3	Glioma with pilocytic features	III	33F	Recent headache, seizure	Right frontal lobe mass with decreased attenuation	13 mo; stable
4*	PXA*	II-III*	31M *	Headache *	Right frontal lobe enhancing mass *	14 years; alive *
5	Astrocytoma	III-IV	29M	Mental status changes	Left frontal lobe mass	6 years; recent status unknown

* indicates patient's age, presentation and follow-up from the 1st recurrence as grade III glioma (9 years after initial diagnosis of PA); mo: month

Conclusions: This study is a collection of gliomas with HGF showing the somewhat rare finding of numerous RF and EGB. While it is difficult to draw definitive conclusions from this small patient sample, 4 of the 5 patients were less than 35 years of age at diagnosis. This is at least 10 years younger than the mean for high grade gliomas. Additionally, most patients had stable follow-up, with the longest being more than 14 years after initial diagnosis. Such gliomas with HGF and RF/EGB could be a unique set of tumors that present acutely yet behave more indolently compared to the usual high grade gliomas.

1639 Osteopontin Immunoexpression in Primary Central Nervous System Lymphoma, and Comparison with Nodal and Extranodal Diffuse Large B-Cell Lymphoma.

J Yuan, K Gu, S Sharma. Medical College of Georgia, Augusta; University Hospital, Augusta, GA.

Background: Primary central nervous system lymphoma (PCNSL) is an aggressive diffuse large B-cell lymphoma (DLBCL) mostly of activated B cell type (ABC), with poor prognosis, yet confined to the CNS microenvironment. Osteopontin, a cell-matrix glycoprotein, is associated with progression, metastatic spread and poor prognosis in several tumors. Osteopontin was the most up-regulated gene in PCNSL compared to nodal and extra-nodal DLBCL (N-DLBCL, EN-DLBCL) in recent cDNA microarray studies. We aimed to validate the protein expression of osteopontin and assess its prognostic value in PCNSL.

Design: We retrieved 19 archival cases of PCNSL, 11 N-DLBCL, and 17 EN-DLBCL from pathology records. Immunohistochemical (IHC) staining was performed for osteopontin and Ki67 on formalin-fixed paraffin-embedded sections using Envision Plus System. Staining for osteopontin was semi-quantitatively stratified and scored both by percentage positivity of tumor cells (0%, 1-25%= score 1, 26-50%=2, 51-75%=3, and 76-100%=4) and staining intensity (none=0, weak=1; moderate=2; intense=3), and an overall score (0 to 12) calculated for each case by multiplying percentage score with intensity score. This data was correlated with Ki67 proliferative indices.

Results: Osteopontin nuclear immune-expression was observed in 18 of 19 (95%) PCNSL cases, 16 of 17 (95 %) EN-DLBCL, and 3 of 12 (25%) N-DLBCL cases. Staining intensity was moderate to strong in most PCNSL cases (especially intense in perivascular and infiltrating neoplastic cells), but weaker and noted in fewer cases sequentially in the EN- or N-DLBCL groups. The overall immunostaining scores were significantly higher in PCNSL group (6.4 ± 3.6) and in EN- (4.4 ± 4.1) than N-DLBCL (0.3 ± 0.7) groups ($p< 0.001$). The difference in osteopontin IHC scores between PCNSL and EN-DLBCL group, was however not statistically significant ($p=0.09$). Further, high osteopontin expression was not associated with high Ki67 proliferation index.

Conclusions: Osteopontin immunoexpression was highest in PCNSL, especially in perivascular and infiltrating neoplastic cells, sequentially followed by EN-DLBCL and N-DLBCL. No association was observed between osteopontin expression levels with proliferative index. Future studies are required to assess the prognostic/predictive role of osteopontin in PCNSL.

1640 Are There Any Differences in the Expression of IDH1 and P53 Proteins between Astrocytoma and Oligodendroglioma?

M Zheng, S Sharma. Medical College of Georgia, Augusta.

Background: Isocitrate dehydrogenase 1 (IDH1) mutation has been well-described in diffuse glioma in recent large studies, with a reportedly similar frequency in astrocytomas and oligodendrogliomas. We compared the expression of IDH1 and p53 in diffuse gliomas to assess any differences between astrocytoma and oligodendroglioma of different grades.

Design: A total of 27 glioma cases were studied, including 20 astrocytomas, 4 oligodendroglioma, 2 anaplastic ependymoma, and 1 ganglioglioma. Autopsy brain tissue with reactive gliosis were used as control. Immunohistochemical staining using IDH1 and P53 antibodies was performed. The percentage positivity of tumor cells showing granular cytoplasmic staining was scored as 1 to 4 (0-25, 26-50, 51-75,76-100%), and staining intensity scored as 1 to 3 (low, medium, strong). A numerical IHC score for each case was derived by multiplying the percentage positivity score with intensity score.

Results: IDH1 immunopositivity was granular cytoplasmic, and seen in 7 of 20 astrocytomas of all grades (35%). Grade-wise distribution was as follows: glioblastoma (1/6), anaplastic astrocytoma (2/6), astrocytoma grade 2 (4/5) and grade 1 (0/3). In contrast, all 4 oligodendrogliomas (100%) showed diffuse strong staining (3 grade-2, and 1 grade-4). No staining was observed in ependymoma (2), ganglioglioma (1) or reactive gliosis (9). IDH1 staining was much more intense in oligodendroglioma as compared with the majority of astrocytomas (*$p=0.0003$*). The expression of IDH1 and p53 proteins in 7 astrocytoma cases was similar (t-test, *$p=0.446$*), whereas the pattern was reversed in 3 oligodendrogliomas with high expression of IDH1 but low p53 protein (*$p=0.003$*).

