**Conclusions:** Racial and ethnic minority population with HIV infection continue to have a high proportion of untreated cases, with high prevalence of both primary parenchymal HIV associated neruopathology as well as secondary opportunistic infections. However we did not find classical HIV encephalitis with multinucleate giant cells or Alzheimer type pneurodegenerative changes in our study.

# Ophthalmic

### 1749 P16 and P53 Expression in Periocular Sebaceous Cell Carcinoma

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**Background:** Sebaceous carcinoma is a malignant neoplasm which often presents in the periocular region. In the United States, this lesion accounts for 1.3 to 4.7 % of malignant eyelid tumors. Histological diagnosis is often difficult, particularly in small biopsies in which tumor is often present only as scattered cells in the squamous or conjunctival epithelium. Determining the extent of such pagetoid spread can also be difficult in mapping biopsies or at margins of larger resections. The goal of this study was to evaluate p53 and p16 as potential immunohistochemical markers of sebaceous carcinoma, particularly intraepithelial tumor, in the ocular adnexa.

**Design:** Sebaceous carcinoma specimens were retrieved from the pathology archives of our institution, including 20 primary and 13 recurrent tumors. All tissues were fixed in 10% buffered formalin, routinely processed and paraffin embedded. Immunohistochemistry was performed using 5-µm sections and a Leica autostainer(Leica)for P16(Cintec)and a Ventana XT autostainer(Ventana Medical Systems)for P53(Ventana).

**Results:** We found 48% of the periocular sebaceous carcinoma cases to have intense nuclear p53 immunostaining. Additionally, we found 70% of sebaceous carcinoma of the periocular region to have intense p16 nuclear reactivity. 4 cases showed only strong p53 staining, while 9 cases showed only strong p16 staining. For both markers, immunoreactivity was relatively diffuse both within and between blocks. It was also roughly equivalent in both large subepithelial tumor nodules, and in the intraepithelial portion of the lesions. Together, our series revealed intense immunoreactivity to either p53 or p16 in 95% of cases, and weak or negative immunoreactivity in 5% of cases.

**Conclusions:** Major pathways implicated in the molecular mechanisms of skin cancer include the p53 and p16 pathways. While the expression of p53 has previously been examined as a potential marker of sebaceous carcinoma, p16 has not been well studied. Our findings confirm expression of p53 in a significant proportion(48%) of periocular sebaceous carcinoma. We found that an even greater proportion of tumors(70%) had intense p16 nuclear reactivity, suggesting that it could represent an additional marker with which to track tumor spread. Because some tumors expressed only p53 or p16, combined staining may represent the most effective way to highlight intraepithelial tumor, with 95% of cases showing immunoreactivity for one of the two markers.

### 1750 Stratifin as a Prognostic Marker in Ocular Surface Squamous Neoplasia

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**Background:** Ocular surface squamous neoplasia (OSSN) is the most common tumour of ocular surface with an incidence of 0.02 to 3.5 per 100,000. It encompasses spectrum of lesions ranging from dysplasia to squamous cell carcinoma (SCC). Stratifin (14-3-3σ)/HEM (human epithelial marker) which is an inhibitor of cell cycle progression, is a target of epigenetic deregulation in many carcinomas. However, its role in OSSN has not been investigated. In the present study, the association of stratifin expression with its promoter methylation status and their correlation with clinicopathological features in ocular surface squamous neoplasia patients was evaluated.

**Design:** Sixty four cases of histopathologically confirmed OSSN (44 SCC and 20 dysplasia) were included in this study. Each tumour was staged according to the AJCC TNM criteria. Immunohistochemistry and methylation specific PCR were used to evaluate expression of stratifin protein and its methylation status. Prognostic significance was assessed using Kaplan–Meier survival and Cox regression analysis.

**Results:** Loss of stratifin immunoexpression was observed in 75% cases (48/64) and promoter hypermethylation in 62.5% (40/64) cases of OSSN. Stratifin promoter hypermethylation was significantly associated with loss of its immunoexpression (38/40) (P=<0.0001). On correlation with clinical parameters, both loss of Stratifin immunoexpression and methylation were significantly associated with recurrence, tumor size ≥2cm (higher T category), orbital or intraocular invasion and reduced disease free survival (P≤0.05). Cox analysis showed stratifin to be an independent prognostic factor for OSSN (p =0.03).

