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CLINICAL EXPERIENCE WITH SOLITARY FIBROUS TUMOR OF CENTRAL NERVOUS SYSTEM: A CASE REPORT.

Oncology

Vikas Gupta* Assistant Senior Medical Officer at Atal Cancer Care Centre, Ambala Cantt., Haryana, India. *Corresponding Author

Minu Gupta Medical Officer at University Health Centre, Kurukshetra University, Kurukshetra, Haryana, India.

Anukriti Jain Junior Resident at M M Institute of Medical Sciences & Research, Mullana,Ambala, Haryana, India.

Roshani Vyas Assistant Senior Medical Officer at Atal Cancer Care Centre, Ambala Cantt., Haryana, India.

Suvetha Chavarkkad Junior Resident at M M Institute of Medical Sciences & Research, Mullana,Ambala, Haryana, India.

ABSTRACT

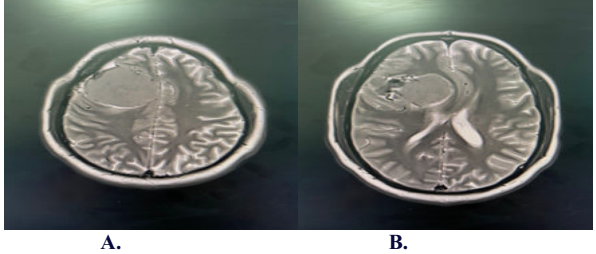
Solitary fibrous tumor (SFT) or Hemangiopericytoma (HPC) are rare mesenchymal tumors in the central nervous system with a high tendency to relapse. Due to the rarity of central nervous system (CNS) HPC, the prognostic factors and optimal treatment remain unclear. The WHO 2021 classification integrated both tumors into one entity but one of the important issues is to demonstrate the standardization of surgery plus adjuvant radiotherapy (RT) as treatment modality. The present study reports the case of a 52-year-old male patient with meningeal SFT also known as Hemangiopericytoma. CEMRI revealed a large enhancing extra-axial right frontal mass lesion causing mass effect and partial effacement of frontal horn of right lateral ventricle and mild leftward shift with subfalcine herniation. He then underwent right frontoparietal craniotomy and total tumor excision. As SFT is difficult to differentially diagnose via imaging, immunohistochemical analysis of CD34, STAT6 and ki-67 index was performed for the definitive diagnosis of SFT. Surgical resection is the preferred treatment for SFT; however, due to the rarity of the tumor, subsequent adjuvant radiation therapy and antiangiogenic drug was administered to reduce the risk of recurrence.

KEYWORDS

INTRODUCTION:

Solitary fibrous tumor (SFT) is a rare spindle cell tumor of mesenchymal origin, initially reported by Klempere and Rabin in 1931.[1] SFT is commonly found in the mediastinum and visceral pleura; however, it can also occur in the pleura external sites, such as the head and neck, pericardium, peritoneum, liver, thyroid, mesentery, and sinuses and orbits.[2]Due to the lack of a true connective tissue component in the central nervous system (CNS), primary SFT of the CNS is rare, accounting for <1% of all primary CNS tumors.[3] SFT has an age-adjusted incidence rate of 0.61 and 0.37 per million persons per year for extrameningeal and meningeal cases, respectively; in other words, we can assume an age-adjusted yearly incidence of 1 new case per million people.[4,5]CNS SFTs account for only 0.09% of all meningeal tumors, while intracranial SFTs (ISFT) are extremely rare.[6] Intracranial SFT occurs most commonly in adults with median age at initial tumor onset at around 42 years with similar incidence rates in males and females.[3]When CNS SFTs occur intracranially, they are frequently extra-axially located.[7] Hemangiopericytomas (HPCs) are also rare mesenchymal tumors that exhibit similar clinical, radiological and histological features to SFTs.[8]Of note, the distinction between the two types of tumours was no longer clinically significant due to the pronounced clinical and histopathological overlap. In the 2021 WHO classification of CNS tumors, the term 'hemangiopericytoma' was removed and replaced with SFT.[9]A solid lesion located in the CNS distinct from fibrous meningioma, termed primary SFT, was initially reported by Carneiro et al in 1996.[10] Intracranially, SFT may occur at the cerebellopontine angle, spinal dura, parasagittal region, meninges and the intraventricular region.[11]

