Meningeal Hemangiopericytoma With Delayed Extra-neuraxial Metastases: Diagnostic Conundrum And Management Using High-precision Simultaneous Multi-target Irradiation On Helical Tomotherapy

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Meningeal Hemangiopericytoma With Delayed Extra-neuraxial Metastases: Diagnostic Conundrum And Management Using High-precision Simultaneous Multi-target Irradiation On Helical Tomotherapy

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Abstract

Introduction: Intracranial meningeal hemangiopericytoma is a rare tumor with variable biological behaviour. Though generally locally aggressive, a subset may fail distantly in the neural axis and even develop delayed extra-neuraxial metastases. It is often difficult to differentiate this entity morphologically from similar lesions such as meningioma, solitary fibrous tumor, and synovial sarcoma with hemangiopericytomatous pattern.

Aims: To highlight the malignant potential of intracranial hemangiopericytoma, associated challenges and dilemmas in accurate diagnosis, and use of helical tomotherapy for simultaneous irradiation of symptomatic metastases.

Case report: A 21-year old man diagnosed previously as a right cerebellopontine angle hemangiopericytoma, treated with surgery followed by post-operative adjuvant stereotactic conformal radiation therapy with no clinico-radiological evidence of progression at the index site, presented 5-years later with disseminated extra-neuraxial metastatic disease. Biopsy from metastatic site was suggestive of synovial sarcoma with hemangiopericytomatous vasculature. Immunohistochemistry profile was overlapping, necessitating molecular genetic studies. Reverse transcriptase polymerase chain reaction did not reveal a SYT-SSX translocation; thereby favouring a diagnosis of hemangiopericytoma over synovial sarcoma. In view of good performance status and long disease-free interval, he was treated with simultaneous multi-target irradiation of symptomatic metastatic sites using image-guided intensity-modulated radiation therapy on helical tomotherapy with good symptomatic relief.

Conclusion: Intracranial meningeal hemangiopericytoma is generally a locally aggressive tumor, but can have variable biological behaviour including delayed extra-neuraxial metastases. Immunohistochemistry and molecular genetic studies are helpful in differentiating it from morphologically similar tumors. There is a potential role of high-precision radiotherapy for targeting multiple metastatic lesions simultaneously for durable symptom control.

Introduction

Intracranial meningeal hemangiopericytoma (HPC) is a rare dural-based central nervous system (CNS) tumor that closely mimics meningioma clinico-radiologically [1,2,3]. Though these tumors are generally locally aggressive, with a tendency for local recurrence [2,4], they can have highly variable biological behaviour with a subset showing propensity to fail distantly in the neural axis and even develop delayed extra-neuraxial metastases [1-4]. It is often difficult to differentiate this entity morphologically from similar lesions such as angioblastic meningioma, solitary fibrous tumor (SFT), and synovial sarcoma (SS) with hemangiopericytomatous pattern. Given their uncertain biological behaviour, aggressive therapy may be warranted even for disseminated disease for sustained tumor control with durable symptom relief.

The purpose of this report is to highlight the potential of intracranial meningeal HPC to present with delayed extra-neuraxial metastases, challenges and dilemmas in accurate diagnosis, and use of helical tomotherapy for simultaneous multi-target irradiation of symptomatic metastases for sustained palliation.

Case Report(s)

