



Intracranial Pleomorphic Malignant Fibrous Histiocytoma, Associated to Systemic Lupus Erythematosus: A Case Report

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Authors' contributions

This work was carried out in collaboration between all authors. Author MLTS designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors CSG and CSL managed the analyses of the study. Author MLTS managed the literature searches. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Background: Pleomorphic Malignant Fibrous histiocytoma (MFH) is a rare neoplasms of the soft tissue and bone composed of fibroblastic and histiocytic components with mitosis figures, nuclear pleomorphism and anaplasia.

Case Presentation: We presented a rare case of MFH in 44 year old woman with history of systemic erythematosus lupus and seizures. Treated with prednisone. The cerebral TAC showed a temporal mass. Craniotomy was performed and the examination of the biopsy sample revealed a giant, pleomorphic and atypical cells. Immunohistochemical analysis showed positivity for vimentin, CD68, Fascin, lysosyme and MIB-1 labeling index of 20%. Pleomorphic malignant fibrous histiocytoma was diagnosed, with involvement of the overlying temporal lobe. We report a case of MFH of the left temporal in adult.

Discussion: The neuroimaging and intra-operative opinion were of a meningioma. Histopathology,

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in conjunction with immunohistochemical evaluation and proliferation marker, confirmed the diagnosis. This is the first case reported of PMFH associated to systemic lupus erythematosus and different histological patterns.

Keywords: Brain tumors; primary intracranial fibrous histiocytomas; pleomorphic malignant fibrous histiocytoma; immunohistochemistry.

1. INTRODUCTION

Primary intracranial fibrous histiocytomas (FHTs) are rare entities some few cases have been reported. The mesenchymal origin of fibrohistiocytic tumors (FHT) remains controversial [1,2]. These tumors can be benign or malignant forms. Malignant fibrous histiocytoma (MFH), is a type of sarcoma, of uncertain origin that arises both in soft tissue and bone. It has been suggested that these may originate from the perivascular pial sheath or mesenchymal cells or primitive mesenchymal cells, and blood vessel walls [2-4]. *Kauffman and Stout* were first which introduced the term of MFH in 1961. Furthermore, *Fletcher* published in 1992 a retrospective series of 159 cases of pleomorphic sarcoma [1]. These tumors were re-assessed morphologically [1]. Histologically MFH is characterized by giant and pleomorphic tumor cells with eosinophilic and foamy cytoplasm with nuclear atypia and mitosis features [1,2]. Histologically have been described four subtypes; Storiform-pleomorphic, Myxoid, Giant cell and Inflammatory [1]. MFH are rare intracranial tumors, they usually presented as a meningeal mass, intraaxially [5-8], mesenchymal [9], or an intraventricular location [10]. Some cases have been associated to radiotherapy [11-17]. Radiation-associated status and incomplete resection has been identified as independent predictors of local recurrence. One complication of local radiotherapy can development of radiation-associated sarcoma (RAS). It can originate in the CNS or arise as a metastasis from a primary extra cranial tumor [1,2]. However, the term of MFH is very controversial and it was proposed name to undifferentiated pleomorphic sarcoma (UPS). *Shirasuna K, et al.* suggested that this tumor originates of neoplastic histiocytes with the high capacity to origin various types of cells, which suggested a possible stem cell origin [5]. This theory has been demonstrated by study of the gene-expression patterns of soft tissue sarcomas failed to find a clear distinction between the genes of MFH, liposarcoma and leiomyosarcoma [1].

Here we reported a rare case of pleomorphic malignant fibrous histiocytoma or UPS in 44

years-old-woman with was treated by 12 year of systemic lupus erythematosus (SLE) and was emergency operated with a temporal mass suggestive of a meningioma.

