Intracranial mesenchymal tumour: case report of a rare intracranial tumour with angiomatoid fibrous histiocytoma-like features and FET::CREB fusion

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Background

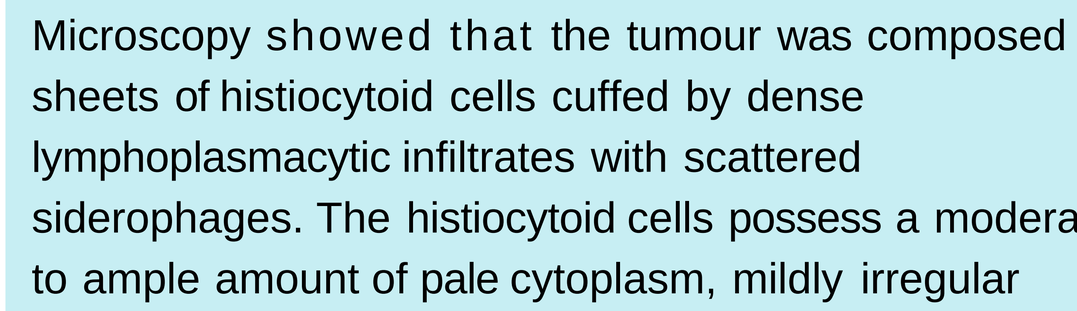
Angiomatoid fibrous histiocytoma (AFH) is a rare mesenchymal tumour that infrequently recurs and rarely metastasizes, mostly occurring in subcutaneous tissue in children and young adults. These tumours are characterized by a distinctive set of histological features. They most frequently harbor EWSR1::CREB1 fusion (in > 90% of cases), less commonly EWSR1::ATF1 fusion. The latest WHO classification of central nervous system tumours includes intracranial mesenchymal tumour, FET::CREB fusion-positive as a provisional entity, which may or may not resemble AFH.