A 21-year-old man presented with recent onset of pain and swelling on the right upper back and mild pain over left lower jaw. Physical examination revealed a 5 X 4 cm firm, non-tender, non-fluctuant swelling over
the right scapular area with ill-defined borders with fixity to deeper structures. A diffuse hard swelling was also palpable overlying the left hemi-mandible corresponding to the site of pain. A computed tomography (CT) scan of the thorax showed a patchily enhancing soft tissue mass in the right posterior chest wall with destruction of the underlying ribs and intra-pleural extension. Another smaller enhancing soft tissue mass was seen in the right para-tracheal region. Patient was a previously diagnosed case of right cerebellopontine (CP) angle HPC treated with gross total resection followed by post-operative focal stereotactic conformal radiation therapy 5 years back. He had been on regular follow up with no clinico-radiological evidence of progression of disease at the index site in the brain. At this time also, he did not have any focal neurological deficits. A tru-cut biopsy from the right posterior chest wall mass showed a markedly cellular tumor with spindle to oval cells with micotitic activity and presence of gaping blood vessels on light microscopy (Figure 1). On immunohistochemistry (IHC) the tumor cells diffusely expressed Bcl-2 and Mic-2 (Figure 2). They stained variably positive for CD34 and were equivocal for epithelial membrane antigen (EMA). The pathological differential diagnosis was between a SS with hemangiopericytomatous pattern versus metastases from a meningeal HPC. The overlapping IHC profile necessitated molecular genetic studies for further diagnosis. SYT-SSX translocation is generally considered specific for SS. However, reverse transcriptase polymerase chain reaction (RT-PCR) did not reveal any such translocation between SYT gene on chromosome 18 and SSX, SSX1 and SSX2 gene on chromosome X (Figure 3). In view of past history of intracranial meningeal HPC as well as negative SYT-SSX translocation, the diagnosis of delayed extra-neuraxial metastases from a previous intracranial meningeal HPC was favoured. Whole-body 18-F-fluoro-deoxy-glucose positron emission tomography/computed tomography (FDG-PET/CT) showed increased FDG-avidity in multiple soft tissue masses and skeletal lesions (Figure 4). The two chest wall masses, seen earlier on thoracic CT also, had maximum standardized uptake value (SUVmax) of 8.0 and 5.5 respectively. In addition, another soft tissue lesion involving the right iliac bone, sacroiliac joint, and adjacent sacrum (SUVmax 7.1) was also noted. FDG-avid lytic bone lesions were also seen at lateral end of left clavicle, left mandible, left 7th rib laterally, D4, D5, D8, and L2 vertebrae. Multiple marrow lesions were also noted consistent with the diagnosis of widely disseminated disease. In view of the multiple painful lesions, long disease-free interval, young age and excellent performance status, he was planned for palliative radiotherapy to symptomatic sites. He received high-precision simultaneous multi-target irradiation of symptomatic metastases (Figure 5) to a dose of 36 Gy in 12 fractions over 2.5 weeks using image-guided intensity-modulated radiation therapy (IG-IMRT) on Helical Tomotherapy Hi-Art II (Tomotherapy Inc, Madison, WI, USA) with good symptom relief. Clinical follow-up 4 weeks after completion of palliative radiotherapy showed significant regression of the swelling over the right upper back and left lower jaw with sustained pain relief.

Discussion

Intracranial meningeal HPCs are relatively rare dural-based potentially malignant hypervascular tumors of uncertain histogenesis [1,2]. Ever since the initial description by Schmidt and subsequent nomenclature by Stout and Murray [5], the medical community has doubted their existence as a separate entity. It is only recently that the World Health Organisation (WHO) classification of brain tumors [6] has recognized them as ‘mesenchymal, non-meningothelial tumours’. Their initially postulated cell of origin was pericapillary cells or pericytes of Zimmerman [5]. However, it is currently believed that HPCs including those that are meningeal in origin do not show any pericytic differentiation but are instead fibroblastic showing a morphologic continuum with SFTs. Traditionally, intracranial meningeal HPC was clinico-radiologically confused with meningioma. Despite the recent WHO classification [6], histologic overlap occurs with tumors with hemangiopericytoma-like vascularity such as angioblastic meningioma, SFT, and SS with hemangiopericytomatous pattern. IHC and electron microscopy can help in the differential diagnosis of HPCs from other vascular neoplasms and mesenchymal tumors [7,8]. Although no single marker is 100% sensitive or specific, the immunoprofile of HPC is sufficiently distinct to differentiate it from meningioma, SS, and SFT. The immunoreactivity of HPC is diverse and several antibodies, which include EMA, CD34, glial fibrillary acidic protein, vimentin, factor XIIIa, Leu7 and S-100 are sometimes positive in HPC [7,9]. Electron microscopy can sometimes be a useful tool in diagnosing HPCs which in several instances show basal membrane-like substances and lack of desmosomes [7]. In recent times, molecular genetic studies have made a big impact on diagnosis
and prognosis in oncology. Several cytogenetic abnormalities have been described in HPCs in the form of breakpoints in 12q13, 12q24 and 19q13, with recurrent t(12;19)(q13;q13) translocations [10]. The presence of SYT-SSX1 or SYT-SSX2 fusion transcripts identified by RT-PCR and a positive t(x;18) (p11.2;q11.2) demonstrated by fluorescence in-situ hybridization is specific for 80% of synovial sarcomas [11].

