Flow Cytometric and Histopathological Correlation of Cystic Meningiomas: Analysis of Three Cases

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Abstract: Cystic meningiomas are rare forms of meningiomas which are generally known as solid and benign tumours.
Preoperative misdiagnosis of such a tumour will affect the surgical management and difficulties in histopathological diagnosis will affect the prognosis.
Flow cytometric studies have more advantages than histopathological studies, in postoperative management and in predicting prognosis. and it is better to use flow cytometry in conjunction with histopathological procedures for predicting the prognosis.
In this acticle we report flow cytometric analysis of three cystic meningioma cases, we correlate them with the histopathological results and discuss the pertinent literature.

Key Words: Cystic meningioma, histopathology, flow cytometry, magnetic resonance imaging

INTRODUCTION

Meningomas are 13-18% of all intracranial tumours (11, 13, 16, 24, 26, 28, 31) and the incidence of cystic meningiomas ir rare 17-9% (2, 7, 11, 18, 19, 26) but increases in childhood (17-30).

Cystic meningiomas can mimic glial and metastatic tumours, hemangioblastoma (11, 20, 27) and neuroblastoma (11, 27) in computerized tomography (CT) and magnetic resonance imaging (MRI) by the presence of cystic and necrotic changes. In addition there can be some difficulties in histopathological diagnosis (4, 14, 18, 24, 25, 34, 37).

The histopathological properties of cystic meningiomas are not certain indicators of prognosis, but flow cytometric findings give some important information and can help in deciding the postoperative treatment and follow up protocols.

PATIENTS AND METHODS

A total of 40 patients with meningioma underwent operations at our department between 1990 and 1995. Review of the imaging studies (CT; MRI, angiography) showed only 3 patients to have cystic meningioma and these were operated in 1994. The surgical pathological findings, the operation notes and follow up of the patients were reviewed to correlate them with the flow cytometric findings. The ages of the patients were 51, 70 and 31, two were women and one was a man. A correct preoperative diagnosis was achieved radiologically in all the three patients.

HISTOPATHOLOGICAL STUDIES

The paraffin blocks were reexamined loss of cellular architecture, focal necrosis, nuclear pleomorphism, increased number of mitotic figures and brain invasion were noted (Table I).

FLOW CYTOMETRY STUDİES

Using a method moodified by May et al. (22), 50 microgram paraffin block sections were placed in gloss centrifuge tubes, dewaxed in xylene for 30

minutes and rehydrated first in 99% alcohol for 45 minutes and then in distilled water for 24 hours. Later the tissue was digested in 0.5% pepsin in phosphate buffered solution (pH 1,5) for 30 minutes at 37°C to release nuclei.

Table I: Malignancy Criteria of the Cases			
Malignancy Criteria	Case 1	Case 2	Case 3
Loss of cellular architecture+	++	-	
Focal necrosis	-	+	-
Nuclear pleomorphism	-	+	-
Brain invasion	-	-	-
Increased number of mitotic figures	+	++	-

The suspension of cells was centrifuged for 10 minutes at 1700 rpm, the pellet was resuspended in distilled water and whole cell DNA staining was performed using propidium, 0.1 mg/ml in phosphate buffered solution pH 7.4 and the resulting suspension was filtered through a 50 microgram steel mesh to remove clumps. Flow cytometric studies were performed with a coulter EPICS ELITE ESP flow cytometer.

Result of cell cycle analysis were expressed as a percentage of the who sample (Table II). The proliferative index (PI) of each tumour was calculated as the sum of the percentage of the cells in the S phase and the G2/M phase of the cycle. [PI (%)=S%+G2%/M].