**Conclusions:** Our results indicate that loss of Stratifin expression occours in OSSN and is caused by aberrant DNA methylation. Further, this loss of stratifin immunoexpression could prove to be a useful poor prognostic marker in OSSN patients after further validation.

### 1751 Ocular Infections, Diversity of Microorganisms and Clinical Associations

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**Background:** Infectious eye disease remains a significant cause of secondary blindness in the United States. Infectious keratitis alone is associated with a 35% risk of secondary blindness. Progression to endophthalmitis requiring enucleation is uncommon in the absence of comorbid conditions. This survey of patients with sight-threatening ophthalmic infections identifies the causative organisms and outcomes.

**Design:** Ophthalmic microbiology results were reviewed on patients with positive cultures from corneal and intraocular specimens over the period 2007-2012; 347 organisms were identified from 167 patients.

**Results:** The most commonly identified organisms in the studied population are listed in Table 1. The most common organisms were distributed over a range. In contact lens wearers, Pseudomonas aeruginosa (24%) was the most common isolated organism. In addition rare fungi, i.e. Aspergillus spp. (6 cases), Candida spp. (3 cases), and the protozoan, Acanthamoeba, were isolated (4 cases). 24 enucleations and eviscerations were identified, three of which had positive cultures for coagulase negative Staphylococcus, Corynebacterium and Pseudomonas aeruginosa. Predisposing factors included a history of trauma and corneal ulcers (45%), previous ophthalmic surgery (26%) and systemic diseases such as diabetes mellitus and sarcoidosis (20%).

Table 1. Positive ocular cultures

| Organism | Prevalence |
|---|---|
| Coagulase negative Staphylococcus | 34% |
| Methicillin sensitive Staphylococcus aureus | 7% |
| Corynebacterium spp. | 6% |
| Streptococcus, alpha-hemolytic | 5.7% |
| Pseudomonas aeruginosa | 5.5% |
| Haemophilus influenza | 5.5% |
| Methicillin resistant Staphylococcus aureus | 4.8% |

**Conclusions:** The significance of CNS identification was not clear. CNS was regarded as a contaminant if recovered as a part of a group of organisms. CNS, MSSA, Corynebacterium spp. and alpha-hemolytic Streptococcus were considered commensal organisms and were clinically treated only if they were the sole organism recovered from the culture of a corneal ulcer. The mechanism of acquisition of MRSA in this location is not clear but MRSA organisms were most commonly resistant to Erythromycin and Clindamycin. A history of contact lens usage was confirmed in majority of the Candida (3/3) and Acanthamoeba infections (3/4). Progression to endophthalmitis was more commonly seen in patients with a history of trauma, ophthalmic surgery and systemic diseases.

### 1752 Glioblastoma of the Optic Nerve

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**Background:** Gliomas of the optic nerve are uncommon neoplasms, comprising approximately 3% of all gliomas, and 2% of all orbital tumors. Most optic nerve gliomas are pilocytic astrocytoma (WHO Grade I). Glioblastomas (GBM) (WHO grade IV) of the optic nerve and chiasm are rare, aggressive tumors that typically present with visual symptoms.

**Design:** We reviewed two cases of GBM arising in the optic nerve. Both patients were adult females who presented with visual complaints.

**Results:** Patient A was a 67-year-old female who presented with headaches, total vision loss in her left eye, and partial vision loss in her right eye. She had no previous ophthalmologic history, and no significant medical history. Magnetic resonance images (MRI) showed enlargement of the optic nerves and chiasm. Biopsy of optic nerve and chiasm demonstrated GBM. Follow-up MRI showed tumor extension to the visual cortex in the occipital pole. She expired 5 months following the biopsy. Patient B was a 61-year-old female who presented with blurred vision in her right eye, without any associated pain, nausea, vomiting, or other symptomatology. She had no previous ophthalmologic history, and had medical history only of hypertension and dyslipidemia. MRI showed evidence of an enhancing lesion of the right optic nerve and optic pathway (Fig. 1). A biopsy of the right optic nerve was performed, demonstrating GBM (Fig. 2). Microscopic examination of biopsies from both patients showed a hypercellular population of malignant astrocytes, characterized by cytological pleomorphism, mitoses, microvascular changes, and pseudopalisading necrosis.

