoma, and (3) the sarcoma must be diagnosed histologically. The case reported fulfills all these criteria.

The case reported had undergone adjuvant RT for testicular seminoma 20 years before presenting with an RT-I intradural MPNST that developed diffuse leptomeningeal, hydrocephalus, and cervicothoracic spinal cord metastases. A literature review of RT-I spine tumor cases was performed in an online database: pubmed.gov (http://www.ncbi.nlm.nih.gov/pubmed/)

[Figure 5]. A total of 30 cases were included, 29 cases reported in the literature from 22 articles and the case presented in this paper [Table 1]. The mean age of RT-I spine tumor cases was 39.36 (±16.74) years at the diagnosis of the induced tumor, and most of them were male (63.3% - 19/29).

According to Toland *et al*.[39] in 643 cases of Hodgkin's lymphoma treated with RT, 18 presented secondary malignancies. RT in the treatment of Hodgkin's lymphoma dramatically increased the patients' survival but also increased the incidence of RT-I tumors cases. The incidence of RT-I tumors was also observed after RT for testicular cancer with a 2.6-fold increased risk.[42] To avoid this complication, the therapy guideline for testicular cancer was modified, for example, by the use of carboplatin as an alternative instead of RT.[2,30,31,43]

The pathology of the primary tumor of the 30 spine tumors cases induced by RT was mainly neural tumors (30%), followed by Hodgkin's lymphoma (16.6%), ankylosing spondylitis (16.6%), seminoma (13.3%), and astrocytoma (10.0%) [Table 1]. The most common site of the primary tumor was the sacral region (21.4%) followed by testicle (14.3%), mediastinum (10.3%), and cervix (10.3%) [Table 1].

Prompt recognition and treatment of radio-induced tumors located in the spine are crucial because they tend to grow rapidly and have a low response to conventional radiation and chemotherapy.[38] However, it is not always easy to recognize them. The clinical presentation frequently mimics benign disc disease, which may lead to a wrong diagnostic and surgical approach only for decompression,[38] or even mimic the recurrence of the original tumor.[8,16] The radiological and pathological findings are indistinguishable from a spontaneous solitary

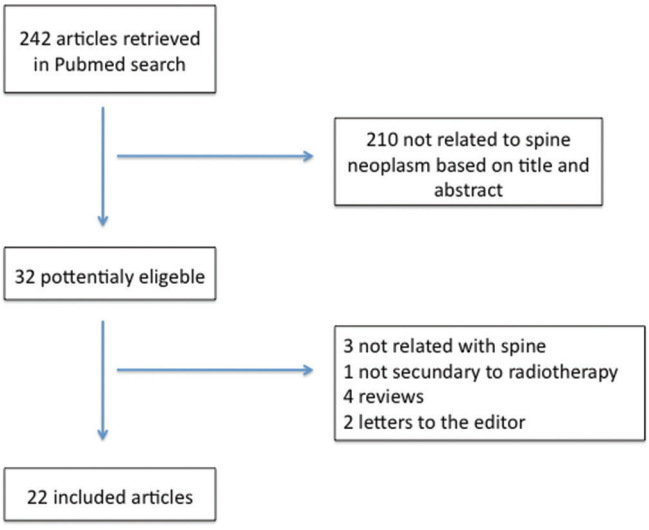

Figure 5: Literature review of radiation-induced tumors of the spine using an online database of pubmed.gov

osteochondroma,[17] and due to its latent period of appearance after the irradiation, the differential diagnosis with late onset metastasis is difficult.[38]

In the reported case, the MRI diagnosis was two small nodular lesions in peripheral nerve compatible with a benign tumor of nerve sheath. This radiological presentation was concordant with the symptoms, and the neurophysiologic study of lower limbs. The genetic analysis was performed to evaluate the presence of neurofibromatosis with a normal result. To identify others lesions in the neuroaxis, brain, cervical, and thoracic MRI were indicated and did not show any tumor except those in the lumbar region. At that time, the patient decides to treat the pain and be closely observed because he was afraid of the chance of residual motor deficit from surgery.