Table II : Flow Cytometric Evaluation of 3 Cystic Meningioma Cases			
	Case 1	Case 2	Case 3
Go/G_1[a] (%)	76.7	90.5	93
CVG_1[b] (%)	9.2	4.3	10.3
S[c] (%)	4.6	0.1	5.5
G_2/M[d]	18.7	9.4	1.5
CV G_2[e] (%)	11.3	9	6.7
DI[f] of Aneuplodic Peak	1.17	0.9	-
PI[g] (%)	23.3	9.5	7
Chi Sq	1.8	0.8	0.9

a: Cells in the resting plase.
b: Variation coefficient of cells in G_1 phase.
c: Cells synthesising DNA.
d: Cells in mitosis.
e: Variation coefficient of cells in G_2 phase.
f: DNA index:
g: Proliferati ve Index = G_2M+S

ILLUSTRATIVE REPORTS OF PATIENTS

PATIENT 1:

A 51-year-old woman presented with left focal motor seizures, left hemiparesis and dysarthria. Physical examination was normal except for a 4x4x4 cm. right frontal mass. neurological examination revealed right grade 2 papil oedema, dysarthric speech, left central facial palsy and mild left hemiparesis. Skull x-rays revealed a hypodense eroded region in the frontal bone (Fig 1). At angiography the feeding artery of the tumour was the superficial temporal artery and tumoural blushing was especially observed in the venous phase (Fig 2). MRI showed a right extraaxial frontal mass with both solid and multicystic components extending to the extracranial area by eroding the frontal bony calvaria (Fig 3). The tumor was type 2 according to the classification of Zee et al. (41).

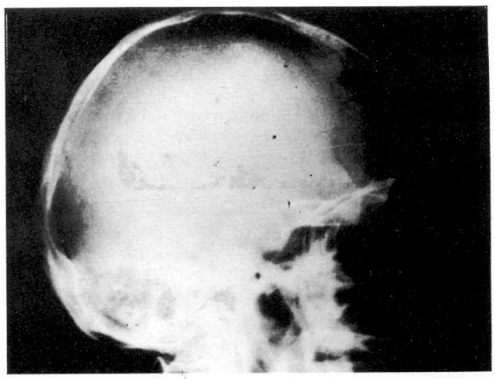

Fig. 1 : Lateral skull x-rays showing a hypodense eroded region in the frontal bone.

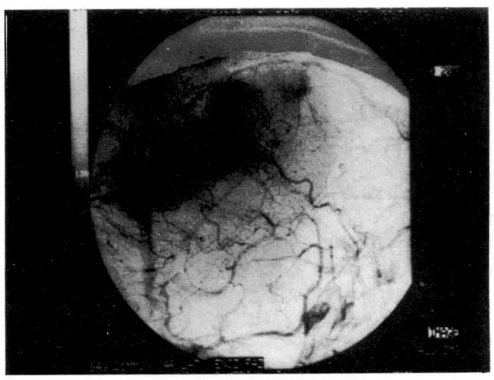

Fig. 2 : Right common carotid lateral angiography showing tumoural blushing in the venous phase.

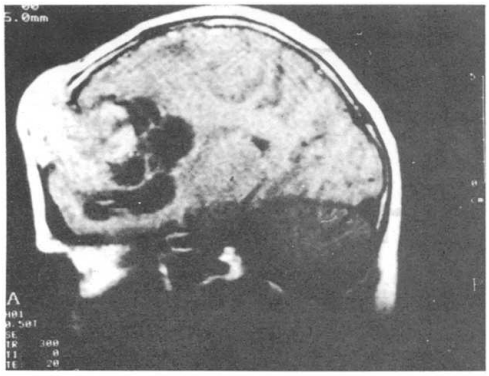

Fig. 3 : Parasaggital MRI (SE 300/20) showing a right frontal lobe mass that has both solid and cystic components. There is a dural thickening in the frontal region and the mass is extending extracranially.

At operation a solid tumour which had eroded the frontal bone was removed totally with the frontal dura. The cysts, contained xanthochromic fluid. A fascia lata duraplasty was performed. Pathological diagnosis was meningothelial meningioma (Fig 4). Three months after surgery, the patients' neurological examination was within normal limits.