Figure 1

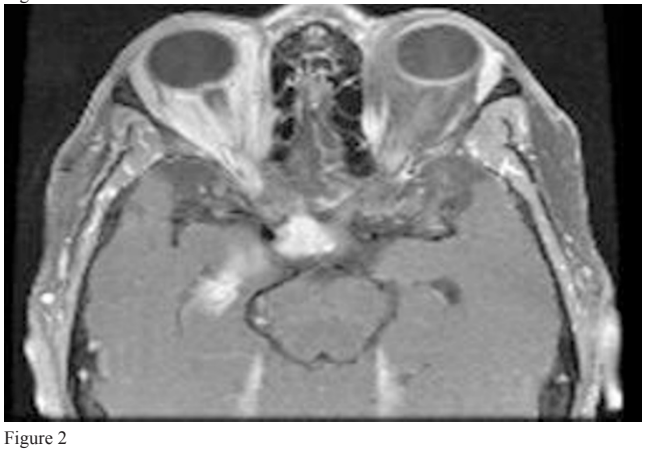
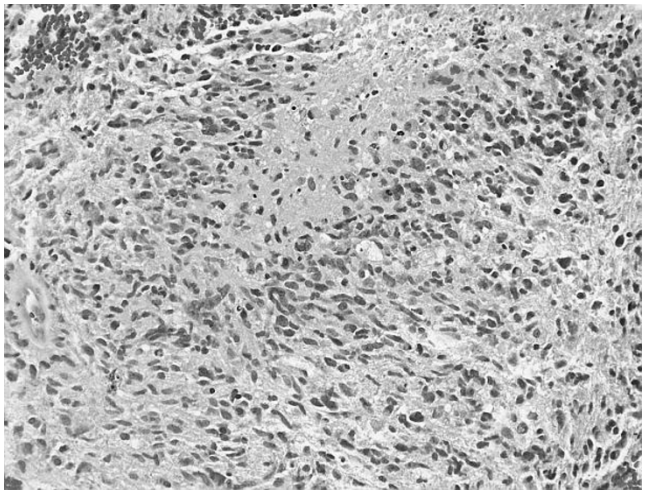


Figure 2



**Conclusions:** Optic nerve GBMs are rare tumors. We present two cases with involvement of the optic nerves and chiasm, both of which presented with visual symptoms. GBM should be considered in the differential diagnosis of optic nerve lesions in adults with visual complaints.

### 1753 Histopathologic Features That May Be Indicators of Prognosis in Ocular Sebaceous Carcinoma

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**Background:** Ocular sebaceous carcinomas are rare, representing approximately 5% of all malignant eyelid tumors. They are locally aggressive with regional and distant metastasis reported in 25% of cases. Our study sought to identify the histologic features associated with worse prognosis (local recurrence, regional lymph node and distant metastasis).

**Design:** Forty biopsy cases of sebaceous ocular carcinomas were obtained from the surgical files of a large tertiary care center in the United States and a European university hospital center over an 11-year period (1999-2010). Slides were obtained and histologic parameters including size, depth of invasion, level of invasion, mitotic count, ulceration, perineural and lymphovascular invasion were assessed. Clinical data was also reviewed when available.

**Results:** Patients showed a female predominance (F:M=3:1) with a mean age of 66.8 yrs (range:37-89). Sites of involvement included the eyelid (40/40, 100%) and additionally the conjunctiva (20/40, 50%). Mean measurement of tumor size was 7.8 mm (range:0.8-40). Tumor size ($p<0.02$) and tumor depth of invasion ($p<0.002$) significantly correlated with sentinel lymph node (SLN) positivity. Lymphovascular invasion was associated with distant ($p<0.03$) and SLN metastasis ($p<0.004$). Tumor necrosis was strongly associated with disease status. Sebaceous differentiation and mitotic activity were not significant histologic markers of prognosis. Pagetoid upward migration, lymphovascular and perineural invasion were not significantly associated with local recurrence.