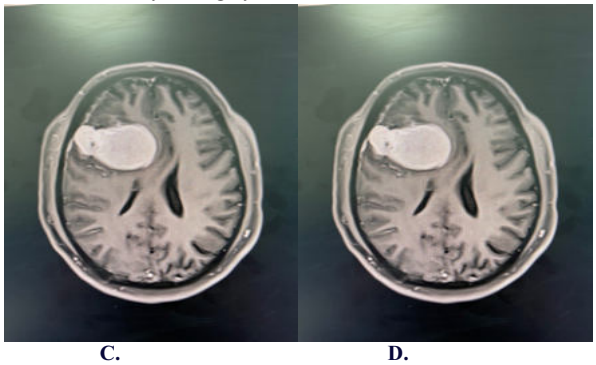
CASE REPORT:



A. B.

A. And B.: Pre-Op MRI T2 weighted images

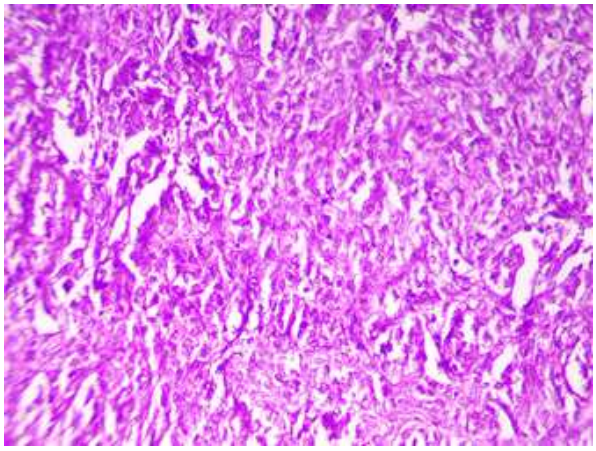
A 52 years old male experienced a single episode of seizure in July 2023. After initial management at emergency, MRI revealed large vividly enhancing extra-axial right frontal mass lesion causing mass effect resulting in partial effacement of frontal horn of right lateral ventricle and mild leftward shift with subfalcine herniation. It measured 5.0 x 4.7 x 5.4 cm (APxTRxCC). Patient then underwent right frontoparietal craniotomy and total tumor excision. During operation, tumor was seen to be dural based, extra-axial, well defined, firm in consistency and highly vascular.



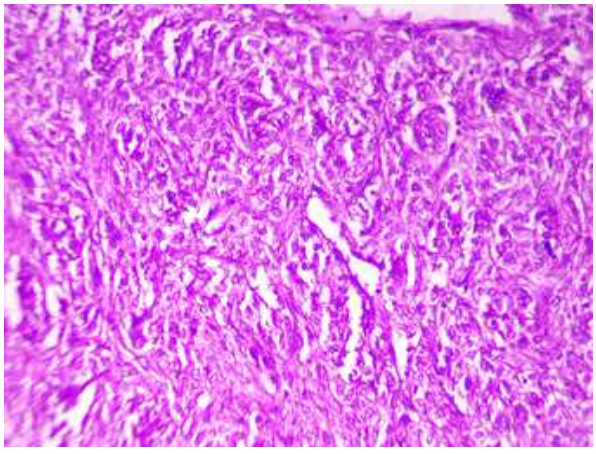
C. D.