The cases of RT-I tumors reported in the literature were diagnosed on average 16.6 (± 9.73) years after the RT (minimum 3 – maximum 40) [Table 1]. The thoracic spine (26.7%) was the most common location involved followed by sacral (23.3%), cervical (20.0%), lumbar (10.0%), and combined spinal segments in the rest of the cases (20.0%) [Table 1].

The most common type of RT-I tumor in the spine was fibrosarcoma (20.0%) followed mainly by MPNST (16.6%), osteosarcoma (13.3%), and osteochondroma (10.0%) [Table 1]. MPNST are extremely rare tumors with an incidence of 0.001% in the general population.[1,44] In the present review, four MPNST (13.3%) located in the spine were reported as secondary to RT, and these tumors are considered aggressive with a poor long-term prognosis.[38]

Surgery is the main therapy in these cases (56.7%), especially because no clear survival benefit has been demonstrated with RT or chemotherapy [Table 1].[44] In the case we reported, there was a two-nodule formation in the right L5 nerve root. Despite aggressive surgical resection, the patient went on to have diffuse leptomeningeal spread and seeding of the cervical spinal cord dysfunction and hypertensive hydrocephaly and died despite prompt treatment.

In patients with a history of previous RT that had a clinical presentation of the spine and/or spinal cord dysfunction and where a lesion is detected, a biopsy should be performed to rule out a second primary neoplasm.[38] In those cases, the current gold standard of the treatment is complete resection with clear margins.[3] Aggressive surgical management significantly improves survival when adequate margins are obtained.[22] However, the possibility of obtaining wide margins for spinal tumors is about 20%, given their proximity to or invasion of the spinal cord, major vessels, and peripheral nerves.[14,20,25]

Table 1: Summary of the systematic review of the 28 cases of radio-induced of the spine reported in the literature

Author (year)	Age (years) - gender	Primary tumor location - histology	Total intensity of radiotherapy for primary tumor	Location of radiation-induced tumor	Histological type	Diagnosis after primary tumor (years)	Treatment option	Survival after diagnosis of radio-induced tumor (months)
Falavigna (2014)	30 - male	Testicle - seminoma		Thoracic and lumbar	Malignant peripheral nerve sheath	20	Surgical	9 DD
Kawanabe *et al.* (2012)[24]	54 - male	Testicle - seminoma	30.6 Gy (T10–T12)	Thoracic	Anaplastic astrocytoma	37	Surgical + chemotherapy	9 DD
West *et al.* (1997)[44]	40 - male	Testicle - seminoma	30.6 Gy (periaortic + sacrum)	Sacral	Malignant peripheral nerve sheath	8	Surgical	7 LLF
Edgar and Robinson (1973)[15] Case 1	26 - male	Sacral - ankylosing spondylitis	5400 r (SI + TL + TC)	Lumbar	Fibrosarcoma	20	Surgical	11 DD
Edgar and Robinson (1973)[15] Case 2	19 - male	Sacral - ankylosing spondylitis	1360 r (SI)	Sacral	Fibrosarcoma	17	Surgical	6 DD
Edgar and Robinson (1973)[15] Case 3	41 - male	Sacral - ankylosing spondylitis	2000 r (CT)	Sacral	Fibrosarcoma/ leiomyosarcoma	15	NR	6 DD
Edgar and Robinson (1973)[15] Case 4	18 - male	Lumbar - ankylosing spondylitis	11,600 r (SI + L)	Lumbar	Fibrosarcoma	9	Surgical	6 DD
Edgar and Robinson (1973)[15] Case 5	47 - female	Sacral - ankylosing spondylitis	15,910 r (SI + TL + TC)	Sacral	Fibrosarcoma	17	Palliative irradiation	3 DD
Noh and Huh (2007)[35] Case 1	59 - female	Uterine - cervical adenocarcinoma	50 Gy (pelvic)	Sacral	Osteosarcoma	16	Chemotherapy + palliative radiotherapy	2 LLF
Noh and Huh (2007)[35] Case 2	66 - female	Uterine - squamous cell carcinoma	54 Gy (pelvic)	Sacral	Sarcoma	7	Palliative	? LLF
Amin *et al.* (2004)[3]	38 - male	Testicular - seminoma	30 Gy (para-aortic)	Thoracic and lumbar	Malignant peripheral nerve sheath tumor	10	Palliative radiotherapy	NR the LLF
Amirjamshidi and Abbassioun (2000)[4]	17 - female	Cerebellar - ependymoma	2000 r (spine)	Cervical	Meningotheliomatous meningioma	15	Surgical + chemotherapy + radiotherapy	58 LLF
Marzbani *et al.* (2013)[29]	65 - male	Thoracic - astrocytoma	50.4+30 Gy (T1–T7)	Thoracic and lumbar	Rhabdomyosarcoma	40	Surgical + radiotherapy	8 DD
Ng *et al.* (2007)[34]	26 - male	Mediastinal - Hodgkin lymphoma	3060 cGy (mediastinal)	Thoracic	Astrocytoma	3	Surgical + radiotherapy + chemotherapy	Several weeks DD
Mut *et al.* (2004)[32]	36 - male	Thoracic - aneurysmal bone cyst	65 Gy (thoracic)	Cervical	Rhabdomyosarcoma	7	Surgical + chemotherapy	13 DD
Gorospe *et al.* (2002)[17]	18 - male	Cerebellar - medulloblastoma	7950 rad (cranial + spine)	Thoracic	Osteochondroma	11	Surgical	<1 week LLF
Leis and Fratkin (1997)[28]	34 - male	Hodgkin lymphoma	4000 (cranial + CT)	Thoracic	Chondrosarcoma	24	Surgical	NR the LLF