**Conclusions:** We present one of the largest case series of ocular sebaceous cell carcinomas with an assessment of histologic parameters for their prognostic significance. Tumor size, depth of invasion, presence of lymphovascular invasion and tumor necrosis all correlated with regional lymph node and distant metastasis. Identification of these histologic features in small biopsy specimens may indicate a higher probability for metastasis and warrant closer clinical follow-up.

### 1754 Molecular Characterization of Ocular Adenexal MALT Lymphoma

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**Background:** Extranodal marginal zone B-cell lymphoma of mucosa associated lymphoid tissue type (MALT lymphoma) is the most common type of malignant lymphoma of the ocular adenexa. Reports on the association of *Chlamydia psittaci (C.psittaci*) with ocular adenexal MALT lymphomas (OAML) vary geographically. Chromosomal aberrations, t(14:18) translocations and IgH clonality are often seen in OAML. We have investigated genomic alterations and immunoglobulin CDR3 sequences in a small subset of primary OAML.

**Design:** Nine patients with ten cases of biopsy proven ocular adenexal MALT lymphoma from over the past 10 years were selected for the study. Formalin fixed paraffin embedded tissue was used for molecular analyses. The presence of *C.psittaci* was determined by real time PCR with primers and FRET probes targeting the *omp 1* gene. t(14:18) analysis was done by interphase FISH and IgH clonality studies were performed by capillary electrophoresis (invivoscribe). Immunoglobulin CDR3 sequences were amplified using a degenerate consensus *FR3* forward primer and a reverse *JH* primer.

**Results:** All nine tissue DNA specimens were negative for *C.psittaci* and *C trachomatis* by realtime PCR. Amplification of the positive control was validated by sequencing. Cytogenetic analyses of 7 cases, showed normal karyotype in 3, deletions in 2, and multiple aberrations including trisomy 3 in 2 cases. Monoclonal populations by flow cytometry, confirmed by DNA analysis were seen in 7/9 cases. Preliminary investigations on CRD3 region did not show any sequence similarity.

**Conclusions:** Primary ocular adenexal MALT lymphoma shows significant molecular heterogeneity. *C.psittaci* was not present in the specimens investigated at our institution. CDR3 usage may be useful in determining antigenic etiology. Larger studies are necessary for determination the role of bacterial infection in the pathogenesis of the disease.

### 1755 Frequency of Chromosome 3 LOH and Partial Loss in Uveal Melanoma by Genomic Microarray Analysis of Frozen Tissue

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**Background:** Molecular cytogenetic alterations, especially monosomy of chromosome 3, are strongly correlated with metastases and death in uveal melanoma (UVM). For prognostic stratification, monosomy 3 is frequently assessed by fluorescence *in-situ* hybridization (FISH). A subset of UVM exhibit only regional chromosome 3 loss or loss of heterozygosity (LOH) resulting from uniparental disomy, that are undetectable by chromosome enumeration probes. Alternatively, CGH/SNP microarray analysis can generate high resolution multi-chromosome data and identify LOH. Here we assessed the frequency of chromosome 3 LOH and partial loss by combined genomic and SNP array analysis of DNA extracted from frozen tissue (FZT) procured from a consecutive series of enucleations performed for UVM.

**Design:** Sufficient FZT DNA for genomic microarray analysis was obtained from enucleations performed for 28/119 patients on clinical trial NCT00952939 with CEP3-FISH results obtained as described (Invest Opthal Vis Sci 2012 Apr 17 Epub PMID 22511634). DNA was fluorescently labeled (Roche) and microarray analysis was performed using a custom designed Roche® NimbleGen® array (OncoChip®v2) with oligonucleotide coverage biased to >2400 cancer features and backbone SNP coverage affording combined oligo and SNP analysis (CGH/SNP).

**Results:** CGH/SNP results were technically successful in all cases. 15/28 aCGH samples showed chromosome 3 monosomy (14/15 concordant with FISH). 13/28 aCGH samples showed chromosome 3 eusomy (7/13 concordant with FISH). Of the 13 cases with chromosome 3 eusomy by aCGH, 1 case (3.5%) demonstrated whole chromosome 3 LOH by SNP analysis, and 1 case (3.5%) showed partial 3q loss. In addition, large terminal 6p gains were seen in all cases with chromosome 3 eusomy. Amplifications involving *TERT* and *NEDD9* genes, deletions involving *CDKN2A/B* and *LUM* genes, and other whole chromosome LOH were also identified.