C. And D.: Pre-Op MRI Flair sequence images

Pathological examination revealed that soft tissue mass measuring 6x5x4 cm which was grey white in colour and fibrous in texture. Microscopic examination showed a cellular neoplasm composed of mostly spindle to oval shaped cells arranged in a haphazard storiform manner with ill defined cytoplasm and oval nuclei. Numerous small vascular channels were seen with in a mesh of reticulin like network. The cells showed no inclusion/pseudoinclusion and inconspicuous nuclei. There was no necrosis but foci of haemorrhage were seen. Focal collections of large foamy cells forming nodules were noted. Tumor appeared to be closely approximated with dura. Findings were consistent with vascular neoplasm or meningioma variant. On Immunohistochemistry, CD34 and STAT6 were positive in tumor cells while CD31 and GFAP were negative in tumor cells with high Ki-67. Morphology and Immunohistochemistry confirmed Solitary Fibrous Tumor, WHO grade III.



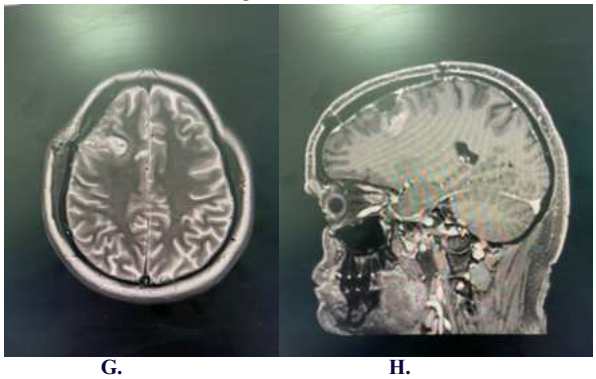
E.



F.

E. And F.: Spindle to ovoid cells arranged haphazardly in a collagenous fibrous stroma with multiple thin walled dilated vessels characteristic of Solitary Fibrous Tumor

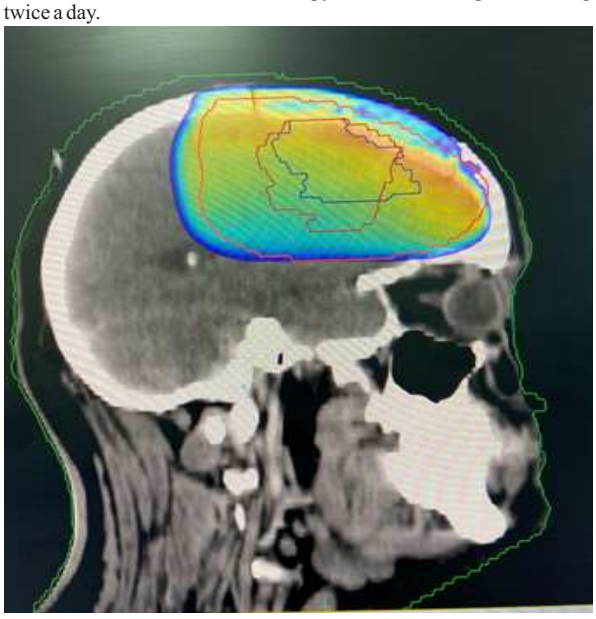
Post operative MRI scan revealed surgical cavity in right frontal region with fluid and late subacute hemorrhagic contents. Hemosiderin rim was seen around cavity. There was mild perifocal edema causing effacement of sulci in right frontal lobe. There was no midline shift seen. No abnormal enhancing lesion was seen.



G. H.

G. And H.: Post Op MRI axial and sagittal view with Tumour cavity seen in sagittal section

In view of high grade and rariety of solitary fibrous tumor of central nervous system, patient was planned for post operative radiotherapy to reduce the risk of recurrence. External beam radiotherapy was delivered via linear accelerator VERSA HD up to a dose of 60 grey in 30 fractions with one fraction per day over five days a week. Target volume delineation involved magnetic resonance imaging (MRI)-based image fusion and planning with a 2.5 cm margin around the tumor cavity for clinical target volume (CTV). An additional 5 mm were added for planning target volume (PTV). Except for mild nausea and hair loss, radiotherapy was well tolerated by patient. Patient was then started on maintainance therapy with Tab. Pazopanib 400mg twice a day.