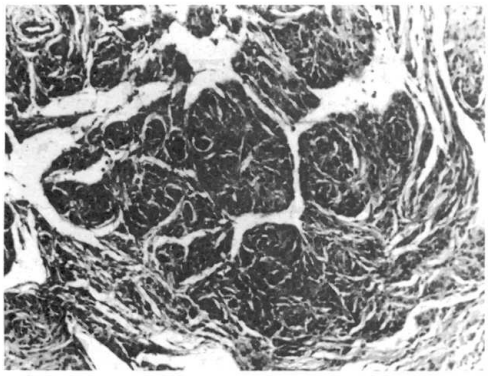

Fig. 4 : The mass was histopathologically revealed as a meningothelial meningioma. Neither atypia nor mitotic activity were observed. (HE X 100).

PATIENT 2

A 7-year-old woman presented with a right frontal mass which had grown in the last year, causing headache, drowsiness and left hemiparesis. Physical examination was within normal limits except a 3x3 cm right frontal mass. Neurological examination revealed a right grade I papil oedema and slight left hemiparesis. A contrast enhancing (CE) CT scan of the brain showed a right frontal cystic mass. An initial diagnosis of glioblastome multiforme was made. CE MRI demonstrated a right frontal lobe multicystic mass causing a midline shift. There was prominent rim enhancement of the cysts (Fig 5). The tumour was type 1 according to the classification of Zee et al. (41), and a preoperative diagnosis of cystic meningioma was made. At surgery a bifrontal craniotomy was performed and the cystic mass which had eroded the frontal bone and invaded the dura and 1/3 of the anterior superior sagital sinus, was removed totally. A craniectomy was performed on the eroded region of the frontal bone and a fascia lata duraplasty was performed for the dural defect. The pathological diagnosis was angioblastic meningioma (Fig 6). Patient's postoperative period

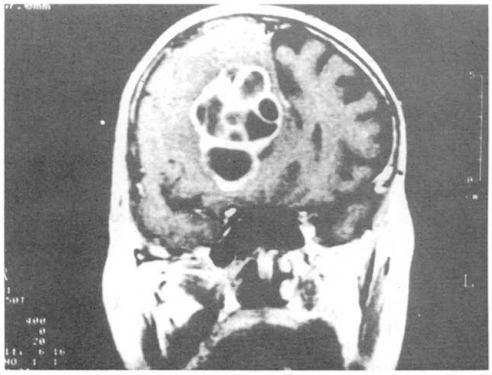

Fig. 5 : CE coronal MRI (SE 400/20) showing a right frontal lobe multicystic mass. There is prominent rim enhancement of the cyst walls. The mass is causing some distortion in the midline structures.

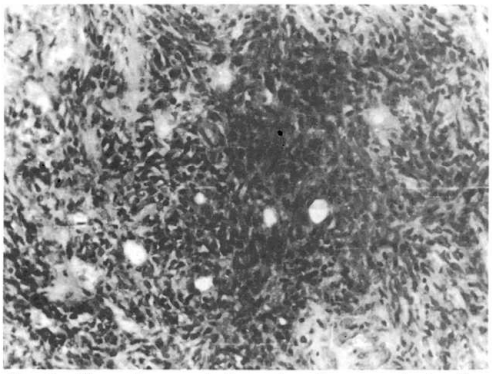

Fig. 6 : Tumoral mass at the cyst wall composed of solitary nodules, each nodule containing numerous slide-like vascular channels which were lined by meningothelial cells. Local pleomorphic changes and cranial bone invasion are seen . (HE X 200).

was uneventful and the patient was discharged at the tenth postoperative day without any neurological daficit and transferred to an oncology department for radiotherapy. No recurrence was observed at the second follow-up visit six months later.

PATIENT 3:

A 34-year-old man presented with a 7-year history of tonic clonic seizures. Neurological examination disclosed a right grade II papil oedema. A CE CT brain scans howed a right temporal ,mass with solid and cystic components and significant mass effect. The solid portion was enhancing homogeneously. CE MRI demonstrated a right temporal lesion with solid and cystic components. There was intense enhancement of the solid portion. Compression and distortion of the third and lateral ventricles was observed (Fig 7). The tumour was type