**Conclusions:** Chromosome 3 LOH and partial loss are rare events that can be detected by CGH/SNP genotyping of DNA from FZT of UVM. Genomic microarray analysis may be warranted as second step testing in UVM cases with apparent chromosome 3 eusomy by FISH. The genome-wide coverage of CHG/SNP identifies complex genomic signatures and provides additional data with potential relevance to UVM biology, diagnosis and prognosis.

### 1756 Uveal Melanoma Metastases: Clinico-Pathologic and Mutational Analysis of 21 Cases

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**Background:** Uveal melanoma is the commonest malignant tumor of the adult eye. It is often diagnosed at an advanced stage, and is associated with a poor prognosis (10-year survival ~40%). Activating mutations of *GNAQ* or *GNA11* occur in 80-90% of uveal melanomas. Metastases of uveal melanoma are generally hematogenous, and most commonly involve the liver. We investigated the clinico-pathologic and genetic features of metastases from uveal melanoma, with emphasis on their distinction from other melanocytic tumors in the differential diagnosis.

**Design:** From the clinical and pathology records of two institutions, 21 patients with metastases from primary uveal melanoma were identified. Pathologic features were evaluated by slide review in 19 cases, and all tumors were subjected to direct sequencing for exons 4 and 5 of *GNAQ* and *GNA11*.

**Results:** In 7 female and 14 male patients, median age at diagnosis of primary uveal melanoma was 59 years (range 14-73 years). The sites of metastasis were: liver (7), skin/subcutis (7), lung (1), brain (1), mediastinum (1), spleen (1), lymph node (1), and unknown (2). The tumors showed sheet-like, nested or lobular growth patterns, and were composed of exclusively epithelioid cells (14), exclusively spindle cells (2) or a mixture of epithelioid and spindle cells (3). Tumor cells contained moderate amounts of amphophilic cytoplasm in the majority of cases, and exhibited moderate to marked nuclear pleomorphism. Melanin pigment was present in 15 cases (moderate to marked in 7), and melanophages were seen in 9 tumors. Tumor necrosis was present in 5 cases. *GNA11* mutations were detected in 11 (52%) cases (exon 4 in 2 cases and exon 5 in 9 cases), and *GNAQ* exon 5 mutations were seen in 4 (19%) cases.

**Conclusions:** Metastases from uveal melanomas show predilection for liver and skin, predominance of epithelioid cells, and conspicuous melanin pigment – features that should prompt consideration of the diagnosis and clinico-pathologic correlation when evaluating melanocytic tumors. The common occurrence of *GNAQ*/*GNA11* mutations is particularly helpful in distinguishing them from metastases of cutaneous melanomas, in the vast majority of which these mutations are absent.

### 1757 Identification of Ocular Sebaceous Neoplasia with Evaluation for Mismatch Repair Proteins

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**Background:** Recognizing sebaceous carcinoma is important because of its risk for metastasis and tumor death. Histopathology alone is often difficult because fresh tissue for oil red-O stain is not always available. Several immunohistochemical stains (IHC) have been evaluated but often the diagnosis is elusive. Furthermore, the diagnosis of a sebaceous adenoma or carcinoma raises the possibility of Lynch syndrome, a cancer predisposition syndrome. Mismatch repair protein(MMR) abnormalities are a feature of Lynch syndrome, and they can be detected with IHC for the MLH1, MSH2, PMS2, and MSH6 proteins.

**Design:** 14 sebaceous carcinomas and 3 adenomas from the eyelid (17 specimens) from 14 patients were evaluated for oil red-O when possible as well as IHC for AR, EMA, BER-EP4, CAM5.2 for diagnosis. MMR for MLH1, MSH2, PMS2, and MSH6 by IHC were evaluated as a possible screening panel for Lynch syndrome. Two patients already had other tissue tested by PCR for microsatellite instability (MSI) for Lynch syndrome.

