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Metaplastic Meningioma Presenting with Anemia in A Young Boy Case Report and Review of the Literature

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Abstract:- Meningioma is the most common extra-axial, Dura-based tumor of the central nervous system. These tumors often present in middle to late adult life, especially in women, and account for 15% - 30% of all intracranial tumors(1). Incidence rate of 18.69 and 0.16 per 100,000 is recorded for patients above 40 years and 0-19 years age respectively(2). The World Health Organization (WHO) in its 2021 classification divides meningioma into Grade I (benign), Grade II (atypical), and Grade III (anaplastic) variants. It further sub-classifies grade I meningioma into 9 subtypes: meningothelial, fibrous, transitional, psammomatous, angiomatous, microcystic, secretory, lymphoplasmacyte rich, and metaplastic(3). Metaplastic meningioma is the rarest subtype, and defined as a tumor containing focal or widespread mesenchymal components including osseous, cartilaginous, lipomatous, myxoid or xanthomatous tissue, singly or in combinations(4). We present a case of metaplastic meningioma with Myxoid, Xanthomatous and Osseous metaplasia presenting with anemia in a 17-year-old boy.

***Keywords*:-** *Meningioma, Anemia, Immunohistochemistry.*

I. CASE REPORT

A 17-year-old boy came to the neurosurgery clinic of a tertiary care hospital at Peshawar with complaints of headache, decreased vision, and weakness. Except from pallor and low visual acuity, rest of the physical examination was unremarkable. Complete blood profile showed microcytic hypochromic anemia with a Hemoglobin level of 9.5 g/dl (see table 1). All other routine investigations were normal. MRI (Magnetic Resonance Imaging) brain with and without contrast showed a 5x4 cm lesion arising from dura and causing midline shift as shown in figure 1 (A & B). The mass was resected (as shown in post-surgery MRI in fig.1 C) and sent to Histopathology department. Gross examination of the Specimen showed multiple, irregular, soft, greyish white tissue fragments collectively measuring 4.5x3x0.9cm. Microscopically a tumor composed of meningothelial cells arranged in nests, sheets and whorls with psammoma bodies suggestive of conventional meningioma, was seen (figure 2A). Other areas showed round cells with amphophilic cytoplasm and vesicular nuclei in a basophilic, myxoid stroma (figure 2B&C). In addition, foci show collection of cells with foamy, vacuolated cytoplasm and central rounded nucleus (figure2. D). Mitotic activity was not increased. Also noteworthy were the scattered mature bony trabeculae which showed well-formed lacunae and osteoblastic rimming (figure 2E). Presumptive histopathologic diagnosis of Metaplastic Meningioma with myxoid, Xanthomatous, and osseous metaplasia was made on Hematoxylin and eosin (H&E) stain. Special stains and immunohistochemical markers were applied for confirmation of diagnosis Alcian blue stain was diffusely positive in areas with myxoid stroma showing the presence of acid mucopolysaccharides (figure2. F). Epithelial membrane antigen (EMA) showed cytoplasmic positivity for tumor cells including nests of cells with foamy cytoplasm (figure3. A). Strong nuclear positivity was also seen on application of progesterone

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receptor antibody (figure2. B). Xanthomatous cells (cells with foamy vacuolated cytoplasm and round nuclei) stained negative for CD68 antibody (figure3. C). GFAP was negative in tumor cells (figure3. D). Tumor cells were strongly immunoreactive for vimentin (Figure3. E and F). Based on special stains and immunohistochemical markers, a final diagnosis of metaplastic meningioma with myxoid, xanthomatous and osseous metaplasia was rendered.

Gradual improvement was noted in the patient's symptoms over the next three months after surgical extirpation of the tumor. His vision improved, headache subsided and Hemoglobin levels returned to normal (See Table 1). There was no sign of recurrence of disease after two years of follow up.

Table 1 Hemoglobin and Other Parameters before and after Surgery

Laboratory Parameters	Before Surgery	After Surgery	Units	Reference Values
Hemoglobin	9.5	14.2	G/Dl	12.5-16.5
Red Blood Cells	4.85	5.8	10^12/L	4.5-6.5
Hematocrit	33.4	48	%	35-65
MCV	68.9	88	Fl	80-100
MCH	19.6	29	Pg	27-33
MCHC	28.4	32	G/Dl	30-35

II. DISCUSSION

Metaplastic meningioma is a subtype of meningioma in which metaplasia of meningothelial cells into stromal cells occurs locally to form bone (osseous), cartilage (cartilaginous), lipids(lipomatous), and mucin (myxoid)(4).