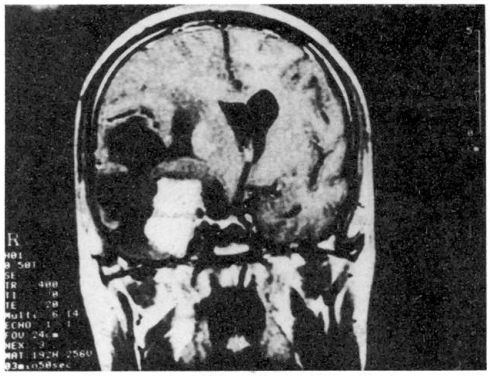

Fig. 7 : CE coronal MRI (SE 400/20) showing a right temporal mass with solid and cystic components. There is intense enhancement of the solid portion. Compression and distortion of the third and lateral ventricles are seen.

3 according to the classification of Zee et al. (41), and a preoperative diagnosis of of 1/3 medial sphenoid wing cystic meningioma was made. At surgery, first the cyst was punctured and the cyst fluid was xanthochromic. The solid portion of the tumor removed subtotally and the cyst wall were removed. The pathological diagnosis was a psammomatous meningioma (Fig 8). The postoperative period was uneventful. In the first year after surgery the patient's neurological examination was normal and he had had no seizures.

DISCUSSION

Different factors are responsible for the occurrence of cystic meningioma. Possible

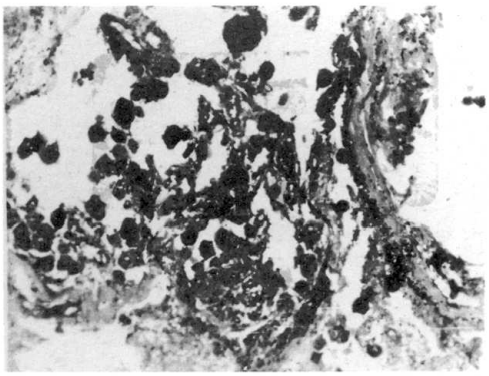

Fig. 8 : Neoplastic tissue composed of meningothelial cells with calcified and non-calcified psammoma bodies in various numbers. There is no sign of atypia and mitotic activity. (HE X 40).

physiopathological mechanisms are; 1) ischaemic central necrosis and cystic degeneration, 2) secretions of functional tumour cells into the tumour, 3) secretions of the proliferated glial cells as a response to the tumour, 4) brain oedema causing peritumoral cystic cavities, 5) CSF loculation, 6) combination of 2nd and 3rd mechanisms with post haemorrhagic cavitation (18, 41).

, Meningioma cysts are classified by Nauta, Rengachary and Worthington et al. according to the ralation of the cyst with the tumour and brain (24, 32, 37). Cystic meningiomas are classified by Ramos et al. according to their CT appearances (29) and by Zee et al. according to their MRI appearences (41).

CT images of cystic meningiomas may simulate glial or metastatic tumour with cystic or necrotic changes (4).

MRI may show the presence of dural attachment, extra axial localisation and cerebral oedema better than CT. Demonstration of dural thickening by MRI is sometimes a useful clue to the nature of a cystic meningioma (36). But unfortunately, it may not be differentiated from partly echanced glioma or metastasis, because of nonenhanced cysts and focal oedema.

It is advisable to use CT, MRI and angiography together for making a correct preoperative diagnosis in cystic meningioma cases. Preoperative diagnosis is important because resection and careful pathological evaluation of the walls of any cysts are mandatory to avoid recurrence (5, 16) and this is supported by the fact that %8 of cystic meningiomas are malignant and % 12 are angioblastic, probably

haemangiopericytic (13).

Histopathological diagnosis can be difficult because of the multipotential character of the arachnoid stem cell, both epithelial and mesenchymal differentiation can occur in the meningioma (32).