**Results:** Oil red-O was done on 6 of 17 specimens and positive in 5 of the 6 (83%). AR was positive in 2 of 3 adenomas (67%) and 5 of 14 carcinomas (36%). EMA was positive in 2 of 3 adenomas (67%) and 11 of 14 carcinomas (79%). BER-EP4 was negative in all 3 adenomas and positive in 7 of 14 carcinomas (50%). CAM5.2 was positive in 1 of 3 adenomas (33%) and 8 of 14 carcinomas (57%). All 17 specimens(100%) showed positive nuclear staining for MLH1 and PMS2, indicative of normal protein expression. In 14 of 17 specimens from 12 patients, MSH2 and MSH6 were also normal. 3 specimens from 2 patients that had rare positive cells for MSH2 and MSH6. Both patients had previous colonic tumors tested for MSI and were found to be MSI-H, indicative of possible Lynch syndrome.

**Conclusions:** Diagnosing sebaceous carcinoma is important prognostically but sometimes challenging with routine histopathology. In our experience androgen receptor (AR) was found to be confirmatory in only 36% of cases and not dependent on the size of the tumor available. The other IHC stains were of marginal benefit and not specific. While none of the cases showed complete loss of expression of a MMR protein, there were 2 patients in with only rare positive cells who had known MSI-H tumors in the colon, suggestive of Lynch syndrome. Additional studies of these eyelid tumors may elucidate the possible role of using them for screening for Lynch syndrome.

# Pancreas

### 1758 International Consensus Study on the Terminology and Diagnosis of Tumoral Intraepithelial Neoplasms ("Adenomas" and "Intracystic Papillary Neoplasms" of WHO-2010) of the Gallbladder

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**Background:** The 7 types of tumoral intraepithelial neoplasms (TINs) of the gallbladder (GB) originally recognized by Dr.Albores-Saavedra in the AFIP fascicle, were recently regrouped in the WHO-2010 under 2 major categories of adenoma vs. intracystic papillary neoplasm.

**Design:** 28 selected examples of TINs were evaluated on a digital platform by 18 authors from 9 countries.

**Results:** There was overwhelming consensus that these were neoplastic lesions (except 1 case), and that they were distinct from conventional (non-tumoral) dysplasia. There was fair agreement on the degree of dysplasia and the presence of invasive carcinoma (κ: 0.36 and 0.35, respectively). However, the terminology was highly problematic. The number of different diagnostic names used per case ranged 4-13 (median 8), and in each case at least half of the authors did not use the WHO terminology, some citing the potential misunderstanding of the term intracystic giving the impression of a tumor arising within a cyst. Furthermore, when forced to use the WHO, there was no agreement on specific subcategories (κ: 0.01-0.19), and even more importantly, agreement on placing the cases into adenoma vs. intracystic papillary neoplasm categories was fairly poor (κ: 0.23), with >25% of the evaluators disagreeing with the others in 43% of the cases. The cell lineage, one of the bases of the WHO classification, also had poor agreement (κ: 0.17) as assessed in routine histology alone.

**Conclusions:** There is consensus on the neoplastic nature of GB-TINs, and fair agreement on the grade of dysplasia and invasiveness. However, as in TINs of pancreas and bile ducts, the growth patterns and cell lineages show significant overlaps, leading to great subjectivity and frequently precluding the reproducible application of WHO classification. A unifying terminology is needed, emphasizing their analogy with pancreatobiliary counterparts.

### 1759 Growth Patterns of High-Grade Gallbladder Dysplasia: Clinicopathologic Associations and Diagnostic Implications in an Analysis of 318 Cases

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**Background:** The diagnosis of dysplasia in the gallbladder (GB) is a well known challenge. Meanwhile, there is virtually no data on the growth patterns of high-grade dysplasia (HGD) of GB, and their diagnostic and clinical significance.

**Design:** 318 cases with unequivocal conventional (non mass-forming) HGD, 189 with accompanying invasion, were analyzed.

**Results:** Various growth patterns were recognized and often occurred in a mixture: Flat/ondulating in 82%, tubular- 66%, micropapillary/tufting-52%, denuding/clinging-19%, tall-papillary-22%, urothelial-like 1%, acantolytic-1%. When analyzed based on the predominant pattern(**also see table**): Tall papillary was commonly associated with invasion (88%; p= 0.001) and the worst clinical outcome, with 5-yr survival of 25%. Denuding/clinging had a similar trend but not statistically significant. In contrast, flat type had the best survival (66%, p=0.002). Hyalinizing cholecystitis ("incomplete" porcelain) cases (n=35) typically had either denuding/clinging or flat patterns, and almost never tall papillary or tubular. Tubular pattern was often difficult to distinguish from invasion, in particular, the foamy-gland, foveolar and attenuated cell variants.