2. CLINICAL CASE

A 44-year-old woman had been treated with steroids for SLE for 12 years. One year ago she presented seizures. She presented headache, nausea, vomiting loss progressive loss of strength in right hemisphere, giddiness, and unsteadiness of gait, of six months' duration, stool or urine incontinence, or sensorineural deficit. The patient presented with a sudden loss of consciousness and vomiting and was admitted in our institution. Neurological examination revealed normal higher mental functions, without any associated sensory deficit or cerebellar signs. However, her gait was ataxic. Hematological and biochemical parameters were within normal limits. Cerebral TAC revealed a well-defined, intensely enhancing extra-axial lesion along the inferior aspect of the left temporal lobe suggestive of a meningioma (Fig. 1). There was intense homogeneous post-contrast enhancement, with focal non-enhancing intralesional areas. No dural attachment was seen. She underwent left temporal craniotomy and Simpson Grade 2 excision of the tumor. Intra-operatively, the neoplasm was highly vascular, soft and necrotic areas shown.

The tumor was processed and five-micron-thick sections were cut from routine formalin-fixed, paraffin-embedded tissue, and stained by hematoxylin and eosin (H&E). Immunohistochemistry (IHC) was performed using streptavidin-biotin immunoperoxidase technique (Envision Kit, M/s Dakopatts, and Carpinteria CA), using the primary antibodies following; vimentin, CD68, cytokeratin (CK), S-100 protein, glial fibrillary acidic protein (GFAP), lysosome and epithelial membrane antigen (EMA), while the proliferation index using ki67.

Microscopic examination of the resected specimen showed various cell patterns; isolated classic giant cells with pleomorphism and cellular atypia, monstrous and giant cells (Fig. 2a) with abundant eosinophilic cytoplasm (Fig. 2b), with

round to elongated nuclei, few of which showed prominent nucleoli and multinuclear features (Fig. 2c), numerous atypical mitotic features were observed (Fig. 2d), with sarcomatous pattern, other pattern was formed by round cells with nucleus to the periphery rejected that looks gemistocytes vs rhabdoid cells (Fig. 2e), and the other one formed by large cells with abundant eosinophilic cytoplasm with astrocytes vs hepatoid appearance (Fig. 2f), and necrosis was also observed. Few bits showed invasion into the bony trabeculae with destruction of the bone. There were xanthomatous areas in the tumor.

Immunohistochemistry results were; the giant cells were positive immunoreaction for vimentin (Fig. 3a, 3b and 3c), CD68 (Fig. 3d), Fascin (Fig. 3e) and lysozyme (Fig. 3f), in conjunction with MIB-1 labeling index (MIB-1LI) of 30% was noted, in the plump and giant cells confirmed the fibrohistiocytic nature of the tumor lacking of GFAP, S-100, EMA and CK-immunopositivity, ACE, AFP, CGH, HMB45. Pleomorphic Malignant Fibrous histiocytoma or undifferentiated pleomorphic sarcoma grade III was diagnosed.

Follow-up. The patient has been on a regular follow-up. At the last review, she was ambulant, and with normal speech with loss of strength in right hemisphere deficit.

3. DISCUSSION

Most of the MFH reported in the literature affected pediatric cases, less than 24 months of

age [4-16]. Radical excision of intracranial FHT, provided it is technically feasible, is considered the optimum therapy for a satisfactory outcome. However, have been suggested the role of adjunctive radiation and chemotherapy in the subsets that invade bone [11-17]. Furthermore, the current case was offered radical excision only. Follow-up results at 12 weeks' postoperatively were satisfactory. Others tumors [3-12] have also noted a recurrence-free status during a follow-up period ranging between 15 months and 6 years. In our case the tumor was resected completely, it was totally resected due soft gross aspect.

Fibrous histiocytomas tumors (FHTs) can showed benign and malign aspect according with the WHO classification [1]. The benign form is formed by storiform pattern of bland spindle cells and foamy histiocytes centered. Variable hemosiderin, multinucleated giant cells, chronic inflammatory cells and pseudoepitheliomatous hyperplasia also have been seen [1,2]. Benign isolated fibrohistiocytic tumors of the CNS are most frequent than MFH form [1-4]. The benign nature of the tumor was supported by the lack of pleomorphism and necrosis, with low mitotic activity and Ki67-li of 2%, as per se the standard accepted criteria [1,2]. Furthermore, tumor cell necrosis, not seen in BFHT [1]. Benign form has been variably described as fibrous xanthoma and fibroxanthoma [1,3,8-12]. Tumors reported as fibrous xanthoma have been reported as xanthoastrocytoma. However although, those tumor expressed GFAP [4].

