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RECURRENT INTRACRANIAL SOLITARY FIBROUS TUMOR WITH LUNG METASTASIS- NOT A "SOLITARY" TUMOUR ANYMORE

Oncopathology

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ABSTRACT

Solitary fibrous tumour is a rare intracranial neoplasm of fibroblastic origin. Histopathology demonstrates spindle to ovoid tumour cells in a "patternless-pattern". Immunohistochemical evaluation shows characteristic STAT6 positivity and molecular analysis confirms the hallmark STAT6:NAB2 gene fusion. Despite complete surgical excision being the mainstay of treatment, local recurrences and rarely distant metastasis may occur and hence its treatment remains challenging.

KEYWORDS

Solitary fibrous tumour, Intracranial solitary fibrous tumour, Central nervous system.

INTRODUCTION

Solitary fibrous tumor (SFT) is a rare mesenchymal ubiquitous tumor of fibroblastic origin, especially in the central nervous system (CNS). According to the fifth edition of WHO classification of tumors of the CNS (2021), the term "hemangiopericytoma" has been removed, with "solitary fibrous tumor" being the terminology used now. The combined term "solitary fibrous tumor/hemangiopericytoma" proposed in the 2016 WHO classification is considered obsolete now[1]. The new terminology is concordant with the nomenclature used for its soft tissue counterparts which emphasizes the biologic similarities between the two. The histogenesis of CNS SFT remains debatable, despite the presence of pathognomonic NAB2:STAT6 gene fusion. Reported herein is a case of CNS SFT in a 27 year old male with lung metastasis.

CASE REPORT

A 27 year old male presented to us with complaints of breathlessness and dry cough since one month. Patient had a history of impaired vision, headache and hearing loss three years ago for which he was evaluated and magnetic resonance imaging (MRI) brain revealed a 6.8 x 6.7 x 5.1 cm multilobulated dural based soft tissue lesion in the left frontal region with erosion of the left frontal bone and mass effect. Imaging findings suggested possible differential diagnosis of meningeal hemangiopericytoma versus meningioma. He had undergone left frontal craniotomy with excision of left frontal lesion in March 2020.

Histopathology report of the left frontal tumor also rendered the same differential diagnosis. On immunohistochemical (IHC) evaluation, the tumor cells showed immunoreactivity to smooth muscle antigen (SMA) and STAT6 while they were immunonegative to CD34, S100 and EMA. Ki-67 labelling index was <5%. The final diagnosis after IHC was solitary fibrous tumor/hemangiopericytoma- grade 2. On routine follow-up, MRI brain showed recurrence in November 2022 for which he underwent re-exploration with near total excision of the tumor on 11/11/2022. He also received adjuvant external beam radiotherapy 30 fractions in February 2023. Later he was referred to us for further treatment.

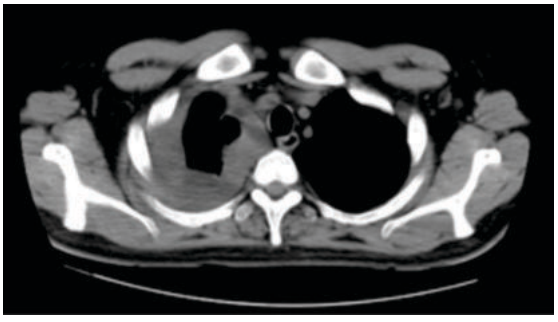

Figure 1: CT Chest Showing Right Anterolateral And Pretracheal Lobulated Mass.

On general examination at presentation to us, patient was afebrile with decreased respiratory sounds on the right side. CT chest showed a large pretracheal lobulated mass lesion measuring 5.4 x 5 cm with multiple lung nodules suggestive of metastatic disease (Figure 1). MRI brain showed grossly residual disease in the left frontal region with mass effect (Figure 2). Initial laboratory findings showed normal complete blood counts, renal and kidney function tests.

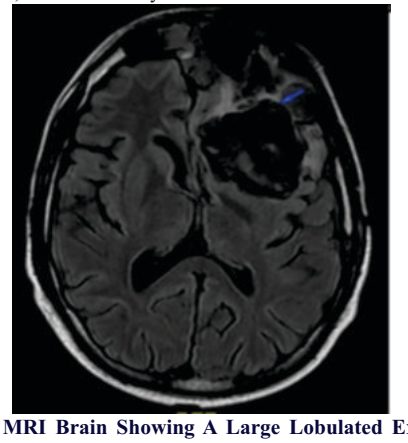

Figure 2: MRI Brain Showing A Large Lobulated Extra-axial Altered Signal Intensity Mass In The Left Frontal Region (Arrow)

The patient underwent computed tomography (CT) guided biopsy from the right pleuropulmonary lesion. Histopathological evaluation showed poorly differentiated malignant cells in sheets and nests with focal perivascular arrangement. The tumor cells were large, polygonal with prominent nucleoli and moderate amount of clear cytoplasm (Figure 3).