Conclusions: Our study supports the observation that IDH1 may be an early event in the development of diffuse glioma, and further shows that IDH1 likely contributes more to the tumorigenesis of oligodendroglioma than astrocytoma, in contrast to p53. IDH1 is neither expressed in reactive gliosis nor in majority of glioblastomas. Therefore IDH1 alongside p53 carries the potential to be a diagnostic marker of low-grade diffuse glioma.

Ophthalmic

1641 Biopsy Negative Temporal Arteries.

AM Bartlett, CT Welsh. Medical University of South Carolina, Charleston.

Background: Giant cell arteritis is the most common form of systemic vasculitis in older adults. The major therapy, prednisone, holds more risk for this age group even than it does in younger patients. The alternative, however, can be permanent visual loss. The literature indicates a range in negative biopsies up to 2/3. Our impression has been that of a much higher negative rate at our institution.

Design: We conducted a retrospective review of all temporal artery biopsies from 1995 to 2010 to determine the actual positive rate, related differences in biopsy material, and any possible clinical associations.

Results: Temporal artery biopsies from 1995 to 2010 numbered 244 total, with 19 displaying active inflammatory infiltrates (8%), 10 demonstrating medial scars (4%) consistent with prior injury to the artery (possibly treated arteritis, and 20 with adventitial perivascular lymphocytic cuffing. Bilateral biopsies were done simultaneously in 99 patients, with both active in 7 (7%), and both negative in 84 (85%). Activity was seen in only one of the two biopsies in 2 patients (2%), and medial scarring in one of two biopsies in two patients (2%). Two patients were biopsied twice with a medial scar in only one of the two (1%), and medial scar followed by active arteritis in 1 (1%). Length of biopsy was surgeon dependent; half the active arteritis biopsies were less than 1.5 cm and half greater than 2 cm. The biopsies containing medial scars were all over 2.7 cm. Biopsies which did not show histologic evidence of activity tended to be larger in general, presumably due to the surgical impression of a lack of focal nodularity.

Conclusions: Only 8% showed active signs of arteritis, and 4% demonstrated medial scars consistent with prior injury suggesting treated arteritis. Even combined, this is still only 12% of biopsies with any suggestion of arteritis, which is considerably lower than reported in the literature. Larger biopsies were no more likely to show active inflammatory changes than quite small biopsies, but medial scars tended to be picked up on larger biopsies. This would tend to indicate that surgeons can intra-operatively identify grossly active lesions. We will compare and contrast the clinical features of the patients with positive and negative biopsies to explain the discrepant rates at which these patients are being referred for biopsy.

1642 Morphoproteomics Provides Correlates of Chemoresistance, Metastatic Potential, Insulin-Like Growth Factor and c-Met Signaling in Uveal Melanoma with Therapeutic Implications.

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Background: Uveal melanoma has a propensity to metastasize to the liver and to be chemoresistant (systemic therapies produced a response rate of <1% in one large study).Insulin-like growth factor(IGF)-1 receptor (R)and c-Met are expressed in uveal melanoma and are significantly associated with metastatic disease and death. Moreover, these are receptors for IGF-1 and hepatocyte growth factor ligands, which are produced by the liver.The majority of uveal melanomas expressed activated MET protein in one study, and the blocking of MET reduced uveal melanoma cell proliferation and migration. Targeting IGF-1R and c-Met has been proposed as a therapeutic option in uveal melanoma.

Design: Three(3)patients with uveal melanoma with metastatic disease(two with metastasis to the liver) were the subject of this study. Representative sections were analyzed using a comprehensive morphoproteomic profile(Brown, RE.*Arch Pathol Lab Med.* 2009;133:568-79). This included a specific focus on chemoresistant and metastasis-associated protein analytes and on molecules linking IGF-1R and c-Met signaling in uveal melanoma, in an attempt to provide therapeutic opportunities.

Results: The anti-apoptotic protein, Bcl-2 was expressed in the cytoplasm of all tumor cells (up to 3+ on a scale of 0 to 3+) with concomitant and correlative expression of CD44 and heat shock protein(Hsp)90 on their plasmalemmal aspect and in their cytoplasmic compartment, respectively. Fatty acid synthase [FAS] expression(up to 2 to 3+) in the cytoplasm was evident in the vast majority of the tumor cells in each case.

Conclusions: Bcl-2 expression provides one explanation for the chemoresistance of uveal melanoma. Because CD44 and Hsp90 contribute to its expression, these present therapeutic opportunities. CD44 is associated with metastasis in melanoma. FAS represents a bridge between IGF-1R and c-Met, being induced at the genomic level by the former and also involved in the expression of c-Met tyrosine kinase. Inhibition of IGF-1R causes regression and attenuates invasion of uveal melanoma cells. Inhibition of FAS retards growth and induces apoptosis of melanoma cells and suppresses c-Met receptor kinase expression. The constellation of findings from our study raises the following therapeutic opportunities in uveal melanoma based on their reported actions: Valproic acid to downregulate CD44 and thereby, Bcl-2; 17-AAG to inhibit Hsp90 and also downregulate Bcl-2; Metformin to inhibit both IGF-1R signaling and FAS expression.

