

Case Report

Hemorrhagic intracranial follicular dendritic cell sarcoma: A case report

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Abstract

Background: Follicular dendritic cell (FDC) sarcoma is an extremely rare neoplasm, which has only been reported once in the literature with an intracranial occurrence. Neither hemorrhagic presentation of an intracranial instance of FDC sarcoma nor its rapid recurrence has yet been published in the literature.

Case Description: We report the case of a 61-year-old female who presented with confusion and headaches secondary to a right frontal hemorrhagic lesion, and her subsequent presentations for recurrence of the lesion and finding of a new intracranial lesion. Immunohistopathologic analysis confirmed the diagnosis based on immunoreactivity for clusterin and CD 35.

Conclusion: As demonstrated in this case report, the presentation and progression of primary intracranial follicular dendritic cell sarcoma can often be misleading, and consideration for this rare entity should be made in cases of hemorrhagic dural-based lesions without a primary source of malignancy.

Key Words: CD 35, clusterin, follicular dendritic cell sarcoma

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BACKGROUND

Follicular dendritic cell (FDC) sarcoma is an extremely rare neoplasm that represents only 0.4% of all soft tissue sarcomas.^[12] Originally recognized as its own cancer in 1986 by the work of Monda *et al.*, FDC sarcoma arises from the antigen presenting cells of B-cell follicles in lymph nodes and extranodal tissues.^[10] The most common site for this rare tumor are cervical lymph nodes. Extranodal sites have also been described, however, most commonly in the head and neck region. This entity has also been described in association with Castleman's disease as well as prior infection with Epstein-Barr virus. Diagnosis of FDC sarcoma is made when a neoplasm manifests variable histological patterns of tumor cell growth,

often associated with an inflammatory infiltrate, with expression of one or more epitopes characteristic of follicular dendritic cells, including clusterin, CD21, CD35, and CD23.^[1,2,4,7,9,13,14] To our knowledge, there is only one other reported case of intracranial FDC sarcoma.^[5] In addition to identifying another case of

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intracranial FDC sarcoma, here we report a unique case of this rare tumor originally presenting with a hemorrhagic mass, and recurring within 2 months of initial resection, which has not yet been seen in the literature.

CASE REPORT

Initial presentation

History

Patient BC is a 61-year-old female with a past medical history of diabetes mellitus and hyperlipidemia who initially presented to the emergency room in June 2015 for periods of confusion and memory problems over the prior few weeks. Upon further questioning, the patient also reported having intermittent, diffuse headaches over the prior week. On initial examination, she was grossly neurologically intact and did not exhibit any noticeable short or long-term memory deficits. A noncontrast head computed tomography (CT) scan revealed a 4 cm right frontal hematoma with associated edema and sulcal effacement along with 3 mm of right-to-left midline shift [Figure 1]. Underlying neoplasm could not be excluded, and therefore, further imaging modalities were sought.

Imaging findings

Magnetic resonance imaging (MRI) of the brain with and without contrast done on the night of admission revealed stable acute hemorrhage in the right frontal lobe with underlying dural-based lesions in the right frontal lobe including a dominant hemorrhagic lesion measuring up to 2.4 cm [Figure 2]. Radiographic characteristics were most consistent with metastatic disease. A screening CT scan of the chest/abdomen/pelvis was done, which demonstrated mild hepatomegaly and calcifications in the right breast, but no signs of obvious malignancy. Positron emission tomography (PET) scan showed no evidence of extracranial disease.



Figure 1: Noncontrast axial head CT of patient on initial presentation

Hospital course

The patient was started on dexamethasone and underwent imaging studies to fully evaluate her intracranial hemorrhage. Evaluation for a primary malignancy source found no other sites of disease. The decision was made to proceed with surgical resection, and the patient underwent a right frontal craniotomy with resection of the dural-based lesion with no adverse events. Postoperatively, the steroids were tapered and she was transferred to an acute rehabilitation facility. Postoperative MRI brain with and without contrast demonstrated enhancement along the margins of the resection cavity, compatible with a resolving residual hematoma [Figure 3].