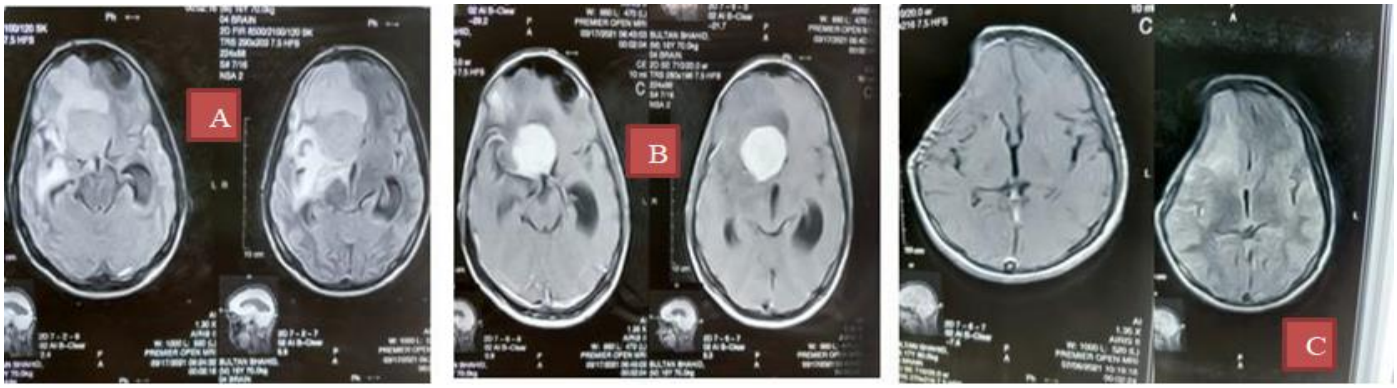

Fig 1 (A & B): Preoperative MRI scan shows a large mass with Dural attachment causing edema and midline shift (C) Postoperative MRI brain showing a defect in skull. No mass or associated edema and midline shift is seen.

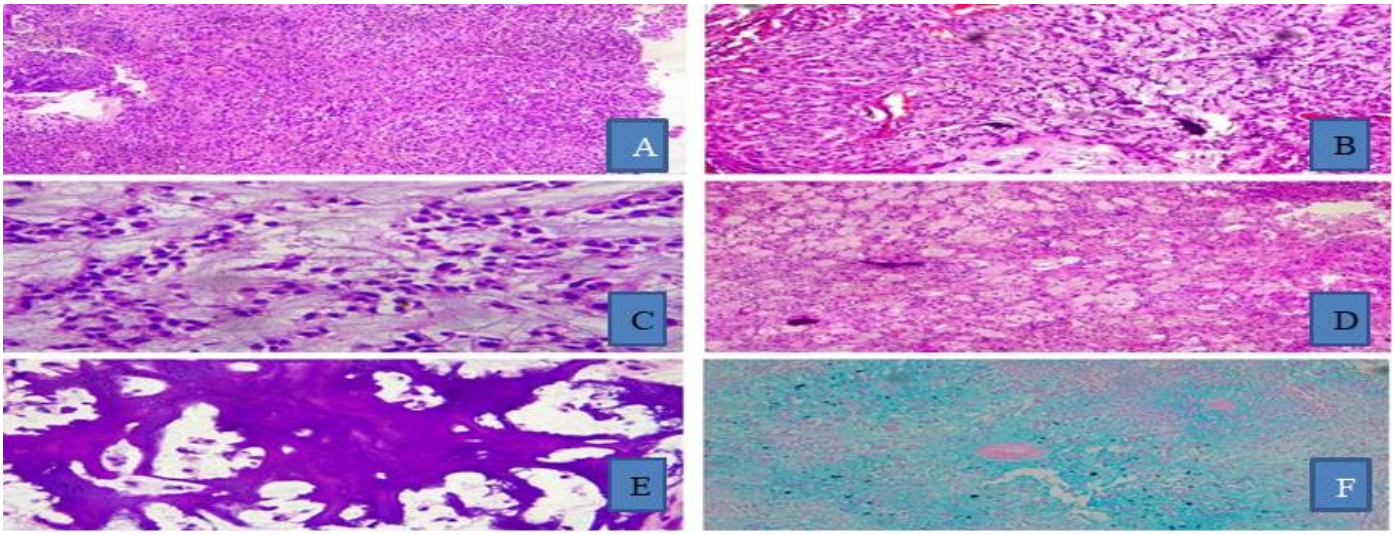

Fig 2 (A) Meningothelial cells are forming vague whorls and sheets (H &E; original magnification x100) (B) Meningothelial cells interspersed in myxoid background (H &E; original magnification x200) (C) High power view showing scattered cells in an abundant myxoid background (H &E; original magnification x400). (D) Sheets of Xanthomatous cells (H &E; original magnification x200) (E) Mature bone with well-formed lacunae and osteoblastic rimming (H &E; original magnification x200) (F) Alcian blue stain showing positivity for acidic mucopolysaccharides in background (Alcian Blue; original magnification x200).