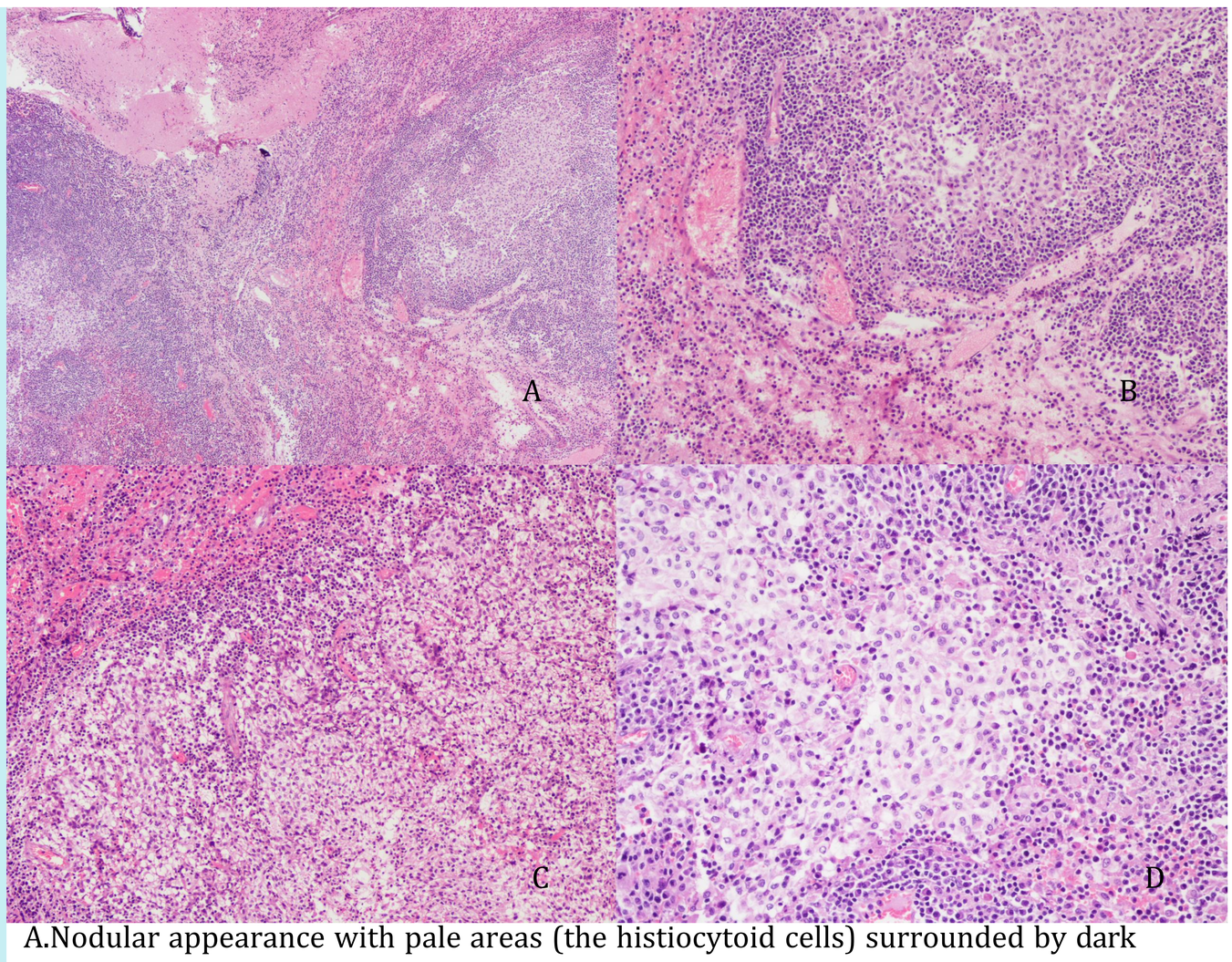
Case presentation

A 65-year-old female presented in 8/2018 with dizziness was found to have a 3 cm right cerebellar lesion. During operation, the mass was found to have a poor interface with the surrounding brain. Residual tumour that had invaded the torcular sinus was left behind. A final diagnosis of angiomatoid fibrous histiocytoma-like tumour was made based on histology and molecular findings. Follow-up MRI in 7/2019 showed interval enlargement. Tumour excision was subsequently performed. Residual tumour was confirmed by histology and molecular studies. No tumour recurrence was found in follow-up MRI scans, the latest performed in 11/2021.

Microscopy showed that the tumour was composed of sheets of histiocytoid cells cuffed by dense lymphoplasmacytic infiltrates with scattered siderophages. The histiocytoid cells possess a moderate to ample amount of pale cytoplasm, mildly irregular nuclei with delicate nuclear membranes and fine chromatin. Scanty nuclear pseudoinclusions were seen. The mitotic count was up to 4 per 10 HPF (22 mm eyepiece). On immunohistochemical study, they are positive for CD68 and EMA. Desmin is negative. Necrosis was inconspicuous. There was no definite tumour invasion into the adjacent cerebellar tissue.

RT-PCR studies for EWSR1-ATF1 and EWSR1-CREB1 transcripts were negative. Illumina Pan-cancer RNA-sequencing panel analysis detected EWSR1-CREM and CRKL-PI4KA fusion transcripts.





A.Nodular appearance with pale areas (the histiocytoid cells) surrounded by dark areas (the lymphoplasmacytic infiltrate) on low power
B.Abundant thin-walled dilated vessels traversing the histiocytoid cells and in the surrounding
C.&D. Sheets of cells with moderate to ample amount of pale cytoplasm, mildly irregular nuclei with delicate nuclear membranes and fine chromatin. They are surrounded by dense lymphoplasmacytic infiltrates.

Discussion

- The provisional entity of intracranial mesenchymal tumour, FET::CREB fusion-positive demonstrates a wide morphological spectrum. The stroma usually contains collagenous areas with reticulin-positive intercellular matrix, with or without myxoid areas. Dense lymphoplasmacytic infiltrates, dilated thin-walled vessels and hemosiderin deposition are usually present. Amianthoid fibres and meningothelial-like whorls may be seen. Tumour cells vary from epithelioid/rhabdoid cells to stellate/spindle cells to monotonous round cells. The mitotic activity is generally low (typically < 5 mitoses/mm^2).
- They demonstrate a polyphenotypic immunoprofiles with the majority positive for EMA and CD99. They show variable S100, synaptophysin, CD68, MUC4 and GLUT1 expression.
- Differential diagnosis can be largely excluded by immunohistochemical studies. They include primary or secondary mesenchymal tumours, for example, myoepithelial neoplasms (positive for cytokeratin, GFAP, S-100), rhabdomyosarcoma (positive for myogenin, MyoD1), solitary fibrous tumour (positive for STAT6), meningioma, especially microcystic/ chordoid, (positive for EMA but also SSTR2A and PR), glial and glioneuronal lesions (GFAP- and OLIG2-positive glial cells; synaptophysin-positive neuronal cells), atypical teratoid / rhabdoid tumor (INI1 loss).
- Small samples that include little to no histiocytoid cells may lead to misdiagnosis as reactive process. Histiocytoid cells may raise the possibility of an infective process or histiocytosis. Therefore, clinical and radiological correlation is important especially during frozen section.
- Only documentation of a pathognomonic gene fusion provides diagnostic confidence for this entity. Hence, it is advisable to obtain a sample of decent size where possible, as well as to preserve tissue for molecular studies.
- The spectrum of clinical behaviour is not well-defined (ranges from slow growth to rapid recurrence). Whether morphological feature or fusion partners is predictive of behaviour is unknown.

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