I.

I.: Colourwash 3DCRT plan depiction of Solitary Fibrous Tumor

On follow up CEMRI scan at 3 months, it was seen that there are Postoperative changes seen in right fronto-parietal calvarium. There is a well-defined T2 heterogeneously hyperintense/ T1 hypointense lesion seen in right frontal convexity probably in the extra-axial space with adjoining hemosiderin staining measuring approx 18 x 20 x 14 mm. It shows a peripheral Hemosiderin Rim and internal heterogeneous enhancement likely representing residual/ recurrent lesion. However no leptomeningeal spread is seen.

Repeat scan at 6 months is suggestive of Postoperative status with evidence of right frontal craniotomy. Surgical cavity measuring approximately 16 x 25 x 12 mm (AP x TR x CC) is seen in the right frontal region with fluid as well as late subacute haemorrhagic contents. Hemosiderin rim is seen around the cavity. There is mild perifocal edema / gliosis. There is no midline shift. On post contrast scans, no abnormal enhancing lesion is seen. Rest of the cerebral hemispheres reveal normal morphology and signal characteristics. No residual/recurrent tumour seen in present scan.

DISCUSSION:

Solitary fibrous tumours are unusual spindle-cell mesenchymal tumours that predominantly occur in the visceral pleura but have been found at other site like peritoneum, pericardium, upper respiratory tract, lung, liver, mediastinum, parotid glands, and thyroid glands. SFT has an age-adjusted incidence rate of 0.61 and 0.37 per million persons per year for extrameningeal and meningeal cases, respectively; in other words, we can assume an age-adjusted yearly incidence of 1 new case per million people.[4,5] Central nervous system (CNS) SFTs account for only 0.09% of all meningeal tumors, while intracranial SFTs (ISFT) are extremely rare.[6] Intracranially, SFT may occur at the cerebellopontine angle, spinal dura, parasagittal region, and the intraventricular region.[11] CNS SFT occurs most commonly in adults with median age at initial tumor onset at 42 years with similar incidence rates in males and females.[3] They are slow growing tumours and patients may present with several non-specific symptoms related to increased intracranial pressure or with the location of the tumor. Only once the lesions become large enough or infringes into the important functional areas, clinical symptoms arise. The symptoms include episodic headaches, gait imbalance, dizziness, sensory disturbance, hemiplegic paralysis, and epileptic seizure.[12] The majority of intracranial SFTs are dural based masses originating predominantly from thick collagen bands, which are produced by fibroblasts.[3]

On MRI, SFTs are well defined, enhancing, homogeneous, or slightly heterogeneous, lesions with intermediate T1-, and low T2, signal. It has been suggested that relatively hypo- and hyperintense areas on T2-weighted images correspond, respectively, to collagenous and

hypercellular regions of tumor. Thickened dural tail, hyperostosis, skull erosion, and capping cysts may all be seen. In general, radiological appearances of SFT are non-specific and would suggest the diagnosis of meningioma.[3]