Contd...

Table 1: Contd...

Author (year)	Age (years) - gender	Primary tumor location - histology	Total intensity of radiotherapy for primary tumor	Location of radiation-induced tumor	Histological type	Diagnosis after primary tumor (years)	Treatment option	Survival after diagnosis of radio-induced tumor (months)
Isler *et al.* (1996)[22]	46 - male	Sacral - chordoma	4960 rad (T4-sacrum)	Lumbar	Neurofibroma/ schwannoma	9	Surgical	24 DD
Kam *et al.* (2013)[23]	68 - female	Breast - carcinoma	15 Gy (thoracic)	Thoracic	Fibrosarcoma	30	Surgical	Not reported
Cree *et al.* (1994)[11]	29 - female	Abdominal - neuroblastoma	2500 rad (10 cm ×15 cm)	Lumbar	Osteochondroma	28	Surgical	3 LLF
Nadeem *et al.* (1991)[33]	36 - male	Cervical - astrocytoma	4500 cGy (cervical)	Cervical	Histiocytoma + ependymoma	12	Surgical + radiotherapy + chemotherapy	NR but DD
Sundaresan *et al.* (1986)[38]	59 - female	Mediastinal - Hodgkin lymphoma	4400 rad (thoracic)	Thoracic	Telangiectatic osteogenic sarcoma	31	Surgical + chemotherapy	3 DD
Dowdle *et al.* (1977)[13]	14 - female	Cervical - astrocytoma	4500 rad (cervical)	Thoracic	Osteosarcoma	11	Surgical	1 DD
Scheiden and Oberthaler (1983)[36]	41 - male	Sacrum - cystic tumor	27000 rad (sacral)	Sacral	Osteosarcoma	20	Surgical	12 DD
Herman *et al.* (1991)[19]	16 - female	Kidney - Wilms tumor	3000 rad (abdominal)	Thoracic	Osteochondroma	15	Surgical	NR
Lang *et al.* (1981)[26]	60 - female	Vocal cord - malign epithelioma	7500 rad (cervical)	Cervical	Osteosarcoma	11	Surgical	3 DD
Adamson *et al.* (2004)[1] Case 1	37 - male	Mediastinal - Hodgkin lymphoma	7200 cGy (mediastinal + para-aortic)	Cervical	Malignant peripheral nerve sheath tumor	6	Surgical + radiotherapy	Few months DD
Adamson *et al.* (2004)[1] Case 2	31 - female	Cervical lymph node - Hodgkin lymphoma	7700 cGy (mantle + para-aortic)	Cervical	Malignant peripheral nerve sheath tumor	16	Surgical	12 DD
Hu *et al.* (2010)[21]	66 - male	Thyroid	7000 cGy (cervical 12 cm ×15 cm)	Cervical	Sarcoma	30	Surgical	29 LLF
Comey *et al.* (1998)[10]	44 - male	Cerebellopontine - triton tumor	34 Gy (cerebellopontine)	Cervical	Triton tumor	4	Surgical	6.5 DD