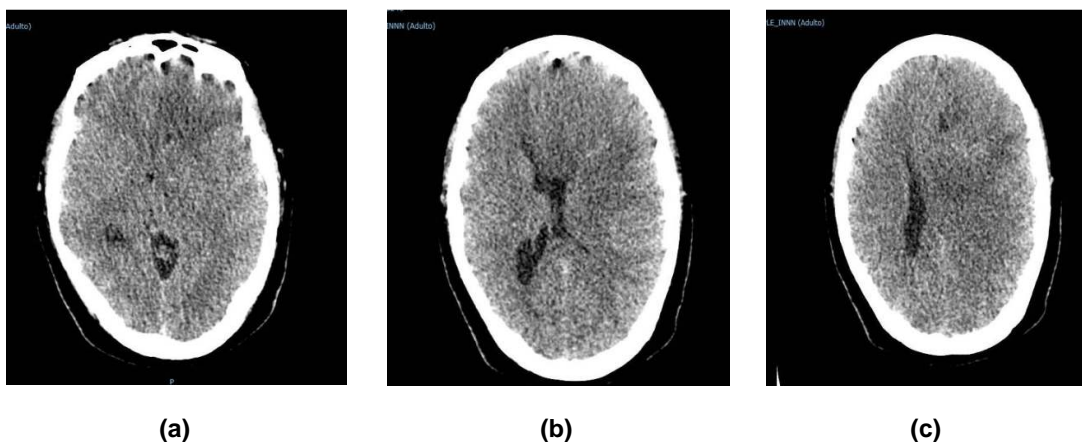


Fig. 1. (a) Cerebral TAC showed a the left fronto-temporal lobe suggestive of a meningioma, (b and c) with peritumoral edema