The characteristic histologic features of SFT include the so-called "pattern less-pattern" of spindle cells, high vascularity, and thick strands of stromal collagen. Alternating hypo- and hypercellular areas is another important clue on low-power examination. The classic histologic features combined with immunohistochemistry are helpful in reaching to a correct diagnosis. Immunohistochemically, SFTs are in most cases diffusely positive for STAT 6 and CD34, while meningiomas are typically reactive for EMA. However, CD34 is not specific for SFTs, as weak and usually patchy staining may be visualized in meningiomas and neurofibromas. Positivity for CD99 and BCL-2 is found in more than half of all cases of SFTs and they also stain strongly with the intermediate filament vimentin, but are usually negative for the neural crest markers S-100, GFAP, EMA, cytokeratin, or vascular antigens.[10]However, Corinne et al found overlapping pathological features and common prognostic factors between SFT and HPC, suggesting that they belong to the same spectrum of tumors.[10] Electron microscopy has not yielded a unique distinctive feature. WHO 2021 classification thus rendered SFT equal to HPC.[9] At present, CD34 is considered the most consistent marker in SFT and positive staining is reported in 95-100% of patients; however, its absence does not rule out this tumor.[13] STAT6 is positive in almost all patients with intracranial SFT.[14]STAT6 may be associated with the fusion of the NAB2-STAT6 gene caused by 12q chromosome rearrangement..[14] Thus, detection of STAT6 or the NAB2-STAT6 fusion gene is recommended for the diagnosis of intracranial SFT.[14] NAB2 and STAT6 are neighbour genes localized on the long arm of chromosome 12 and transcribed in opposite directions.[14] In SFT, an intrachromosomal inversion places the genes in the same orientation, which results in an in-frame fusion transcribed from the NAB2 promoter, leading to STAT6 nuclear expression that may be detected by IHC.[14] The expression of STAT6 in intracranial SFT tissue was detected using IHC staining, and the NAB2-STAT6 fusion gene was accurately detected with both high specificity and sensitivity.[14] STAT6 IHC is both a highly specific and sensitive surrogate for NAB2-STAT6 gene fusions, and the specificity and sensitivity of nuclear STAT6 for SFT/HPCs were 100 and 96.6%, respectively.[14] In the present study STAT6 expression was detected by IHC instead of detecting the NAB2-STAT6 fusion gene. Therefore, the lack of NAB2-STAT6 fusion gene detection was a possible limitation of the present report. The SFT tissue of the patient described in the present study was positive for CD34 and STAT6, which was consistent with the results of previous reports. Histological features such as necrosis, hypercellularity and mitoses did not affect the rate of recurrence. A high proliferation index should be considered as a prognostic parameter. Michele et al advocated inclusion of high Ki-67 (i.e. > 5%) as an adverse prognostic parameter in assessing the prognosis of SFT of the CNS.[15]

Surgery offers the best first-line treatment and achieves excellent local control. Total excision of the mass is clearly superior to subtotal resection, with a 16-fold increase in recurrence ratio with subtotal resection (STR) (without adjuvant therapy), compared to total resection.[16] In many reported case series, intracranial SFT have been shown to recur even after complete gross tumor resection (GTR). Therefore, several authors have recommended adjuvant RT for a better outcome.[17,18] Yu et al retrospectively studied patients treated for intracranial SFT between January 2009 and June 2019[19] and their results demonstrated that patients with reduced WHO grading, and who underwent gross total resection and adjuvant radiation therapy exhibited prolonged progression-free survival (PFS).[19] Results of a multi-centre study demonstrated that postoperative radiotherapy, including 2-dimensional conventional radiotherapy, 3-dimensional conformal radiotherapy and intensity-modulated radiotherapy, may significantly improve the PFS of patients with SFT, irrespective of the surgical extent and grade.[20] The prognosis of SFTs remains yet to be fully elucidated since follow-up data of the few reported cases are limited. Recurrence, malignant transformation, or cerebrospinal fluid dissemination has also been described, though seemingly not as frequently but more associated with higher grade of CNS SFT. In these cases, meticulous and complete resection is believed to be the most important prognostic factor and may preclude downstream malignant behavior.[21] Based on the grades and extent of resection (EOR), CNS SFT are divided in following risk categories: low risk—grade 1 with any EOR and grade 2 with GTR; intermediate risk—grade 2 with biopsy/STR; high risk—grade 3 with any EOR. These risk categories improved the prognostic value compared with any single risk factor.[22]