1643 Fine Needle Aspiration Biopsy of the Eye: A Single Institution's Experience.

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Background: Typically, a microscopic diagnosis of tumor is required prior to treatment. Treatment decisions of intraocular lesions, however, are often based on clinical examination due to the difficulty and potential complications in performing

ocular biopsies. Recently, fine needle aspiration (FNA) biopsy has been introduced as a diagnostic modality. The purpose of this study is to evaluate our experience with FNA biopsies of ocular lesions.

Design: The Department of Pathology database was queried and 26 cases of FNA biopsy of the eye were obtained from 2009-2010. The cytomorphologic features of aspirates were evaluated on cytospin or Thin Prep slides. Immunostains with melan A or flow cytometry were performed when indicated and additional material was available. The FNA diagnoses were classified into malignant (melanoma, lymphoma, metastatic tumor) or benign (reactive/inflammatory). The FNA diagnosis was compared with clinical and surgical follow ups that were available in 20 cases. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated.

Results: Of the 26 cases obtained, there were 12 males and 14 females with ages ranging from 20 to 94 years. Eight cases were diagnosed as malignant or suspicious for malignancy (6 melanoma, 1 lymphoma, and 1 metastatic tumor) and 18 cases diagnosed as benign or atypical (3 atypical and 15 negative). Of the 20 cases with follow up there were 10 melanoma cases, 1 lymphoma case, and 9 benign cases. The correlation between the FNA diagnosis and follow up was shown in table 1.

Correlation between FNA Diagnosis and Follow up

FNA Diagnosis	# of Cases	Benign Follow Up	Malignant Follow Up
Negative/Atypical	13	9	4
Malignant/Suspicious	7	0	7

Overall, the FNA diagnosis had a calculated sensitivity of 64%, a specificity of 100%, a PPV of 100%, and a NPV of 69%.

Conclusions: Our data demonstrates that FNA is an effective tool for the diagnosis of ocular tumors with a high specificity (100%) and good sensitivity (64%). Material obtained by FNA biopsies can be used in ancillary studies. A definitive FNA diagnosis can be used in guiding clinical management of intraocular lesions.

1644 DNA Mismatch Repair in Periocular Sebaceous Carcinoma.

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Background: Sebaceous carcinomas of the eyelid are rare but aggressive tumors. While sebaceous neoplasms can be associated with Muir-Torre syndrome, such systemic features are uncommon in patients with ocular adnexal sebaceous carcinoma. Patients with Muir-Torre syndrome most often demonstrate loss of one of several mismatch repair genes, leading to genomic instability in the form of microsatellite instability. However, the role of mismatch repair gene abnormalities in sporadic sebaceous carcinomas of the ocular adnexa remains poorly understood. The aim of our study was to assess mismatch repair in sporadic periocular tumors.

Design: Hematoxylin-and-eosin stained slides from eleven sebaceous carcinomas of the ocular adnexa were reviewed to verify the diagnosis as well as to note their extent. Ten of these were sporadic cases, and one was from a patient with known Muir-Torre syndrome. Immunohistochemistry was used to analyze the presence of four mismatch repair (MMR) proteins (MLH1, MSH2, MSH6, and PMS2) in these tumors. The tumors demonstrated either strong positive staining or total lack of staining for these MMR proteins, which was interpreted as either MMR intact or MMR deficient respectively. DNA was extracted from 7 of the larger tumors as well as adjacent normal control tissue, and subjected to microsatellite instability (MSI) analysis using 5 highly sensitive mononucleotides and 2 pentanucleotides.

Results: All ten of the presumed sporadic ocular adnexal sebaceous carcinomas maintained strong staining of all four of the mismatch repair genes tested. The Muir-Torre syndrome associated tumor showed loss of staining for the mismatch repair genes MSH2 and MSH6. MSI testing of seven tumors showed low microsatellite instability in the Muir-Torre associated tumor, and no microsatellite instability in the remaining cases.

Conclusions: Sporadic sebaceous carcinoma of the ocular adnexa are neither associated with a loss of mismatch repair genes, nor microsatellite instability. This distinguishes them from those associated with Muir-Torre Syndrome, and from sporadic tumors at other sites.

1645 Primary Mucinous Carcinoma of the Skin: Coming Back for More for 27 Years.

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Background: Primary mucinous carcinoma of the skin is a rare adnexal neoplasm, often with periocular involvement. It is slow growing and locally destructive, at times forming tumor satellites. It frequently recurs locally, however lymph node as well as distant metastases are rare. We discuss the pathologic and clinical features of a patient with mucinous carcinoma of the skin with an unusually long history of recurrences and successful local management.

Design: A 53 year old African American presented to us initially in 1993 with a 3-month history of a right lateral canthal mass. He noted that he had had two previous operations at the site in 1983 and 1989 for a "rare cancer without spread", which he was told 'may, or may not come back'. We reviewed all prior recurrences and later recurrences, in all a total of seven times, including the latest occuring this year, occurring over a period of over 27 years.