LLF: Live at last follow-up, DD: Died from disease, SI: Sacroiliac, TL: Thoracolumbar, TC: Thoracocervical, NR: Not reported

Table 2: The analysis comparing neural and nonneural tumors

	Neural tumor (%)		*P*
	Yes (36.7)	No (63.3)	
Age (mean±SD)	36.27 (±10.14)	41.15 (±19.63)	0.377¥
Gender			
Male (63.3%)	9 (47.4)	10 (52.6)	0.140Ω
Female (36.7%)	2 (18.2)	9 (81.8)	
Time for diagnosis (mean±SD)	12.72 (±9.58)	18.89 (±9.32)	0.095¥
Survival in months (median±IQR)	9.0 (±17.0)	6.0 (±8.3)	0.039§

¥T-test, ΩChi-square test, §Mann–Whitney U-test. SD: Standard deviation, IQR: Interquartile range

The overall prognosis for patients with secondary RT-I tumors in the spine is dismal because there are no proven benefits of chemotherapy, RT, intraoperative electron irradiation, and brachytherapy, with a 5-year survival rate of around 20%.[5,37,41,45] The mean survival after the diagnosis of the secondary tumor was 10.7 months (±13.27). The majority of the patients (63.3%) died from the disease, and 26.6% were alive at the last follow-up [Table 1]. The analysis comparing neural and nonneural RT-I tumors showed a longer survival period of 9.0 (±17.0) months in neural tumor cases, compared to 6.0 (±8.3) months in patients with nonneural tumors ($P = 0.039$) [Table 2]. The age, sex, and time of diagnosis were similar in the neural and nonneural groups.