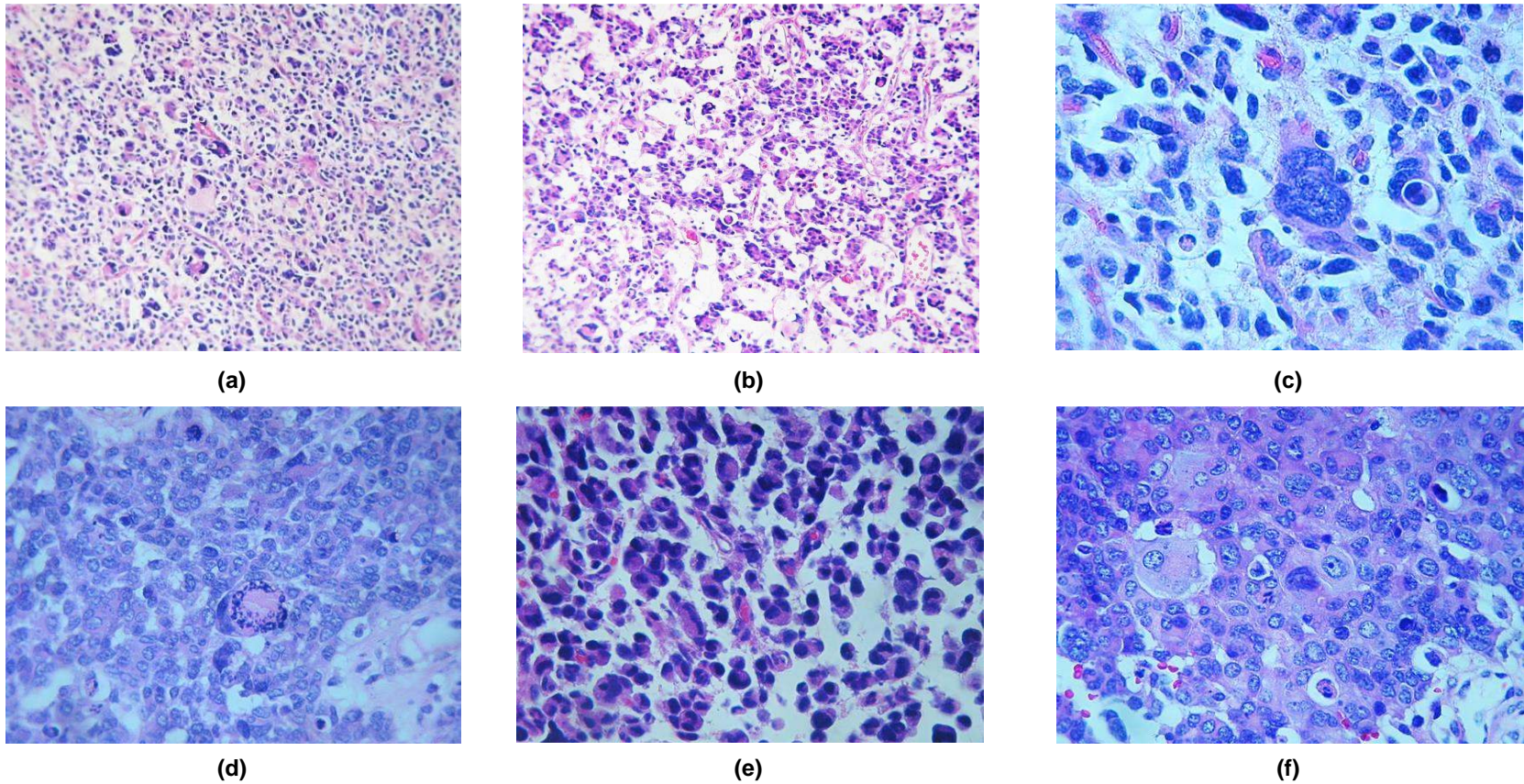
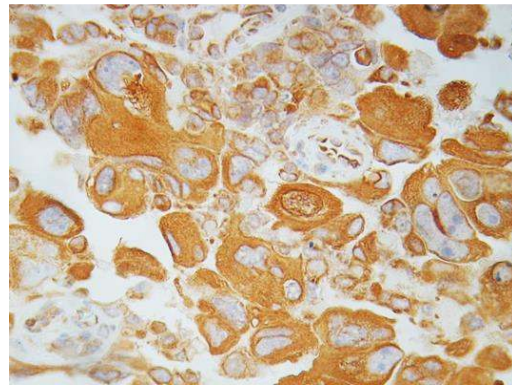
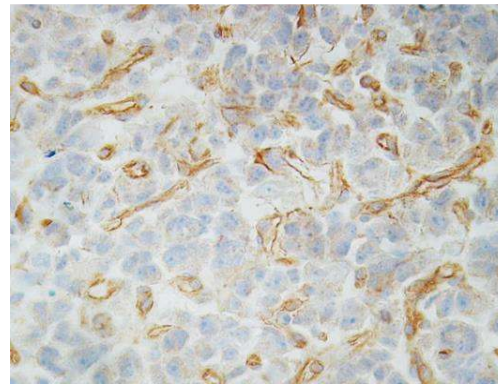


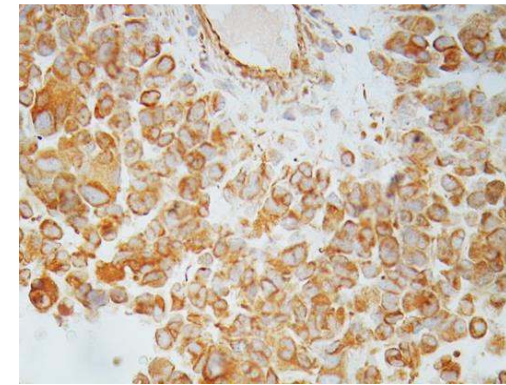
Fig. 2. Histopathological features. (a) Photomicrograph revealed tumor anaplastic proliferation of spindle-shaped cells admixed with atypical giant cells arranged as individual cells of varying sizes (b). These cells contained a typical hyper-chromic nuclei with moderate cytoplasm, in some areas showed a lipoid appearance (H&Ex200). (c) Showed mitotic figures, easily identified and multinuclear cells were also observed (H&E 400x). (d) Other histological pattern with homogenous and sarcomatous appearance with atypical mitotic features were observed. (e) Some areas showed a cells with gemistocytic or rhabdoid appearance and in (f) also showed and other histological pattern with homogeneous and clear cells and hepatoid appearance (H&Ex400)