Although the standard treatment for intracranial meningeal HPC is aggressive surgical resection, total excision can sometimes be difficult to achieve, especially when it arises from the skull base or involves venous sinuses. The high rates of local recurrence even after gross total resection necessitates the use of post-operative adjuvant radiation therapy for maximizing local tumor control [3]. Some authors have speculated that the extensive vascular supply of these tumors generally facilitate their favourable response to radiation therapy. Helical TomoTherapy (HT) has recently emerged as a promising and novel technology for the planning and delivery of highly conformal doses to target volumes across various sites with excellent conformal avoidance of surrounding organs-at-risk. A 6 MV linear accelerator mounted on a ring gantry continuously rotates around the patient to deliver radiation in a helical mode as the patient translates through the ring. Moreover, daily image-guidance using megavoltage CT helps minimize inter-fractional set-up uncertainties. An additional advantage of HT is that it can treat multiple physically separately located targets simultaneously in one plan in a single set-up. A systematic review of the index medical literature could not identify any previous report of disseminated hemangiopericytoma treated using HT. However, simultaneous multi-target irradiation is well described with HT in various other tumors treated with curative intent as well as in the palliative setting [12]. The biological behaviour and natural history of meningeal HPC can be highly variable. Sometimes it can be locally aggressive with tendency for local recurrence with rapid progressive course resulting in fatal outcome. On the other hand, it may be associated with prolonged survival even in the face of extensive metastatic disease. Metastases may be multiple to many organ systems [13] including bone, lung, kidney, pancreas, adrenal, liver, and rarely to breast, thyroid, or lymph nodes. The interval from initial diagnosis to detection of distant metastases may range from 1-26 years. The use of salvage chemotherapy even for disseminated HPC remains somewhat controversial with contradictory reports on its efficacy [3,14]. Due to the relatively insensitive nature of HPC to conventional cytotoxic chemotherapy, molecularly targeted agents are necessary for improving outcomes in advanced disease. Inhibition of angiogenic pathway may provide a novel therapeutic mechanism for targeting these tumors [15].

**Conclusion**

Intracranial meningeal HPC is generally a locally aggressive tumor, but can have variable biological behaviour including delayed extra-neuraxial metastases. Immunohistochemistry and molecular genetic studies are helpful in differentiating it from morphologically similar tumors. There is a potential role of high-precision radiotherapy for targeting multiple metastatic lesions simultaneously for durable symptom relief. Deeper insights into the molecular biology and pathology of these tumors are necessary to pave the way for development of molecularly targeted therapy.

**Authors contribution(s)**

Dr Vimoj Nair prepared the first draft of manuscript
Dr Tejpal Gupta did literature search, revised the initial draft and prepared the final manuscript
Dr Rakesh Jalali was responsible for decision-making for treatment and critical review of manuscript
Dr Sridhar Epari provided microphotographs and interpreted the pathology findings
Dr Sangeeta Desai and Dr Bharat Rekhi were responsible for the IHC and translocation studies

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Illustrations

Illustration 1

H&E X 100: Cellular tumor(A) with oval cells(B), mitotic activity(C)& gaping blood vessels(D)

Illustration 2

Variable CD34 positivity(A), diffuse Mic-2(B)& Bcl-2(C) positivity on IHC. EMA(D) was equivocal
Illustration 3

Absence of SYT-SSX translocation on RT-PCR

Illustration 4

Whole body PET/CT(A) showing multiple FDG-avid soft tissue(B-D) & skeletal lesions(E,F)
Illustration 5

Conformal dose-wash of multi-target irradiation(A,B) sparing parotid(C), lung(D), & kidney(E)
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