Results: In all instances, histologic examination revealed non-encapsulated, poorly circumscribed tumor with thin delicate fibrous trabeculae enclosing large pools of mucin. Over 90% of the mass was comprised of mucin, which was PAS positive. Nestled within these pools were benign-appearing epithelial islands forming branching- and duct-like structures. The epithelial cells were strongly positive for CK7 and ER, but negative for all other markers tested. No 'dirty' necrosis, foci of acute inflammation or mitotic figures were identified. To date the patient is clinically well, and no lymph node or distant metastases have been detected.

Conclusions: The long follow-up in the present case, not hitherto reported in the literature, highlights the biologic behavior of these uniquely indolent malignancies. We believe the clinical management of this case may offer insight into the optimal treatment of these lesions. Clinicopathologic and immunohistochemical differentiation from metastatic mucinous carcinoma from the breast, colon are pancreas is discussed

1646 Ocular Lymphoma in Patients with Systemic (Non CNS) Lymphoma: Unusual Presentations.

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Background: Intraocular lymphoma is rare. The primary form is considered a subset of primary CNS lymphoma and the secondary form is the result of ocular involvement in systemic lymphoma, which occurs in advanced stages of disease, often with concomitant CNS involvement. Vitreous-retinal infiltrates only are characteristic of the primary form, but are unusual without associated choroidal involvement in secondary ocular lymphoma. Furthermore, lymphoma transformation presenting in the eye is extremely rare, with only a few cases reported.

Design: Clinical history, cytological and histological preparations, immunostudies and outcome of 3 patients with systemic lymphoma and ocular involvement were reviewed.

Results: All patients were men, ages 54, 66 and 73 years, with complaints of blurred vision and floaters for several weeks before the diagnostic vitrectomy. Ophthalmic examination revealed clumps of vitreous cells, but no choroidal involvement. Patient 1 had no prior history of lymphoma; the diagnosis of ocular lymphoma prompted staging studies unveiling nodal disease a week later. Patient 2 carried the diagnosis of marginal zone lymphoma involving his bone marrow for 29 months, and patient 3, CLL for 7 months prior to the ocular symptoms. The diagnosis of secondary ocular lymphoma was based on the cytomorphological features and immunophenotype of the vitreous cells. Patients 1 and 3 had large B-cell lymphomas. Patient 2 showed clinical features consistent with transformation, but histological classification of the B-cell lymphoma was precluded by cellular degeneration. Patients 2 and 3 were found to have CNS involvement on MRI, 2 and 1 month following the diagnosis in the eye. All patients were treated with intraocular injections (rituximab, patient 1 and methotrexate, patients 2 and 3) in addition to systemic chemotherapy. All patients are alive; patient 1 without disease, and patients 2 and 3 with disease, after 22, 11 and 5 months follow-up after the diagnosis of ocular involvement.

Conclusions: We report 3 patients with systemic lymphoma and unusual ocular presentation. In one patient, the ocular symptoms and diagnosis preceded the systemic disease. In the other 2 patients with systemic low-grade lymphoma/leukemia, the ocular lymphoma was the presenting site of a higher grade process, consistent with transformation in the eye/CNS.

1647 Lymphomas of the Orbit.

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Background: Lymphoma, the commonest malignant tumor affecting the orbit, may arise primarily from the orbit, extend from contiguous structures, or develop as a metastasis of a systemic lymphoma. Primary lymphoma of the ocular adnexa represents 5-15% of all extranodal non-Hodgkin lymphomas, yet only 1% of all non-Hodgkin lymphomas. Current literature suggests marginal zone lymphoma to be the most commonly diagnosed non-Hodgkin lymphoma affecting the orbit. Herein we describe our experience with a large series of orbital lymphomas arising from or secondarily involving the orbit.

Design: Retrospective chart review of clinical and pathologic features of 32 biopsy proven orbital lymphomas evaluated in a single tertiary referral institution from 2001 to 2010. Diagnosis was based on histomorphology, immunohistochemistry, and cytogenetic analysis and classified according to the World Health Organization classification.

Results: Thirty-two patients ages 29-86 years (68.6, mean; 73 median) showed male to female ratio of 1.46:1. Presenting signs and symptoms included pain, proptosis, restrictive strabismus or diplopia, eyelid mass or swelling, "salmon patch" conjunctival lesion, ptosis, hypoglobus, optic neuropathy and vision loss. Anatomic locations of the lesions included the eyelid, canthus, orbit (intra and extraconal), lacrimal gland and conjunctiva. All 32 lymphomas were of the non-Hodgkin type and of B cell origin. Among all cases, 11 were mucosa associated lymphoid tissue (MALT) lymphomas, 9 were diffuse large B-cell lymphoma, 6 were mantle cell lymphoma, 3 were follicular lymphoma and, 3 were small lymphocytic lymphoma. Staging revealed the site of origin to be isolated orbital or orbital with extension to contiguous structures (11 cases), orbital with systemic disease found on initial staging (3 cases), orbital with subsequent dissemination (6 cases), secondary orbital lesions of known systemic disease (8 cases) and staging not known (4 cases).

Conclusions: Orbital lymphoma is a disease of the elderly and the vast majority are non-Hodgkin lymphomas of B-cell phenotype. While the diagnosis of these lesions can be challenging, morphology and ancillary studies can assist in determination of phenotype. MALT lymphoma is the most common type in our study which is consistent with several other large studies.