| Variables (Units) | Denuding (n=12) | Flat (n=190) | Glandular/ Tubular (n=51) | Micro-papillary (n=32) | Tall Papillary (n=33) | p-value |
|---|---|---|---|---|---|---|
| Age, mean (±SD), year | 68.2 (7.4) | 59.7 (14.9) | 66.7 (12.9) | 62.6 (11.4) | 68.0 (9.8) | **0.001** |
| Male / Female | 2 (17%) / 10 (83%) | 37 (21%) / 142 (79%) | 8 (18%) / 35 (78%) | 8 (27%) / 22 (73%) | 9 (27%) / 24 (73%) | 0.1139 |
| Presence of Invasion | 10 (83 %) | 91 (48%) | 38 (75%) | 21 (66%) | 29 (88%) | **<0.0001** |
| Invasion Size, mean (±SD), mm | 28.9 (16.1) | 32.0 (23.0) | 15.7 (14.4) | 24.8 (19.2) | 22.4 (17.0) | **0.0053** |
| Stage of Invasive Tumor | | | | | | |
| T1 | 0 | 10 (12%) | 4 (12%) | 2 (10%) | 3 (11%) | 0.9223 |
| T2 | 8 (80%) | 41 (50%) | 20 (59%) | 10 (48%) | 14 (50%) | |
| T3 | 2 (20%) | 31 (38%) | 10 (29%) | 9 (43%) | 11 (39%) | |
| Survival Rates | | | | | | |
| 1-year | 50% | 76 % | 88% | 69% | 68% | **0.002** |
| 3-year | 25% | 70% | 65% | 54% | 30% | |
| 5-year | 25% | 66% | 58% | 54% | 25% | |
| Median Survival (mos) | 18 | N/A | N/A | N/A | 19% | |

**Conclusions:** HGD of GB occurs in various growth patterns. Tall papillary examples are significantly more commonly associated with higher frequency of invasive carcinoma and adverse outcome. Clinging/denuding pattern also appears to be aggressive, is common in hyalinizing cholecystitis and needs to be carefully searched for. Tubular examples often mimic invasive carcinoma but are more indolent in behavior. Recognition of these patterns would allow accurate diagnosis and guide more targeted pathologic examination and prognostication.

### 1760 High-Grade Neuroendocrine Carcinomas of the Pancreas: A Clinicopathologic Analysis of 60 Cases

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**Background:** In the pancreas, data regarding the types and significance of high-grade neuroendocrine carcinoma (HGNEC) has been very limited.

**Design:** Ninety-three cases, biopsied or surgically resected at 12 different institutions from 1988-2012, that had been diagnosed as HGNEC were reassessed with the morphologic criteria employed in the lung as well as IHC labeling with NE (chromogranin/synaptophysin) and acinar (trypsin/chymotrypsin) markers. Thirty-three were excluded, most being reclassified as acinar cell carcinoma (ACC). Remaining 60 were assessed as HGNEC for clinicopathologic features and survival outcomes.

**Results:** The mean age of patients qualified as HGNEC was 58 (range, 27-84). M/F ratio was 1.2. Increased serum hormone levels were present in only 3 (5%) patients (insulin in 2, VIP in 1). Sixty percent of the tumors were localized in the head of the gland, 10% in the body and 30% in the tail. Median size was 4.5 cm (range, 2.3-20). The majority (92%) of the tumors was pure NEC, 38% of which were small cell type. There was an associated adenocarcinoma component in 4, and an IPMN in 1. The incidence of vascular and perineural invasion were 71% and 62%, respectively. In 55%, one or more, usually the retroperitoneal, surgical margin was positive. Sixty-three percent of the patients had metastatic disease at presentation and an additional 28% subsequently developed metastases, usually to the regional lymph nodes and liver. Follow-up (F/U) information was available in 37 (62%) patients. 26 died of disease, with a median survival of 11 mos (range, 0-77); 11 patients were alive with disease, with a median F/U of 17 mos (range, 0-50). The median survival for all cases was 15.1 mos, with 5-yr survival of 17%.