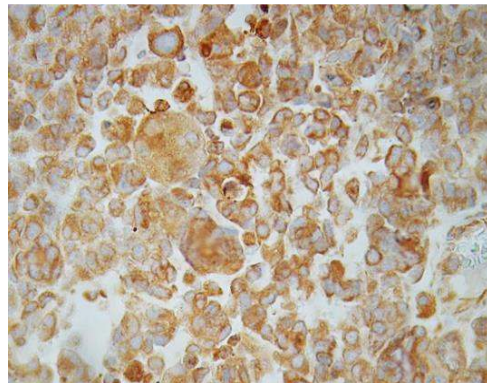
(a)



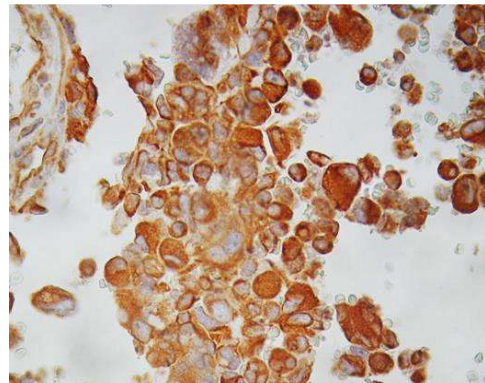
(b)



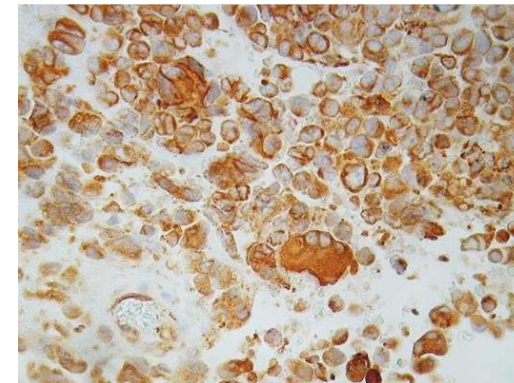
(c)



(d)



(e)



(f)

Fig. 3. The immunophenotyping studies. (a) Observed that the cells like hepatocytes where intensely positive vimentin showed a strong positive reaction for vimentin, (b) sarcomatous pattern the vimentin was observed positive immunoreaction only in the blood vessels, and was also positive in the rhabdoid like patterning(c). (d) Tumor was also positive staining for CD68, (e) fascin and (f) lysozyme immunoexpression were observed (IHQ stain x400)

However, the malignant form is characterized by giant, bizarre, atypical, pleomorphic tumor cells with abundant and foamy cytoplasm, numerous mitotic figures, with a collagenous stroma [1], storiform growth pattern multinucleated giant cells may be seen. Pleomorphic MFH (PMFH) subtype is composed of fibroblasts, myofibroblasts and histiocytic-like cells [1], may represent end stage of various sarcomas with common morphologic pleomorphism features classify as MFH-giant cell [1,2]. PMFH usually shows highly aggressive behavior, recurrence, resistance to radiotherapy or chemotherapy treatment and metastasis [1]. MFH usually affect older adults (age over 50+ years) with slight male predominance; is more common location in lower extremities, rarely retroperitoneum, head and neck, breast, and usually have large and deep-seated with progressive enlargement. Some few intracerebral cases have been published [1].

Diagnosis based on histology and clinical criteria alone is sometimes difficult to do. Immunohistochemistry help to distinguish these lesions. The diagnosis of MFH is based primarily upon excellent sampling in conjunction with a panel of immunohistochemistry, usually is a diagnosis of exclusion. PMFH usually expressed; vimentin, alpha-1-antitrypsin, lysozyme, alpha-1-antichymotrypsin, Factor XIIIa, CD68, CD10, CD34, CD99 [1]. And are usually negative immunoreaction to keratins, melanocytic markers, CD45, S100, muscle [1,2,5,9]. Epidermal growth factor receptor overexpressed in MFH [15]. CD99 can help distinguish atypical fibroxanthoma (AFX) from MFH [17]. In our case the immunohistochemical stain expressed positive immunoreaction for vimentin, CD68, CD68, lysosome and fascin with MIB-1 high labeling index (MIB-1LI) of 20%.

By ultrastructure description relatively undifferentiated fibroblastic, myofibroblastic or primitive mesenchymal cells, some with phagocytic properties have been observed [1,3].