CONCLUSION

RT-I tumors of the spine, peripheral nerve, and spinal cord are not common. Twenty-nine cases have been reported in the literature. Better awareness of this entity and its potential for metastasis to the central nervous system may enable physicians to perform early intervention. The current gold standard therapy is complete resection with clear margins, since most tumors do not respond to chemotherapy and RT. The neural type of RT-I tumor presented a longer survival.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Adamson DC, Cummings TJ, Friedman AH. Malignant peripheral nerve sheath tumor of the spine after radiation therapy for Hodgkin's lymphoma. Clin Neuropathol 2004;23:245-55.
2. Albers P, Albrecht W, Algaba F, Bokemeyer C, Cohn-Cedermark G, Fizazi K, *et al.* EAU guidelines on testicular cancer: 2011 update. Eur Urol 2011;60:304-19.
3. Amin A, Saifuddin A, Flanagan A, Patterson D, Lehovsky J. Radiotherapy-induced malignant peripheral nerve sheath tumor of the cauda equina. Spine (Phila Pa 1976) 2004;29:E506-9.
4. Amirjamshidi A, Abbassioun K. Radiation-induced tumors of the central nervous system occurring in childhood and adolescence. Four unusual lesions in three patients and a review of the literature. Childs Nerv Syst 2000;16:390-7.
5. Baehring JM, Betensky RA, Batchelor TT. Malignant peripheral nerve sheath tumor: The clinical spectrum and outcome of treatment. Neurology 2003;61:696-8.
6. Beck A. About this issue, roentgen sarcomas also contribute to the pathogenesis of sarcoma. Muench Med Wonchensehr 1922;69:623-5.
7. Cahan WG, Woodard HQ. Sarcoma arising in irradiated bone; report of 11 cases. Cancer 1948;1:3-29.
8. Canellos GP, Arseneau JC, DeVita VT, Whang-Peng J, Johnson RE. Second malignancies complicating Hodgkin's disease in remission. Lancet 1975;1:947-9.
9. Coleman CN. Secondary neoplasms in patients treated for cancer: Etiology and perspective. Radiat Res 1982;92:188-200.
10. Comey CH, McLaughlin MR, Jho HD, Martinez AJ, Lunsford LD. Death from a malignant cerebellopontine angle triton tumor despite stereotactic radiosurgery. Case report. J Neurosurg 1998;89:653-8.
11. Cree AK, Hadlow AT, Taylor TK, Chapman GK. Radiation-induced osteochondroma in the lumbar spine. Spine (Phila Pa 1976) 1994;19:376-9.
12. Davies AM, Sundaram M, James SLJ. Diagnostic Imaging in: Imaging of Bone Tumors and Tumor-Like Lesions: Techniques and Applications, Techniques and Applications. Berlin, Germany: Springer; 2009. p. 503..
13. Dowdle JA Jr, Winter RB, Dehner LP. Postradiation osteosarcoma of the cervical spine in childhood. A case report. J Bone Joint Surg Am 1977;59:969-71.
14. Ducatman BS, Scheithauer BW, Piepgras DG, Reiman HM, Ilstrup DM. Malignant peripheral nerve sheath tumors. A clinicopathologic study of 120 cases. Cancer 1986;57:2006-21.
15. Edgar MA, Robinson MP. Post-radiation sarcoma in ankylosing spondylitis. A report of five cases. J Bone Joint Surg Br 1973;55:183-8.
16. Ferguson DJ, Sutton HG Jr, Dawson PJ. Late effects of adjuvant radiotherapy for breast cancer. Cancer 1984;54:2319-23.
17. Gorospe L, Madrid-Muñiz C, Royo A, García-Raya P, Alvarez-Ruiz F, López-Barea F. Radiation-induced osteochondroma of the T4 vertebra causing spinal cord compression. Eur Radiol 2002;12:844-8.
18. Halperin EC, Greenberg MS, Suit HD. Sarcoma of bone and soft tissue following treatment of Hodgkin's disease. Cancer 1984;53:232-6.
19. Herman TE, McAlister WH, Rosenthal D, Dehner LP. Case report 691. Radiation-induced osteochondromas (RIO) arising from the neural arch and producing compression of the spinal cord. Skeletal Radiol 1991;20:472-6.
20. Hruban RH, Shiu MH, Senie RT, Woodruff JM. Malignant peripheral nerve sheath tumors of the buttock and lower extremity. A study of 43 cases. Cancer 1990;66:1253-65.
21. Hu CK, Kuo LT, Hong WC, Lee JC, Tu YK. Sarcoma of the cervical spine after radiation treatment for thyroid cancer. Spine (Phila Pa 1976) 2010;35:E363-7.
22. Isler MH, Fogaça MF, Mankin HJ. Radiation induced malignant schwannoma arising in a neurofibroma. Clin Orthop Relat Res 1996;325:251-5.
23. Kam LS, Anthony MP, Shek H. Radiation-induced sarcoma in spine. Pol J Radiol 2013;78:69-71.
24. Kawanabe Y, Sawada M, Yukawa H, Ueda S, Sasaki N, Koizumi T, *et al.* Radiation-induced spinal cord anaplastic astrocytoma subsequent to radiotherapy for testicular seminoma. Neurol Med Chir (Tokyo) 2012;52:675-8.
25. Kourea HP, Bilsky MH, Leung DH, Lewis JJ, Woodruff JM. Subdiaphragmatic and intrathoracic paraspinal malignant peripheral nerve sheath tumors: A clinicopathologic study of 25 patients and 26 tumors. Cancer 1998;82:2191-203.
26. Lang G, Kehr P, Paternotte H, Aebi J. Radiation-induced sarcoma of the sixth cervical vertebra (author's transl). Rev Chir Orthop Reparatrice Appar Mot 1981;67:691-3.
27. Laskin WB, Silverman TA, Enzinger FM. Postradiation soft tissue sarcomas. An analysis of 53 cases. Cancer 1988;62:2330-40.
28. Leis AA, Fratkin J. Chondrosarcoma of the spine and thyroid carcinoma following radiation therapy for Hodgkin's lymphoma. Neurology 1997;48:1710-2.
29. Marzbani E, Jones RL, Fink J, Chamberlain MC. Delayed development of a rhabdomyosarcoma following radiation for a spinal cord glioma. J Neurooncol 2013;112:115-8.
30. Mead GM, Fossa SD, Oliver RT, Joffe JK, Huddart RA, Roberts JT, *et al.* Randomized trials in 2466 patients with stage I seminoma: Patterns of relapse and follow-up. J Natl Cancer Inst 2011;103:241-9.
31. Motzer RJ, Agarwal N, Beard C, Bolger GB, Boston B, Carducci MA, *et al.* NCCN clinical practice guidelines in oncology: Testicular cancer. J Natl Compr Canc Netw 2009;7:672-93.
32. Mut M, Cataltepe O, Söylemezoglu F, Akalan N, Ozgen T. Radiation-induced malignant triton tumor associated with severe spinal cord compression. Case report and review of the literature. J Neurosurg 2004;100:298-302.
33. Nadeem SQ, Feun LG, Bruce-Gregorios JH, Green B. Post radiation sarcoma (malignant fibrous histiocytoma) of the cervical spine following ependymoma (a case report). J Neurooncol 1991;11:263-8.
34. Ng C, Fairhall J, Rathmalgoda C, Stening W, Smee R. Spinal cord glioblastoma multiforme induced by radiation after treatment for Hodgkin disease. Case report. J Neurosurg Spine 2007;6:364-7.
35. Noh JM, Huh SJ. Two cases of post-radiation osteosarcoma of the sacrum after pelvic irradiation for uterine cervical cancer. Eur J Gynaecol Oncol 2007;28:497-500.
36. Scheiden R, Oberthaler W. Radiation induced osteosarcoma of the sacrum following radiation of an undiagnosed bone lesion. Arch Orthop Trauma Surg 1983;102:128-30.
37. Sim FH, Cupps RE, Dahlin DC, Ivins JC. Postradiation sarcoma of bone. J Bone Joint Surg Am 1972;54:1479-89.
38. Sundaresan N, Huvos AG, Rosen G, Lane JM. Postradiation osteosarcoma of the spine following treatment of Hodgkin's disease. Spine (Phila Pa 1976) 1986;11:90-2.
39. Toland DH, Coltman CA, Moon TE. Second malignancies complicating Hodgkin's disease: The Southwest Oncology Group Experience. Cancer Clin 1978;1:27-33.
40. Tsang RW, Laperriere NJ, Simpson WJ, Brierley J, Panzarella T, Smyth HS.