Adjuvant radiation seems to be effective in inhibiting tumor progression, but recurrence remains a common treatment outcome regardless of initial strategy in intermediate and high risk cases as observed in other case series. Anlotinib, a newly multitargeted tyrosine kinase inhibitor with anti-neoplastic and anti-angiogenic activities, inhibits tumor angiogenesis and proliferation.[21] Anti-angiogenesis may be a potential option for the treatment of SFT.[23] Surgery, radiotherapy and Anlotinib alone are effective in the treatment of malignant intracranial SFT.[23] Pazopanib, a multi-target receptor tyrosine kinase inhibitor with potent anti-angiogenic properties, is approved for the treatment of advanced renal cell carcinoma and certain subtypes of advanced soft tissue sarcoma.[24] Of note, pazopanib is effective in treating patients with metastatic or unresectable SFT.[25] The present study demonstrated that surgical resection is the optimal choice for the treatment of SFT, and postoperative radiotherapy may significantly improve PFS in patients. Molecular targeted therapy, such as tyrosine kinase inhibitors anlotinib and pazopanib, is a promising approach for malignant, unresectable or metastatic SFT. However, the present article reports one case and further research and larger randomized controlled trials are required to verify its findings.

REFERENCES:

1. Klemperer P & Rabin C. (1931). Primary neoplasms of the pleura: A report of five cases. *Arch Pathol,* 11, 385-412.
2. Goodlad JR & Fletcher CD. (1991). Solitary fibrous tumour arising at unusual sites: Analysis of a series. *Histopathology,* 19, 515-522.
3. Wang Y, Zhang J, Liu Q, Liu F, Zhu X & Zhang J. (2019). Solitary fibrous tumor of the pineal region with delayed ectopic intracranial metastasis: A case report and review of the literature. *Medicine (Baltimore),* 98:e15737.
4. Kinslow CJ & Wang TJC. (2020). Incidence of extrameningeal solitary fibrous tumors. *Cancer,* 126, 4067.
5. Kinslow CJ, Bruce SS, Rae AI, Sheth SA, McKhann GM, Sisti MB, Bruce JN, Sonabend AM & Wang TJC. (2018). Solitary fibrous tumor/hemangiopericytoma of the central nervous system: A population-based study. *J. Neuro-Oncol,* 138, 173–182.
6. Sanno N, Shimura T, Maeda S & Teramoto A. (2001). A case of solitary fibrous tumor of the meninges. *Brain Tumor Pathol,* 18, 43–47.
7. Claus E, Seynaeve P, Ceuppens J, Vanneste A & Verstraete K. (2017). Intracranial solitary fibrous tumor. *J Belg Soc Radiol,* 101, 11.
8. Zeng L, Wang Y, Wang Y, Han L, Niu H, Zhang M, Ke C, Chen J & Lei T. (2017). Analyses of prognosis-related factors of intracranial solitary fibrous tumors and hemangiopericytomas help understand the relationship between the two sorts of tumors. *J Neurooncol,* 131, 153-161.
9. Louis DN, Perry A, Wesseling P, Brat DJ, Cree IA, Figarella-Branger D, Hawkins C, Ng HK, Pfister SM, Reifenberger G, et al. (2021). The 2021 WHO classification of tumors of the central nervous system: A summary. *Neuro Oncol,* 23, 1231-1251.
10. Carneiro SS, Scheithauer BW, Nascimento AG, Hirose T & Davis DH. (1996). Solitary fibrous tumor of the meninges: A lesion distinct from fibrous meningioma. A clinicopathologic and immunohistochemical study. *Am J Clin Pathol,* 106, 217-224.