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Till date, most of reported cases of metaplastic meningioma were either pure myxoid (9 case reports), or osseous(12 case reports), lipomatous (64 case reports), and xanthomatous (6 case reports) (5)(6)(7)(8). Metaplastic meningioma with myxoid, xanthomatous and osseous metaplasia is extremely rare and to our knowledge, this is the first case to be reported. Moreover, this is the first case where metaplastic meningioma was the cause of unexplained microcytic hypochromic anemia in a young boy. Clinical, radiologic, histopathologic and immunohistochemical correlation is important for diagnosis and exclusion of other entities like various other subtypes of meningioma, osteosarcoma, mucinous tumors, and histiocytic tumors(5).

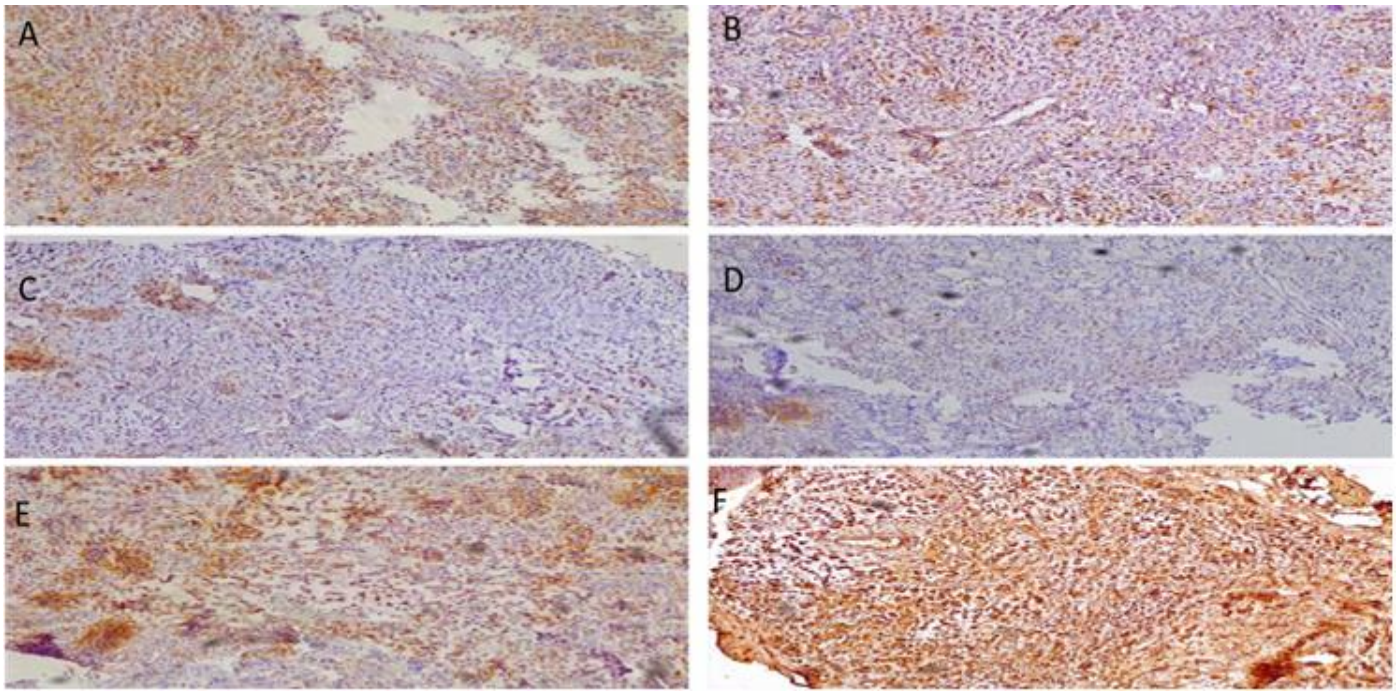

Fig 3 (A-F) Application of various immunohistochemical markers (A) Tumor cells show positivity for epithelial membrane antigen (EMA; original magnification x200). (B) Progesterone receptor showing nuclear positivity in tumor cells [PR; original magnification x20] (C) CD68 stain showing Negativity in Xanthomatous area [CD68; original magnification x20] (D) GFAP showing negative staining [GFAP; original magnification x20] (E &F) Vimentin strong positivity in tumor cells [VIM; original magnification x20].