Histopathology

Histologic examination revealed a mitotically active neoplasm with spindle and epithelioid components, conspicuous infiltration by chronic inflammatory elements, including many lymphocytes, and with associated hemorrhagic necrosis. On immunohistochemical staining, there was focal labeling for CD35 and more diffuse expression of clusterin [Figure 4]. The tumor cells focally expressed smooth muscle actin, minimally and focally expressed CK7, but not CK20 or CAM5.2, retained INI 1 expression, and did not express ALK, CD20, CD21, CD31, Chromogranin, EMA, ERG, GFAP, HMB45, Melan A, MyoD1, Myogenin, NeuN, SOX10, STAT6, or Synaptophysin. These findings are consistent with FDC sarcoma. The findings are not those of a melanoma, carcinoma, meningioma, tumor of neuroepithelial origin, other type of sarcoma or lymphoma. Foundation One report noted STAG2, PTEN mutation, MDM2 amplification, and DKC4 amplification.

Second presentation

History

The patient was sent to the emergency room from the clinic in August 2015 for confusion, urinary frequency, and hyperglycemia. She was still complaining of difficulty

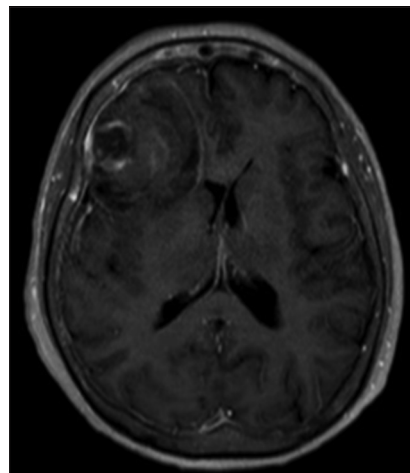


Figure 2: T1 post-gadolinium axial MRI of patient on initial presentation

with her memory, as well as feeling drowsy, which was slightly worse than previous. She also complained of an episode of feeling shaking and confusion, which she was concerned was a seizure. On neurologic examination, she was once again grossly intact. She had not yet started radiotherapy or any adjuvant therapy for her brain tumor. CTH was performed in the ED, which demonstrated vasogenic edema in the right frontal lobe and 9 mm of the midline shift [Figure 5].

Imaging findings

MRI brain with and without contrast on admission demonstrated increasing enhancement and edema in the region of the right frontal resection cavity, including a new 1.4 cm nodular focus of enhancement along the falx cerebri [Figure 6]. Radiographic findings were most suspicious for tumoral progression.

Hospital course

The patient's Keppra dose was increased and she was restarted on dexamethasone. She underwent repeat right

frontal craniotomy for resection of both the frontal and midline dural-based masses with no adverse events. The patient received her first dose of fractionated frameless stereotactic radiosurgery, and was discharged on a dexamethasone taper and instructions to follow-up for further radiotherapy.

Histopathology

The specimen was similar to that of the previous resection, consisting of dura attached to granulation tissue, with associated large neoplastic pleomorphic cells in nests and areas of necrosis. The neoplasm once again expressed vimentin. Immunohistochemical staining was positive for p53 and CK7. Stains for AE1/3, BCL2, CAM5.2, CD21/31/34/35, Clusterin, CK20, and Synaptophysin were negative.