Glioma arising after radiation therapy for pituitary adenoma. A report of four patients and estimation of risk. Cancer 1993;72:2227-33.
41. Valdueza JM, Hagel C, Westphal M, Hänsel M, Herrmann HD. Primary spinal malignant schwannoma: Clinical, histological and cytogenetic findings. Neurosurg Rev 1991;14:283-91.
42. van den Belt-Dusebout AW, de Wit R, Gietema JA, Horenblas S, Louwman MW, Ribot JG, *et al.* Treatment-specific risks of second malignancies and cardiovascular disease in 5-year survivors of testicular cancer. J Clin Oncol 2007;25:4370-8.
43. van Leeuwen FE, Stiggelbout AM, van den Belt-Dusebout AW, Noyon R, Eliel MR, van Kerkhoff EH, *et al.* Second cancer risk following testicular cancer: A follow-up study of 1,909 patients. J Clin Oncol 1993;11:415-24.
44. West DA, Parra RO, Manepalli A, Bernardi RJ, Cummings JM. Development of a malignant peripheral nerve sheath tumor following treatment for testicular seminoma. Urology 1997;50:292-4.
45. Wong WW, Hirose T, Scheithauer BW, Schild SE, Gunderson LL. Malignant peripheral nerve sheath tumor: Analysis of treatment outcome. Int J Radiat Oncol Biol Phys 1998;42:351-60.