1648 Chronic Progressive External Ophthalmoplegia: A Report of 2 Cases.

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Background: Chronic progressive external ophthalmoplegia (CPEO) is a rare mitochondrial myopathy characterized by chronic ophthalmoparesis and exercise intolerance.

Design: Two cases of CPEO diagnosed from deltoid skeletal muscle biopsies were evaluated by enzyme histochemistry, electron microscopy, PCR and Southern blot.
Results: A 65-year-old male presented with a 10 year history of progressive diplopia and lower extremity weakness. A 55-year-old female reported bilateral ptosis and blurred vision. Several years later, she experienced hoarseness, difficulty swallowing and right arm weakness. Neurological examinations showed bilateral limited elevation and abduction of each eye. Deltoid muscle biopsies showed red ragged fibers and increased number of cytochrome oxidase (COX) negative fibers. Electron microscopy showed increased numbers of morphologically abnormal mitochondria with paracrystalline inclusions, dense bodies, and concentric forms. PCR and Southern blot techniques identified multiple deletions in mitochondrial DNA.
Conclusions: Chronic progressive external ophthalmoplegia is a rare disorder of mitochondrial DNA. Ragged red fibers, increased COX negative fibers, and ultrastructurally abnormal numbers of mitochondria with paracrystalline inclusions are diagnostic features on muscle biopsies. The high volume of mitochondria in extraocular muscles results in the typical ocular findings in CPEO. There is currently no definitive treatment for the muscle weakness associated with CPEO; although, clinical trials of exercise training and coenzyme Q supplementation are being conducted in some metabolic myopathies.

1649 Use of Special Stains and Immunohistochemistry To Diagnose Giant Cell Arteritis.

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Background: Giant cell arteritis (GCA) is usually diagnosed on temporal artery biopsy using slides stained with hematoxylin and eosin (H&E), yet pathologists at times implement special stains and immunohistochemistry to confirm the diagnosis when it is in question, and little is reported on the frequency with which that is done. We present here trends from our institution of the use of these additional tests in diagnosing giant cell arteritis.
Design: Retrospective chart review of temporal artery biopsies from January 2008 to September 2010.
Results: Over a 2 ½ year period, 95 temporal artery biopsy specimens were received, of which 65 (68.4%) were negative for either active or treated GCA, 21 (22.1%) showed evidence of healed/treated GCA, 7 (7.4%) were positive for active GCA, and 2 cases (2.1%) had insufficient tissue for diagnosis. The mean age of patients with active GCA was 81 years old. Half of the positive cases of active GCA (4/7) required no additional special stains or immunohistochemistry to confirm the diagnosis following hematoxylin and eosin (H&E) slide preparation. Movat's pentachrome stain was the most commonly used special stain (55 cases, 57.9%). Immunohistochemistry with CD68 to stain macrophages was used in 15 cases (15.8%), always in conjunction with Movat's pentachrome. CD3 to highlight T lymphocytes was used in 9 cases (9.5%) in which healed/treated arteritis was suspected based on histologic features such as fibrosis of the tunica media and breaks in the internal elastic lamina without significant giant cell reaction.
Conclusions: Giant cell arteritis can be diagnosed on temporal artery biopsy using H&E stain alone, yet almost half of the positive cases from our institution required additional tests to confirm the diagnosis. When not seen easily, Movat's pentachrome stain provides excellent visualization of the internal elastic lamina, including segmental absence of elastic lamina associated with muscular layer fibrosis as seen in GCA. Correlating those results with histiocytes (CD68) and T cells (CD3) present at the intima-media junction allows for further confidence in the diagnosis.

1650 Giant Cell Arteritis with Fatal Involvement of the Coronary Arteries.

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Background: Giant cell arteritis (GCA) most often presents as sudden painless vision loss due to arteritic anterior ischemic optic neuropathy (arteritic AION). Systemic involvement rarely occurs. We report here a case of concomitant arteritic AION and myocardial infarction in which the patient was found to have temporal and coronary arteritis, myocarditis, aortitis, and cerebral vasculature involvement.
Design: Case Report
Results: An 83 year-old man presented with a twelve day history of sudden, painless vision loss of the left eye and jaw claudication. He was presumptively diagnosed with GCA based on physical exam and radiologic findings as well as mildly elevated erythrocyte sedimentation rate (28 mm/hr, normal 0-10 mm/hr) and C-reactive protein (1.9 mg/dL, normal 0-1 mg/dL). The patient was admitted and started on high dose methylprednisolone. A left temporal artery biopsy confirmed the diagnosis of GCA. Despite dramatic improvement in the patient's vision in both eyes on steroids, five days after admission he experienced a fatal myocardial infarction (MI). At autopsy, the coronary arteries demonstrated stenosis of the left anterior descending ostia (>90%) and right circumferential artery, but only mild atherosclerosis. Histology revealed thickened vascular walls with transmural inflammation and scattered multinucleated giant cells at the intima-media border of the coronary vessels. MOVAT pentachrome stain was remarkable for interrupted elastic lamina of the coronaries. Similar findings were seen in a vessel surrounding the pituitary gland as well. The wall of the thoracic aorta and the myocardium were thickened and demonstrated areas of chronic inflammation marked by lymphocytes and histiocytes.
Conclusions: Giant cell arteritis is a systemic granulomatous vasculitis that, when diagnosed on temporal artery biopsy, must be treated aggressively to prevent further morbidity and mortality. Although reports have been published regarding mortality from MI due to giant cell arteritis, to our knowledge this is the first case of GCA in which the patient suffered a fatal MI so rapidly despite an excellent initial response in vision to corticosteroid therapy.