Metaplastic meningioma with myxoid differentiation is characterized by acidic mucopolysaccharides in the cytoplasm of tumor cells and in the stroma, in addition to the usual morphologic features of meningioma like nests of cells with syncytial appearance, nuclear inclusions, and psammoma bodies. Alcian blue stain is used for identification of these acidic mucopolysaccharides(5). Strong positivity for Alcian blue stain was seen in our case, thereby confirming myxoid metaplasia (Fig 2-F). Metaplastic meningioma with myxoid areas needs to be differentiated from metastatic carcinoma, sarcoma, chordoma, and especially Chordoid meningioma(9). Metastatic carcinoma and sarcomas can present with myxoid background, however these tumors usually display features of malignancy like anaplasia, mitoses and necrosis. Carcinomas show immunoreactivity for Cytokeratin (CK) which in our case was negative (picture not given). The tumor cells, in the current case, were very monomorphic and did not show any pleomorphism. Ki67 (Picture not given) was applied which showed 1% positivity. Chordoma are usually seen in sacral region in old age and are composed of large physallipharous cells which were not seen in this case. Chordoid meningioma, a grade 2 tumor with high recurrence potential, usually presents in first two decades of life(9). Chordoid meningioma is particularly difficult to differentiate from metaplastic meningioma with myxoid areas since immunohistochemical markers offer no help. Lobules of large cells with eosinophilic vacuolated cytoplasm in a myxoid stroma, dense lymphoplasmacytic infiltrate, association with castleman's disease and retarded somatic/ sexual development characterize Chordoid meningioma(9). Cells in myxoid areas, in our case, were small, monomorphic, rounded and did not show any cytoplasmic vacuoles or epitheloid morphology. Xanthomatous and osseous metaplasia has not been described in cases of Chordoid meningioma. Moreover, the patient was followed for two years and no tumor recurrence was noted. His vision improved and his hemoglobin levels returned to normal (see Table 1).

Xanthomatous meningioma, a variation in the theme of metaplastic meningioma, show localized collections of cells with foamy vacuolated cytoplasm and centrally placed nucleus along with areas showing conventional morphologic features of meningothelial meningioma(10). These foam cells need to be distinguished from macrophages. CD68 is a histiocytic lineage marker which stains macrophages as well as many other histiocytic tumors(11). Xanthomatous areas in our case were CD68 negative (Figure 3-C) while EMA (Figure 3-A) and vimentin (Figure 3-E, F) positive, thereby confirming the meningothelial nature of these cells, which have undergone Xanthomatous metaplasia. Some authors

have used adipophylin positivity as evidence of Xanthomatous nature of these cells(12). However, we did not use this marker in our case, because the Xanthomatous appearance of the cells was obvious and these were proved, by EMA, Progesterone and vimentin positivity, to be meningothelial cells. Grade 2 Clear cell meningioma was also considered in differential diagnosis. Clear cell meningioma, is a childhood tumor usually affecting cerebellopontine angle and lumbosacral region(13). Morphologically these are cellular tumors composed of cells having rounded to polygonal shape and clear cytoplasm with broad bands of collagen in perivascular and interstitial locations(14). In our case, the morphology was suggestive of meningothelial meningioma at places. More over Myxoid, Xanthomatous and bony metaplasia, seen in our case, are not found in clear cell meningioma.

The process of ossification in meningioma is uncertain; many researchers have supported the view that it is the result of metaplasia of meningothelial cells into osteoblasts(15). Increased expression of bone morphogenetic protein-2 (BMP-2) was shown, in a study, as the possible cause of bone formation. However direct involvement of this protein in the ossification process is still unclear(16). Small ossified areas may be seen in Psammomatous meningioma, however, metaplastic meningioma with significant woven bone formation is exceedingly rare(16). Formation of mature woven bone lined by osteoblasts and having well defined lacunae were seen in present case study. Osteosarcoma was considered in differential diagnosis. However, no pleomorphism or immature osteoid was seen in our case.

The association of microcytic hypochromic anemia with metaplastic meningioma, in our case, could not be explained. We assumed that anemia might have developed, due to poor dietary intake, as a result of anorexia caused by this low grade, yet space occupying neoplasm. Despite extensive literature search, we could not find any case of metaplastic meningioma causing anemia in a patient. Cases of lymphoplasmacyte rich meningioma and clear cell meningioma presenting with hypogammaglobulinemia and microcytic hypochromic anemia with associated castleman's disease have been described. However our case did not show any lymphoplasmacytic infiltrate or clear cell meningioma morphology.

III. CONCLUSION

Due to limited number of reported cases, the behavior of metaplastic meningioma is poorly understood. The prognosis of metaplastic meningioma, according to current literature, is not different from other grade 1 meningioma. Knowledge of the mesenchymal metaplastic elements in Meningioma is important to avoid mislabeling of the patient with sarcomas, grade 2 meningioma and other malignant tumors. Investigating microcytic hypochromic anemia in a patient may remotely include grade1 meningioma, especially metaplastic meningioma, in the list of underlying causes. We believe this case will widen our horizon and will help us in better understanding of metaplastic meningioma.

- *Conflict of Interest*
  The Authors do not have any Conflict of Interest.

- *Acknowledgement:*
  This Work has not been Presented at any Conference/Symposium.

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