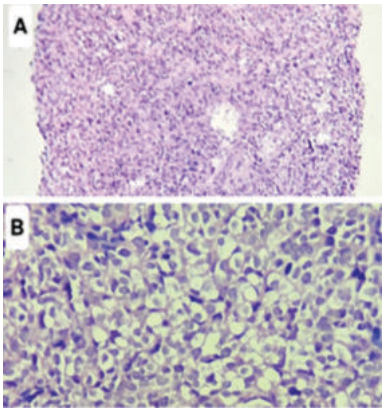

Figure 3: Haematoxylin And Eosin Stain. A) Poorly Differentiated

Tumour Cells In Sheets And Nests (100 X). B) Large Polygonal Tumour Cells With Prominent Nucleoli And Moderate Amount Of Clear Cytoplasm (400 X)

Mitotic count was 6/10 HPF. Necrosis was not seen. Histopathological diagnosis was poorly differentiated malignancy. On IHC, the tumor cells were immunoreactive to Vimentin, CD99, STAT6 and Pan-CK (focal). CD34, CD31, TTF1 and TLE1 were negative. Ki-67 index was 80% (Figure 4). With these results, a diagnosis of metastatic SFT-grade 3 was made. Next generation sequencing (NGS) also detected NAB2/STAT6 fusion which confirmed the diagnosis. Patient has been started on palliative chemotherapy with Holoxan and Adriamycin and is stable at eight months of follow-up.

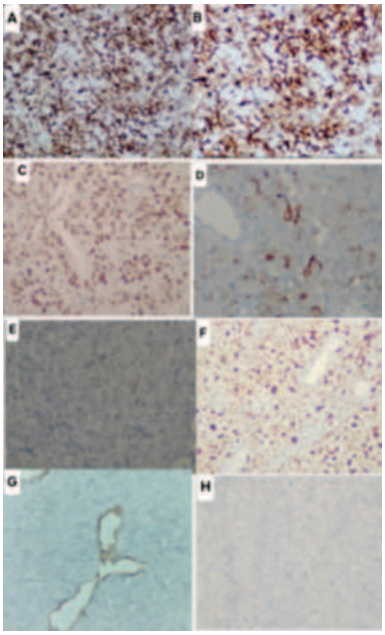

Figure 4: Immunohistochemistry A) Vimentin, B) CD 99, C) STAT 6, D) Pan-CK, E) TLE 1, F) Ki-67, G) CD 34 and H) TTF 1.

DISCUSSION

Intracranial SFT (ISFT) is a rare extra-axial brain tumor of mesenchymal origin, accounting for less than 1% of all primary intracranial tumors[2]. Both genders have equal sex predilection with tumours occurring at a median age of 40-50 years[3]. Patients have nonspecific clinical symptoms depending on the location, size, and invasion of the tumor. Extracranial metastasis is seen in approximately ~13–55% of the cases[4].

Computed tomography and magnetic resonance imaging are important imaging modalities for the diagnosis of SFT. Of late, multimodality imaging, in particular positron emission tomography/computed tomography (PET/CT) has shown an increasingly significant role, considering the high tendency of SFT's for loco-regional recurrence and distant metastasis[5].

Surgery i.e. gross total resection (GTR) remains the mainstay in the management of ISFT, often supplemented with radiotherapy, chemotherapy and molecular targeting[6].

The diagnosis of SFT primarily relies on histopathological examination, corroborated with IHC and molecular studies. Histopathology shows tumour composed of spindle to ovoid cells, interspersed with staghorn shaped blood vessels with perivascular arrangement of tumour cells in a collagenous stroma. Mitotic activity is usually low but maybe variable[7]. In our case, although the CNS tumour was diagnosed priorly, the biopsy from the lung lesion did not show classic histomorphological features, hence making an indubitable diagnosis of metastatic disease difficult.

On IHC, tumour cells demonstrate strong nuclear staining of signal transducer and activator of transcription 6 (STAT6) which is characteristic of SFT. Other immunohistochemical markers used in diagnosis are CD 34, CD 99, vimentin and BCL 2[8]. The expression of CD34 is strong and diffuse in more than 80% of SFT tumors, but its expression can be lost in the most aggressive SFTs which was true to our case[9].

The molecular hallmark of these tumors is the recurrent fusion of NAB2 and STAT6 genes located at chromosomal region 12q13, detected by next generation sequencing (NGS) and RT-PCR techniques. The resultant fusion protein, in which a repressor domain of NGFI-A binding protein 2 (EGR1 binding protein 2) (NAB2) is replaced by a transactivation domain from the carboxy terminal part of signal transducer and activator of transcription 6, interleukin-4 induced (STAT6), is believed to act as a transcriptional activator through early growth response (EGR)-mediated pathways[10]. In our case too, NGS confirmed the pathognomonic NAB2:STAT6 fusion but did not identify any other actionable mutation. Being a metastatic disease now with an aggressive behaviour, identification of specific actionable mutation might have helped in providing targeted therapy to the patient.

CONCLUSION

ISFT is an extremely rare intracranial neoplasm. Currently, histopathology combined with IHC and molecular confirmation of NAB2:STAT6 gene fusion is essential for a definitive diagnosis. Despite surgical excision followed by adjuvant radiotherapy, recurrences are quite common. Metastatic tumors are even more difficult to treat with targeted therapy emerging as a beacon of hope. Albeit challenging, studies evaluating novel therapeutic options including personalized medicine in advanced and metastatic settings are warranted to pave the way for future.

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Conflicts Of Interest
None.

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