1651 Lacrimal Gland Choristoma of the Ciliary Body Presenting as Secondary Glaucoma.

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Background: Lacrimal gland choristoma is a rare entity that can be difficult to diagnose clinically, usually requiring enucleation for definitive diagnosis. Described here is a case of lacrimal gland choristoma of the ciliary body presenting as secondary glaucoma in a young child.
Design: Case report.
Results: A one year-old boy presented at 6 months of age with unilateral glaucoma of the left eye.
After showing no response to medical treatment, a glaucoma filtering device was surgically implanted into the left eye. He then developed a cataract that required lensectomy. A ciliary body mass was noted during the cataract surgery. It was decided to enucleate the eye with the problable diagnosis of medulloepithelioma. The cut surface of the eye showed the implanted reservoir on the superior surface, irregular synechia of the iris to the cornea, and a yellowish mass in the inferior area of the ciliary body associated to opaque whitish bands of vitreous. Histologic sections showed a ciliary body mass composed of benign-appearing lacrimal (serous) glandular tissue with iris tissue lined by cuboidal ductal-type epithelium. Immunohistochemistry analysis (pankeratin, p63, S100, CEA) revealed staining patterns of normal lacrimal gland, consistent with a lacrimal gland choristoma of the ciliary body. PAS and CEA stains were positive in the droplets of glandular secretions in the vitreous.
Conclusions: Although a rare lesion, lacrimal gland choristomas should be in the differential diagnosis of children with unilateral glaucoma and a ciliary body/iris mass. Histologically the choristoma may contain all the structures of the lacrimal gland including the ductal epithelium, basal myoepithelial cells and serous cells with production of secretions like in this case.

1652 KIT Mutations in Ocular Melanoma.

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Background: KIT and BRAF mutations are known to occur in cutaneous and mucosal melanomas. The anatomic location of the melanoma appears to correlate with the mutation present. BRAF mutations are most closely associated with melanomas arising in non-sun damaged skin while those arising at acral sites and on sun damaged skin are more often associated with KIT mutations. Melanomas with mutations in the KIT or BRAF genes may benefit from treatment with specific inhibitors. Little is known about the mutational characteristics of ocular melanomas.
Design: Forty-nine ocular melanomas (38 choroidal, 4 iris, 4 ciliary body and 3 conjunctival) were selected from the files of the Department of Ophthalmology and Pathology. High resolution melting curve analysis was performed to detect mutations in exons 9, 11, 13, and 17 of KIT and exons 12 and 18 of the PDGFRA gene. Results of the mutational analysis were correlated with the anatomical site of the ocular melanoma.
Results: Eight ocular melanomas contained mutations in either the KIT or the PFGFRA gene. Six of 38 (16%) choroidal melanomas were associated with mutations (KIT exon 11 = 1; KIT exon 13 = 1; KIT exon 17 = 2; PDGFRA exon 18 = 2). Two of 4 (50%) iris melanomas had KIT mutations both occurring in exon 11. Histologic type of melanoma did not correlate with the presence or site of the mutation.

KIT and PDGFRA Mutations in Ocular Melanoma

Tumor Site	Percentage with Mutations	Exons Involved (Number of Cases)
Choroidal	16%	KIT exon 11 (1) KIT exon 13 (1) KIT exon 17 (2) PDGFRA exon 18 (2)
Iris	50%	KIT exon 11 (2)
Ciliary Body	0%	N/A
Conjunctiva	0%	N/A

Conclusions: KIT and PDGFRA mutations occur in ocular melanomas. Fifty percent of melanomas of the iris in our series were associated with a mutation in KIT exon 11. A lower percentage of choroidal melanomas demonstrated KIT or PDGFRA gene mutations, which occurred at a frequency similar to that seen in some mucosal or cutaneous sites. Imatinib therapy may represent a viable treatment option in some patients with ocular melanoma.

1653 Cytologic Examination of Vitreous Fluids: A Retrospective Review of Our 15 Years Experience.

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Background: Cytologic analysis of vitreous fluid is requested in a variety of ocular disorders. This is rare in a busy cytology practice and interpretation may be challenging due to lack of exposure of pathologists and residents during their training to these samples. The purpose of this study is to review our 15 years experience of cytologic evaluation of vitreous fluids.
Design: Our department electronic records were searched for vitreous fluids and review of pathology, clinical reports and cytologic slides was performed. Indications, mode of preparation, cytologic patterns, ancillary studies and diagnoses were assessed to appreciate the usefulness of this technique and our ability to identify pathology specific to these fluids.
Results: 15 years review of vitreous fluids samples revealed 132 fluids from 116 patients, 65 females, 51 males, age 3-83 year-old. Seventy-nine samples (60%) were examined

