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CASE REPORT

Clear-cell meningioma: Intraoperative diagnosis by squash cytology: Case report and review of the literature

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ABSTRACT

Clear-cell meningioma (CCM), an unusual subset of meningioma has prominent, clear-cell morphology. It is a wolf in sheep's clothing characterized by benign histologic attributes, but tendency for recurrence (61%) and metastasis. Therefore, WHO has classified it as grade II meningioma. Fine-needle aspiration cytology diagnosis is simple, rapid, cost-effective and reliable procedure primarily aimed at preoperative diagnosis of advanced and metastatic extracranial tumor. Preoperative and/or intraoperative cytodiagnosis of CCM demand expertise in the evaluation of cytology smears. However in case of intra operative evaluation of squash smears there is a time constraint and a very small tissue material obtained by stereotactic biopsy are available for interpretation. Knowledge of clinical features including age, anatomical locations, neuroimaging findings and cytomorphologic features, are prerequisites for arriving at definitive cytodiagnosis. We describe intra operative squash cytology of CCM in a 16-year-old female, located in cerebello-pontine angle. The diagnosis of CCM offered on squash cytology was subsequently confirmed on histopathology and immunohistochemistry. It typically showed pattern less sheets and groups of polyhedral, clear cells with monomorphic, round nuclei having a bland chromatin and inconspicuous nucleoli. Separation of CCM from other tumors having clear -cell morphology and variants of meningioma is important because of its high recurrence rate and mortality.

Key words: Cerebello-pontine angle, clear-cell meningioma, intraoperative diagnosis, squash cytology

Introduction

Clear - cell meningioma (CCM), a newly described subtype is categorized as WHO grade II tumor.[1] It accounts for 0.2% amongst all meningiomas.[2] in contrast to other variants, it affects young adults including children (mean age 29 years) and is often located in the descending order of frequency in spinal canal (50%), cerebello-pontine (CP) angle (21%), supratentorium (21%) and foramen magnum (7%) and exceptional cases may be associated with cranial nerves, spinal roots and cauda equine.[3] CCM is predominantly a dura based (92%), extra axial tumor. WHO has described 15 variants of meningiomas reflecting the mesenchymal and epithelial potential of arachnoid cap cells, the latter being histogenic cells of meningioma. CCM expresses the epithelial differentiation of arachnoid cap cells. A mixture of clear-cells and meningothelial features are keys to the diagnosis. The cytologic features were first described by Imley *et al*. in 1998 by fine needle aspiration biopsy. It is known for aggressive behavior, and the recurrence rate is 61%.[3] Although the histologic features are well documented,[3] cytological features on squash smears are rarely reported in the literature. We describe the intraoperative squash cytology of CCM located at CP angle in a young girl.

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Case Report

The 16-year-old female complained of a headache, vomiting and diminished hearing in right ear since 2 months. She also gave a history of giddiness and diplopia of 1-month duration. Her higher functions were normal. The cerebellar signs such as Romberg's test, Tandem walk, Finger nose Finger tests were positive. Magnetic resonance imaging revealed a well-defined, extra axial, solid mass in right posterior fossa at the level of CP angle with extension into the foramen magnum. Radiological diagnosis was schwannoma [Figure 1]. Intra-operative findings: Tumor was subdural soft, reddish to greyish white sulkable mass without well-defined plane from surrounding brain parenchyma. Multiple, tiny, greyish white tissue bits aggregating 0.5 cc were received for intra operative diagnosis. Four squash smears were prepared, immediately fixed in 95% ethyl alcohol for 2 min. Three out of four smears were stained with rapid H and E stain. Intra operative cytology: Moderately cellular smears revealed neoplastic cells predominantly in diffuse patternless sheets. Focal whorl pattern was also seen against a clean background [Figure 2]. The cells were predominantly polygonal with a moderate amount of clear cytoplasm and central, uniform, round nuclei with inconspicuous nucleoli [Figure 2]. Also seen were few spindle-shaped cells. There was no evidence of atypia, mitosis or necrosis. The intra-operative diagnosis of CCM was offered on squash cytology. Subsequently, partial excision of the tumor was done as it was adherent to surrounding structures. We received a partly encapsulated 4 cm × 3 cm tumor mass, having greyish white, firm and homogeneous cut surface. Histology revealed tumor cells arranged mostly in diffuse sheets and at places in whorls. Cells were polygonal to spindle with moderate to abundant clear cytoplasm. The nuclei were round, monomorphic with inconspicuous nucleoli [Figure 3]. There was no evidence of atypia, mitosis or necrosis. On immunohistochemistry (IHC), the tumor cells displayed membranous positivity for epithelial membrane antigen (EMA) [Figure 4].