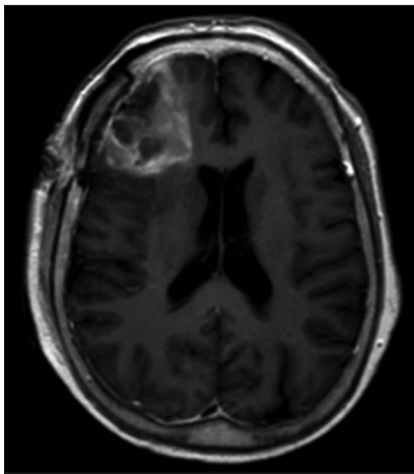


Figure 3: T1 post-gadolinium axial MRI of patient obtained within 48 hours of first resection surgery

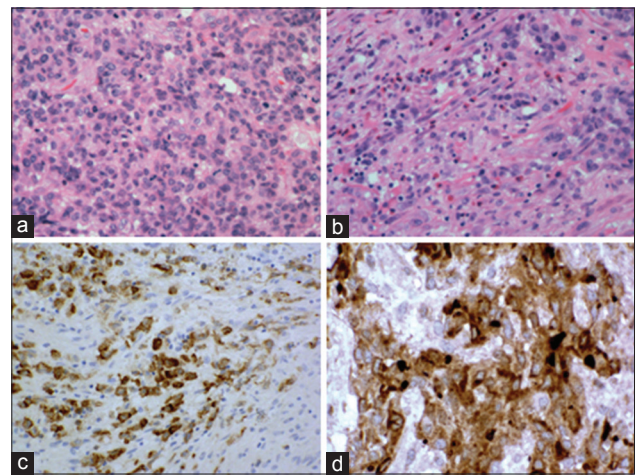


Figure 4: Histopathology demonstration of resected mass at initial presentation. (a) Much of the neoplasm consisted of uniform cells with pink cytoplasm and vesicular nuclei having single small nucleoli and many mitoses. H and E, $\times 375$. (b) In other areas, the tumor was infiltrated by an inflammatory cell reaction rich in eosinophils. H and E, $\times 375$. (c and d) Immunohistochemical marker studies were unrevealing except for CD35 and clusterin. Photography courtesy of Dr. M. Rosenblum, Memorial Sloan Kettering Cancer Center, New York, NY. X375

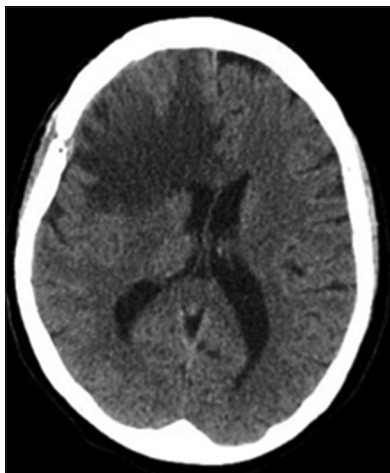


Figure 5: Noncontrast axial head CT obtained on readmission 2 months after initial presentation and surgery

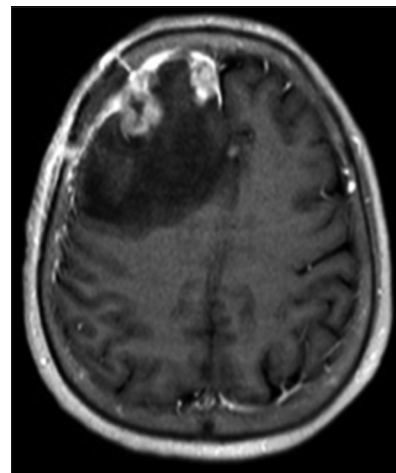


Figure 6: T1 post-gadolinium axial MRI obtained on readmission 2 months after initial presentation and surgery

Third presentation

History

The patient presented again to the emergency room in December 2015 with dizziness and urinary urgency. She was found to have a UTI, but CTH on presentation demonstrated a new 1.5 cm hyperdense lesion in the right middle cranial fossa and a 5 mm lesion in the right high frontal convexity, with associated worsened vasogenic edema and midline shift, concerning for recurrent neoplasm. The patient once again complained of gradually worsening headaches and confusion, with difficulty in memory.