due to clinical signs of infection/inflammation, 18 samples (14%) were submitted to rule out intraocular lymphoma, 9 fluids for reasons like intravitreal foreign bodies or vitreous opacities, 9 samples for intraocular hemorrhage (7%), 6 fluids to rule out amyloidosis (4%), 4 to rule out melanoma (3%), and in 7 samples (5%) no clinical history was provided. The amount of fluid received varied from 0.5 – 150 cc and cytospins and Thin Preps were the methods of preparation used. Fluids displayed few patterns: paucicellular (37%), mixed chronic inflammation (36%), acute inflammation (17%), malignant (4%) and hemorrhage (4.5%). GMS stain performed in 56% of fluids where infection was suspected showed presence of fungal hyphae in 4 cases. No viral inclusions were seen (in 2 cases PCR for herpes simplex and CMV viruses was negative) and one fluid showed present Gram positive cocci on Gram stain performed. Flow cytometry studies were attempted in 72% of cases where intraocular lymphoma was in the differential diagnosis; 5 of them had insufficient cellularity or were technically suboptimal, 7 were negative for a B-cell proliferation and 1 was positive. In 2 cases immunohistochemical stains were performed on smears or concomitant biopsy. Two cases showed high grade lymphoma (1.5%), one large cell B-cell type, one high grade T-cell type, natural killer phenotype. Three cases (2%) were positive for malignant melanoma and abundant amyloid deposition was found in 1 case by Congo Red stain.
Conclusions: Cytologic analysis of vitreous fluid is very useful in evaluation of ocular pathology. The addition of special stains and modern techniques like flow cytometry or PCR, further expands the diagnostic possibilities.

Pathobiology

1654 Targeted Disruption of the CSF-1 Gene Leads to Osteopetrosis and Osteoblast Defects .

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Background: CSF-1, a key determinant of osteoclast-mediated bone remodeling, is highly expressed by osteoblasts and osteocytes. CSF-1 deficiency in spontaneous mutant op/op mice decreases macrophages/osteoclasts and leads to osteopetrosis and a pleiotropic phenotype. The effect of CSF-1 knockout (KO) in all tissues or conditional KO of CSF-1 using a Cre/loxP system has not been explored. Objective: To determine the effect of inactivation of CSF-1 and develop a strategy for examining the biologic effect of CSF-1 KO in bone using Cre-lox technology.
Design: A targeting vector for generating a conditional KO allele for CSF-1 (deleting exons 4,5,6) was used to generate heterozygous mice harboring the floxed construct without a neo cassette (fx allele). CSF-1fx/CSF-1fx mice were bred with Meox2Cre mice to produce mice homozygous for the KO allele(hCSF-1KO). (Meox2 promoter drives expression of Cre throughout the epiblast). At 3 weeks, hCSF-1KO and WT littermates were analyzed for CSF-1 protein and F4/80+ macrophages. Hind limbs were examined by x-ray, microCT, histology and stained with TRAP and CD31 to identify osteoclasts and vessels, respectively.
Results: Homozygous (h)CSF-1KO showed absence of CSF-1 in all tissues, reduced macrophages in most organs, decreased circulating monocytes and osteopetrosis with failure of tooth eruption similar to op/op mice. Radiographs of hCSF-1KO showed marked skeletal sclerosis and, by microCT, %BV/TV and trabecular number were increased and cortical bone thickness was decreased; bone mineral density was increased by DEXA scan. Histologically, hCSF-1KO bones showed an expanded growth plate, increased bone trabeculae with prominent cartilage cores replacing the marrow cavity, narrow vascular sinusoids and poorly formed cortical bone. Numerous TRAP+ osteoclasts were identified in WT, whereas rare mononucleated osteoclast-like cells were detected in CSF-1KO bone. In CSF-1KO, osteoblasts showed loss of polarity; matrix formation and collagen fibrils were disorganized and abnormal clusters of osteocytes entrapped in matrix were identified.
Conclusions: Results provide the first evidence that global CSF-1KO using a Meox2Cre-based system leads to osteopetrosis and alters osteoblast function. Conditional KO of CSF-1 in bone cells is feasible and will be crucial for elucidating the mechanisms by which CSF-1 exerts pleiotropic effects and regulates bone turnover and repair.

1655 Immunophenotypic Characterization of Epithelial-Stromal Interface Cells.

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Background: In visceral organs, the epithelium and the stroma are separated by a layer of stromal cells and the basement membrane. These epithelial-stromal interface (ESI) cells are known to play significant regulatory roles in the organogenesis, differentiation and homeostasis of the overlying epithelium. In the gastrointestinal tract as well as in other viscera, these cells are also postulated to play critical roles in inflammation, restitution, and regeneration of damaged epithelium and also involved in neoplastic transformation and proliferation of the epithelial cells in the process of carcinogenesis and tumorigenesis respectively. However, the histogenesis and the biology of these cells are yet to be elucidated. Hence this study, to characterize the immunophenotypic features of these cells in skin adnexae and visceral organs.
Design: Benign samples were obtained from resection specimens of the following organs: Skin (n=10), breast (n=10), parotid gland (n=10), pancreas (n=10), prostate (n=10), small bowel (n=10) and colon (n=15). The tissue samples were fixed in formalin solution and paraffin-embedded for routine H&E. Representative sections were immunostained for the followings: 5 cytokeratins that are reportedly expressed in myoepithelial cells (CK5, CK7, CK8, CK14, CK18, CK19 and K903), 6 non-keratin related structure-specific microfilaments and intermediate filaments (alpha smooth muscle [SMA], calponin, desmin, H-caldesmon, smooth muscle myosin heavy chain [SMMHC], and vimentin) and 7 nonstructural proteins (CD10, CD34, CD117, GFAP, maspin, p63, and S100). Immunohistochemistry was done using avidin-biotin detection method with antigen retrieval.
Results: ESIs in both small and large intestinal mucosa expressed smooth muscle–related microfilaments and intermediate filaments ([SMA, calponin, H-caldesmon, SMMHC) and vimentin; but stained negative with desmin, all the cytokeratins and the nonstructural proteins.
Conclusions: ESIs in the small and large bowel have similar immunophenotypic features; but in their lack of expression of the keratins and the non structural proteins studied, are distinctly different from the corresponding (myoepithelial) cells in other glandular organs such as breast, prostate and skin adnexal structures where they have been proposed to be the progenitor cells for the epithelium. Our results also show that the immunophenotypic features and the biology of the interface subepithelial stromal cells appear to vary from organ to organ. Therefore, reports of observations of such cells in one organ may not necessarily be true for the counterpart cells in another organ.