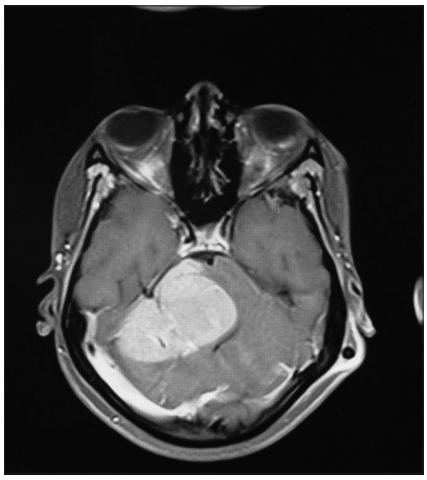

Figure 1: Magnetic resonance imaging - revealed a well-defined, extra axial, solid mass in right posterior fossa at the level of cerebello-pontine angle with extension into the foramen magnum. Impression: Schwannoma

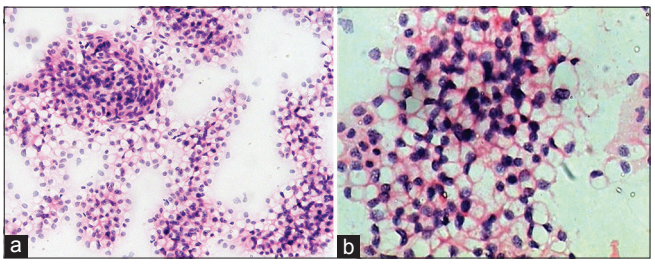

Figure 2: Squash cytology - cells predominantly in diffuse pattern less sheets, at places in whorls (H and E, ×20). Inset: Polygonal cells with moderate amount of clear cytoplasm. The nuclei are centric, uniform, round with inconspicuous nucleoli (H and E, ×40)

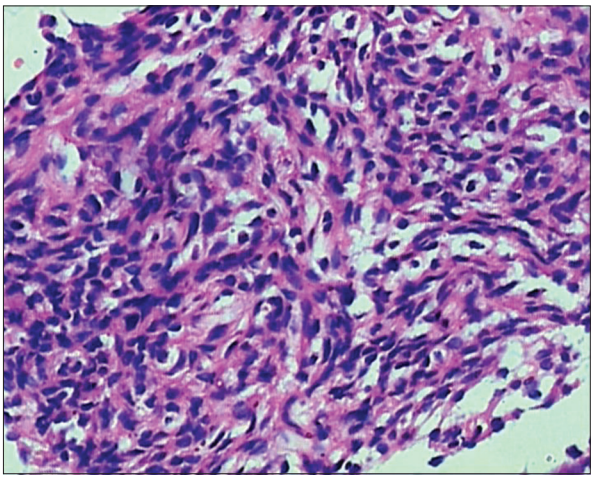

Figure 3: Histology - Meningothelial cells arranged in diffuse syncytial sheets with focal whorling pattern. Polygonal to spindle cells with indistinct borders and moderate to abundant clear cytoplasm. The nuclei are round, monomorphic with inconspicuous nucleoli (H and E, ×20)

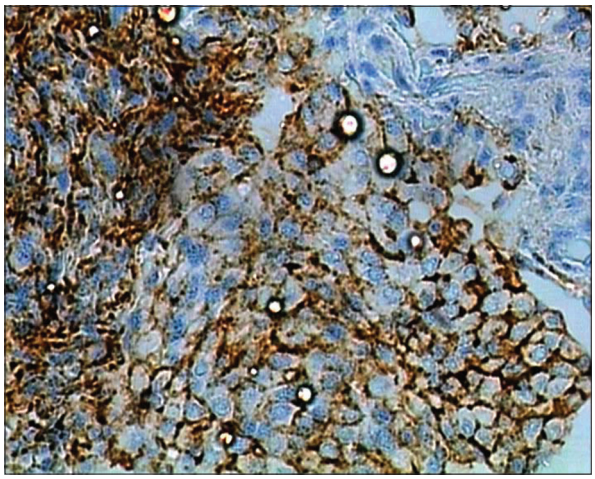

Figure 4: Immunohistochemistry: The tumor cells shows membranous positivity for epithelial membrane antigen (Epithelial Membrane Antigen, ×40)