When cystic meningioma cases reported in literature are examined; different histopathological types are observed, such as; angioblastic (3, 18, 26), meningothelial (14, 18, 19, 25, 35, 37, 38), transitional (24, 2, 31, 35), fibroblastic (3,9,25), psammomatous (19,26), fibroblastic and transitional (26), sarcomatous (3), meningothelial and fibroblastic (3, 26), fibrous syncytial (31), syncytial (9, 24, 31, 37), endotheliamatous (21, 23). In one case the subgroup was not reported (21). Such a wide variety of subgroups may make histopathological diagnosis difficult, in addition to the highly protean microscopical appearances of meningiomas and their capacity for mimicking the histopathoogical features of other neoplasms (33). Myxomatous and microcystic forms may closely resemble picture of a protoplasmic astrocytoma or the cells of cynctial meningiomas may be confused with carcinoma, chordoma, paraganglioma and pilocytic astrocytoma (33). In addition, 4.2% of initially histopathologically benign meningiomas recurr and differentiate into histopathologically malign neoplasms (9). For these reasons, an electron microscope, special stain for fibrous connective tissue and immun histochemical studies are helpful for accurate histopathological diagnosis.

Initial prediction of the degree of malignancy and recurrence is quite difficult (40). Flow cytometric DNA analysis has been studied as a supplementary technique to provide additional prognostic information (32).

The relationship between the flow cytometric features and clinical behaviour of meningiomas was determined by Ahyai et al. (1), Crone et al. (6), Frederiksen et al. (12) and Ironside et al. (15). Especially the presence of aggressive clinical situations like aneuploidy, brain invasion, or cerebral oedema can be diagnosed by routine flow cytometric studies. in 1989, May et al. (22) reported that, PI of 20 % or greater, even in the presence of total macroscopic resection and benign histopathological appearance is strongly suggestive that the tumour will recur.

When histopathological evaluation of cases with malignancy criteria was made (Table I) and compared with flow cytometric results (Table II), in case 1, loss of cellular architecture and an increased number of mitotic figures were observed (TableI) and the patient's PI was 23.3% (Fig 9) (Table II). We can estimate that this patient will have a recurrence and must be closely followed up. In case 2, loss of cellular architecture and increased mitotic figures were more than in, case 1 and in addition, focal necrosis and nuclear pleomorphism were observed (Table I) but the PI was 9.5% (Fig 10) and less than case 1 (Table II). Although the tumour seems histopathologically more malign than case 1 the chance of recurrence

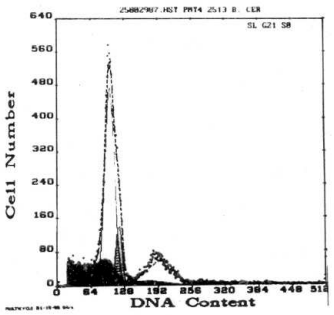

Fig. 9 : Flow cytometric histogram of case no: 1.

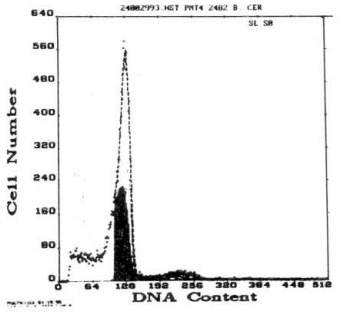

Fig. 10 : Flow cytometric histogram of case no: 2.

seems less than case 1, but a close follow up will also be necessary. In case 3 no malignancy criteria were observed and the PI was 7% (Fig 11); lowest of the three cases. Although the prognosis is good histopathologically and the risk of recurrence is low flow cytometrically; as the tumour was removed

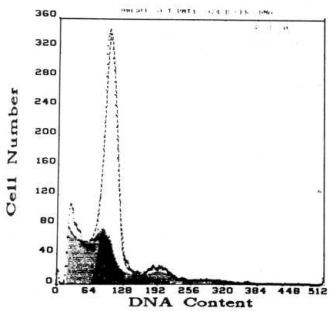

Fig. 11 : Flow cytometric histogram of case no: 3.

subtotally there is still a high risk of recurrence. We hope long term follow up of these patients may add to our present knowledge.

In conclusion; cystic meningiomas can be evaluated with flow cytometric studies for postoperative follow-up. Flow cytometry can be very helpful in predicting recurrence when used in combination with other diagnostic procedures in estimating patients at risk and remodelling follow-up protocols.

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