Imaging findings

MRI brain with and without contrast demonstrated increased size of the midfrontal enhancing lesion, as well as a new area of enhancement in the right anterior temporal lobe, with associated edema and mass effect [Figure 7].

Hospital course

The patient was started on high dose steroids and antiepileptics and improved clinically. After discussion with the patient, the decision was made to not pursue further neurosurgical intervention. The patient was initiated on bevacizumab and irinotecan.

Clinical course

Based on the patient and family wishes, the patient was made DNR/DNI prior to discharge with the decision for no further aggressive or invasive measures. She succumbed to her illness and expired in April 2016.

DISCUSSION

We have reported here the original case of this 61-year-old woman presenting with a right frontal hemorrhagic lesion, which diagnosed as FDC sarcoma because of its patterns of tumor cell growth, association with an inflammatory infiltrate, and expression of clusterin and CD35 in the absence of evidence for any other diagnosis. We suspect

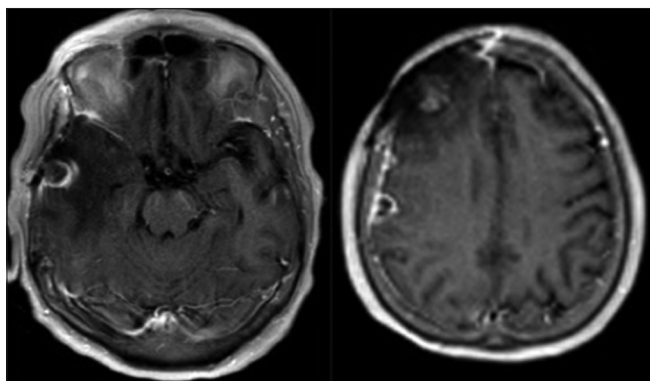


Figure 7: T1 post-gadolinium axial MRI obtained on third and final admission in December 2015

that given its radiographic similarities with other entities, such as meningioma, intracranial FDC sarcoma may in fact be an underdiagnosed entity and has been mistaken for an inflammatory pseudotumor,^[3] inflammatory myofibroblastic tumor,^[6] and histiocytic sarcoma,^[16] all of which have been seen to occur within the central nervous system as well. In addition, FDC sarcoma may also be mistaken for interdigitating dendritic cell sarcoma, which is classically negative for dendritic cell markers such as CD21/35, and which has been reported once before with a primarily intracranial presentation.^[7,16]

While the differential diagnosis for solitary intracranial lesions is often headed by entities such as meningioma, gliomas, or metastases of unknown primary, this case report highlights key features of FDC sarcoma which may guide the evaluation of this entity. First, clinical presentation of hemorrhage in meningioma is relatively rare (1–3%).^[8,15] Presence of hemorrhage in a dural-based lesion should, therefore, initiate further investigations into metastatic or alternate etiologies. Second, while a diagnosis of FDC sarcoma may not be easy to make on initial presentation, a complex clinical course may be a further clue of an uncommon process. The importance of identifying an accurate diagnosis in the case of FDC sarcoma is further supported by our findings in this case of aggressive regrowth and delayed neurologic deficit. This aggressive nature of FDC sarcoma is supported in extracranial studies of this entity as well showing frequent recurrence and metastasis (approximately 25%).^[11] Pinpointing an early diagnosis of FDC sarcoma in unclear lesions will also allow for more directed therapies. Recent multicenter studies showing *BRAF*^{V600E} positivity in almost 20% of FDC sarcoma cases as well as studies demonstrating epidermal growth factor receptor (EGFR) expression by FDC sarcomas suggest new potential targets for treatment in this otherwise elusive entity. As seen in this case, intracranial FDC sarcoma is an unrelenting process, with a wide differential diagnosis, for which clearly delineated target therapies are still only in the initial stages. We present this case to shed light on this scarcely documented entity and promote further efforts to improve treatment.

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Conflicts of interest

There are no conflicts of interest.

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