1656 Anatomic Study of the Renal Sympathetic Nervous System.

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Background: Hypertension affects millions of patients worldwide causing an enormous disease burden. Despite extensive pharmacologic therapy, the contribution of hypertension to death, stroke, myocardial infarction, and congestive heart failure remains significant. Despite these many pharmacologic therapies, blood pressure control remains suboptimal. This has prompted novel device therapies for blood pressure control. A renal nerve ablation catheter has been developed that can destroy the innervation of the kidneys using radiofrequency energy, which has been associated with significant decreases in blood pressure. The anatomic substrate for this device has been poorly described even though the therapy holds great promise. We report the first detailed anatomic study of the renovascular wall and nervous system in renal arteries studied at autopsy.
Design: Left and right renal arteries (n=6) were obtained at autopsy from patients who died at our institution from natural causes. Unusual anatomic variants and arteries that demonstrated significant atherosclerosis or other structural compromise due to underlying pathology were excluded. Representative proximal, middle, and distal cross sections were obtained from each artery. The distance of peripheral nerves within the adventitia and surrounding soft tissue were measured relative to the lumen using an Olympus ocular micrometer.
Results: The distance from the lumen to closest nerve assessed was 0.4mm and the distance from the lumen to the farthest nerve assessed was 3.1mm. The average percentage of total nerves existing at increasing intervals from the artery lumen was 43.3±10.4% from 0.4-1.0mm, 28.5±8.3% from 1.0-1.5mm, 14.3±3.7% from 1.5-2.0mm, 7.99±2.3% from 2.0-2.5mm, and 5.80±3.3% at >2.5mm.
Conclusions: Our data shows that individual nerve fibers are more prevalent at closer intervals to the renal artery lumen, which could be due to increasing segmentation of peripheral nerves as they travel into and through the adventitia. If radiofrequency energy is sufficient to ablate nerves up to 1.5mm from the lumen, approximately 70% of nerves within 3mm will likely be affected. Likewise, if radiofrequency energy is sufficient to ablate nerves up to 2.5mm from the lumen, approximately 95% of nerves will be affected. This could suggest that relatively conservative radiofrequency energies could be used to still ablate a significant proportion of nerves.

1657 Development of a Scoring System for PTEN Immunohistochemistry in Breast Cancer.

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Background: Loss of expression of PTEN, which inhibits the PI3K pathway, occurs in many types of cancer, including breast cancer. Patients with PTEN-deficient cancers may potentially benefit from PI3K pathway inhibitors, which are rapidly being developed and tested clinically. In breast cancer, loss of PTEN expression is associated with resistance to anti-hormonal therapy and Herceptin. Therefore, accurate identification of the subsets of breast cancer patients with PTEN loss is clinically important. Currently, there is no standardized protocol for pathological reporting of PTEN immunohistochemical results in breast cancer. Therefore, we wanted to design a practical scoring system with reliable clinical implications on patient outcome.
Design: Forty formalin fixed paraffin embedded breast carcinomas were immunohistochemically stained for PTEN using the Dako 6H2.1 antibody. Immunohistochemistry for anti-phosphorylated (serine 235/236) S6 ribosomal protein (pS6), a downstream member of the PI3K pathway, was scored as % positive. Cochran-Armitage trend and Fischer's exact tests were used for statistical analyses. The breast cancer results were compared to those from our previous study of 154 endometrial carcinomas.
Results: A 3-tiered scoring system (negative, reduced, positive) was devised. In all cases, the stroma stained strongly positive for PTEN. Positive was defined as tumor PTEN expression comparable to stroma PTEN expression. Negative was defined as a tumor with complete lack of PTEN. Reduced was defined as a tumor with less PTEN expression compared to internal control stroma. Significantly elevated pS6 expression in the negative tumors helped to validate this scoring system. Positive PTEN was present in 27.5% of cases; this correlated with ER positivity (p=0.009) and the absence of the triple negative subtype (p=0.04). The expression pattern of PTEN in the in situ component tended to reflect that of the invasive component. Interestingly, the reduced PTEN category is not identified in endometrial carcinoma.
Conclusions: Positive PTEN expression in breast cancer is associated with ER expression and the lack of the triple negative subtype, factors indicative of a better clinical outcome. The accuracy of our 3-tiered scoring system relies, in part, on careful comparison of tumor PTEN expression to stromal PTEN expression. The pattern of