Discussion

Meningiomas are dura based, slow growing meningothelial neoplasms most commonly encountered in middle or late adult life. These extra-axial tumors are found along the convexities of brain.[1] WHO graded them from grade I to III according to their biological behavior. The cytological features of CCM in the form of patternless sheets with abundant clear cytoplasm and monomorphic nuclei were first described by Imlay *et al*.[3] The cytoplasmic clearing is due to the presence of abundant glycogen, the latter is periodic-acid Schiff positive and diastase labile. The typical meningothelial attributes such as whorls and nuclear pseudo inclusions may not be seen. However, if present can be a valuable clue to the diagnosis of CCM. Increased mitosis and necrosis are unusual.[4,5]

The differential diagnosis of CCM includes clear- cell ependymoma and metastasis of renal cell carcinoma (RCC). Clear-cell ependymomas are intra-axial and ventricular tumors, the squash smears of which show typical perivascular rosettes, poorly formed acini, cords and fibrillary processes of tumor cells.[5,6] On IHC, they are glial fibrillary acid protein (GFAP) reactive and show dot like positivity for EMA. Metastatic RCCs on cytology reveal large polyhedral clear-cells arranged in small groups, in tubular or glandular fashion having large vesicular nuclei with prominent nucleoli. The endothelial cells traversing the cell groups are characteristic features.[5] The cells show positivity for cytokeratin and EMA. In contrast, CCMs have spindled to polygonal cells in sheets with clear vacuolated d cytoplasm and bland-appearing nuclei with inconspicuous nucleoli.[4] On IHC, they show membranouspositivity for EMA and negativity for cytokeratin.[4] CCM should also be separated from hemangioblastoma the later present as a cyst with mural nodule having leptomeningeal attachment. Cytologically it shows anastomosing network of blood vessels separated by stromal cells with medium to large nuclei having foamy cytoplasm. Hemosiderin laden macrophages are seen in the background. The stromal cells are positive for S100 protein, neuron-specific enolase and to inhibin alfa a recent marker.[6] The other tumors showing clear-cell morphology are neurocytomas and oligodendrogliomas. The neurocytomas are intra axial tumors located around the ventricles affecting young adults and on the squash cytology reveals round, uniform-sized cells set in the background of fibrillary matrix of neuropils. The tumor cells display finely stippled granular chromatin, prominent micronucleoli, and ill-defined cytoplasm.[7] IHC studies show positivity for neural markers such as synaptophysin and negativity for GFAP and EMA. Oligodendrogliomas on the other hand are intra-axial predominantly cortical based tumors, which on squash cytology show round cells, with monomorphic vesicular nuclei and ill-defined scant, wispy cytoplasm against a characteristic background of fibrillary matrix. Further, they show a population of fibrillary astrocytes or minigemistocytes.[7]

The importance of squash cytology in intra operative diagnosis of central nervous system tumors has its own advantages over the frozen section. It provides good morphologic details. Small stereotactic biopsies of soft lesions can be smeared easily and requires less technical expertise. There are no freezing artifacts. It is simple rapid, reliable and inexpensive[8] However, it also has limitations; that is, tissue architecture is not apparent and with firm tissue, smear preparation becomes a difficult task. The utility of the imprint/squash preparation technique could be beneficial in centers where a facility for frozen sections is unavailable, in case of a power break-down, or a lack of trained technical personnel.[8]

The patients of CCM need regular follow up because of aggressive behavior and high recurrence, despite its benign morphologic features.[9] Our patient is being followed up regularly since past 2 years. She has no signs and symptoms or radiological features suggestive of recurrence.

Although, CCM is a rare subtype, it is practically possible to offer this diagnosis on squash preparations based on the typical features of patternless sheets and a few whorls of clear-cells with monomorphic nuclei and inconspicuous nucleoli when interpreted in the correct clinico-radiological setting.

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Conflicts of interest
There are no conflicts of interest.

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