11. Hu SW, Tsai KB, Yang SF, Lee KS & Chai CY. (2005). Unusual solitary fibrous tumors in the central nervous system: A report of two cases. *Kaohsiung J Med Sci,* 21, 179-184.
12. Fargen KM, Opalach KJ, Wakefield D, Jacob RP, Yachnis AT & Lister JR. (2011). The central nervous system solitary fibrous tumor: a review of clinical, imaging and pathologic findings among all reported cases from 1996 to 2010. *Clin. Neurol. Neurosurg,* 113, 703–710.
13. Vogels RJ, Vlenterie M, Versleijen-Jonkers YM, Ruijter E, Bekers EM, Verdijk MA, Link MM, Bonenkamp JJ, van der Graaf WT, Slootweg PJ, et al. (2014). Solitary fibrous tumor-clinico- pathologic, immunohistochemical and molecular analysis of 28 cases. *Diagn Pathol,* 9, 224.
14. Georgiesh T, Namløs HM, Sharma N, Lorenz S, Myklebost O, Bjerkehagen B, Meza-Zepeda LA & Boye K. (2021). Clinical and molecular implications of NAB2-STAT6 fusion variants in solitary fibrous tumour. *Pathology,* 53, 713-719.
15. Bisceglia M, Galliani C, Giannatempo G, Lauriola W, Bianco M, D'angelo V, Pizzolitto S, Vita G, Pasquinelli G, Magro G & Dor DB. (2011). Solitary fibrous tumor of the central nervous system: A 15-year literature survey of 220 cases (August 1996-July 2011). *Adv Anat Pathol,* 18, 356-392.
16. Sung KS, Moon JH, Kim EH, Kang SG, Kim SH, Suh CO, et al. (2018). Solitary fibrous tumor/hemangiopericytoma: treatment results based on the 2016 WHO classification. *J. Neurosurg,* 130, 418-425.
17. Ghose A, Guha G, Kundu R, Tew J & Chaudhary R. (2017). CNS Hemangiopericytoma: A Systematic Review of 523 Patients. *Am J Clin Oncol,* 40, 223-227.
18. Stessin AM, Sison C, Nieto J, Raifu M & Li B. (2013). The role of postoperative radiation therapy in the treatment of meningeal hemangiopericytoma - experience from the SEER database. *Int J Radiat Oncol Biol Phys,* 85, 784-90.
19. Yu Y, Hu Y, Lv L, Chen C, Yin S, Jiang S & Zhou P. (2022). Clinical outcomes in central nervous system solitary fibrous tumor/hemangiopericytoma: A STROBE-compliant single-center analysis. *World J Surg Oncol,* 20, 149.
20. Lee JH, Jeon SH, Park CK, Park SH, Yoon HI, Chang JH, Suh CO, Kang SJ, Lim DH, Kim IA, et al. (2022). The role of postoperative radiotherapy in intracranial solitary fibrous tumor/hemangiopericytoma: A multi-institutional retrospective study (KROG 18-11). *Cancer Res Treat,* 54, 65-74.
21. Martin AJ, Fisher C, Igbaseimokumo U, Jarosz JM & Dean AF. (2001). Solitary fibrous tumours of the meninges: case series and literature review. *J. Neurooncol,* 54, 57–69.
22. Kinslow CJ, Rae AI, Kumar P, McKhann GM, Sisti MB, Bruce JN, Yu JB, Cheng SK & Wang TJC. (2023). Risk Stratification for Management of Solitary Fibrous Tumor/Hemangiopericytoma of the Central Nervous System. *Cancers (Basel),* 15, 876.
23. Shen G, Zheng F, Ren D, Du F, Dong Q, Wang Z, Zhao F, Ahmad R & Zhao J. (2018). Anlotinib: A novel multi-targeting tyrosine kinase inhibitor in clinical development. *J Hematol Oncol,* 11, 120.
24. Schutz FA, Choueiri TK & Sternberg CN. Pazopanib: Clinical development of a potent anti-angiogenic drug. *Crit Rev Oncol Hematol* (2011), 77, 163-171.
25. Martin-Broto J, Cruz J, Penel N, Le Cesne A, Hindi N, Luna P, Moura DS, Bernabeu D, de Alava E, Lopez-Guerrero JA, et al. (2020). Pazopanib for treatment of typical solitary fibrous tumours: A multicentre, single-arm, phase 2 trial. *Lancet Oncol,* 21, 456-466.