The reduced number of glial and meningeal cells is helpful in separating MFH from other meningeal non-sarcoma neoplasms [2]. However, differentiating MFH from malignant tumors with a similar degree of cellular pleomorphism such as anaplastic carcinoma and pleomorphic sarcoma is difficult [2]. The differential diagnoses that we have to consider are the following tumors: anaplastic large cell lymphoma (CD30+), atypical fibroxanthoma:

cutaneous, small and superficial pleomorphic leiomyosarcoma (vimentin+ and smooth muscle actin+), leprosy, histiocytoid: prominent histiocytes but no prominent atypia or atypical mitotic figures, special stains may reveals pleomorphic liposarcoma (S100+ or smooth muscle actin+), Myxofibrosarcoma (vimentin+), rhabdomyosarcoma (smooth muscle actin+), metastatic renal cell carcinoma, (keratins+) and melanoma (melan +, HBM45+) and choriocarcinoma (ACE+, AFP+ GCH+) and with other tumor with pleomorphic and giant cells like glioblastoma multiforme (GFAP + and IDH1+) [1,2]. And become differentiated to any histological type of sarcoma.

PMFH may have different histological patterns that complicate the diagnosis, may have features suggestive of other sarcoma types (myxofibrosarcoma, leiomyosarcoma, dedifferentiated liposarcoma, fibrosarcoma, malignant peripheral nerve sheath tumor) but it is insufficient for definitive classification [1]. Cytogenetic analyses have been revealed highly complex karyotypes lacking specific structural or numerical aberrations [18]. As well as the recurrent tumors are reported cytogenetic abnormalities, associated in chromosome bands 1p36, 1q11, 1q21, 3p12, 11p11, 17p11, and 19p13 [18], furthermore, some genes analyzed (FU-MFH-2) genes, WNT1, WISP2, G protein-coupled receptor 64 (GPR64) and Tenascin XB (TNXB) have been identified for various biologic and molecular pathogenetic behavior [18], novel approaches targeting c-Met, MEK/extracellular-regulated kinase (ERK) and/or AKT should be considered for a subset of undifferentiated pleomorphic sarcoma/malignant fibrous histiocytoma (UPS/MFH) [19]. Histologic and genetic advances regarding with the diagnosis of MFH being replaced by undifferentiated pleomorphic sarcoma [19]. Recently, the 2016 CNS WHO has expanded these categories to parallel those in the corresponding Hematopoietic/Lymphoid WHO classifications and are within the category of mesenchymal tumor non-meningeal, molecular parameters are used to establish brain tumor diagnoses [2]. Nevertheless, some tumors with a histological appearance more similar to traditional solitary fibrous tumor can also display malignant features and be assigned a WHO grade III [2], consequently, be required to fine-tune this grading system [2].

There is increasing evidence in support of an association between systemic lupus

erythematosus (SLE) and malignancy. Lymphoma is the most common tumor associated to SLE, few reports of have been published [20], this is the first case of PMFH associated SLE, in a patient who has not been radiated but if you have used steroids for 12 years. It is cause or effect or pure coincidence? Imaginable pathogenic paths linking SLE and cancer include supposed links with medicaments used, patients treated with immunosuppressive or steroid agents, or prolactin and viral contacts, or post-transplantation suggests and toxicity of gamma knife radiosurgery may play a role in the pathogenesis of SLE in some patients. However, risk factors like immunosuppressant, steroid and hormones could be predisposing factors for the development of meningioma during adult life are well known [21].

4. CONCLUSION

In conclusion, this case report documents a rare entity in an intracranial location. In a patient with SLE, with round cells with nucleus to the periphery rejected that looks gemistocytes vs rhabdoid like cells and other cells with astrocyte vs like hepacytes appearance, owing to the rarity of PMFH, one should be aware of its defining morphological and immunohistochemical characteristics for definitive diagnosis. Also genetic marker could help with the diagnosis.

CONSENT

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this paper and accompanying images.

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

ETHICAL APPROVAL

It is not applicable.

The authors have obtained all necessary ethical approval from suitable Institutional or State or National or International Committee. This confirms either that this study is not against the public interest, or that the release of information is allowed by legislation.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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