

Tumour-to-tumour metastasis: a rare cause of apparent intratumoural heterogeneity in conventional clear cell renal cell carcinoma

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Case: We describe a case of a 51 year-old woman with a 3 year history of locally advanced and metastatic breast cancer who was noted to have a growing renal mass. The case was discussed at a multidisciplinary tumour board from which a recommendation was made to biopsy the renal lesion. The biopsy revealed renal cell carcinoma (RCC) of conventional clear cell type, which warranted surgical resection. The resection specimen showed metastatic breast carcinoma that was found within a conventional clear cell type renal cell carcinoma, highlighted by immunohistochemical staining with PAX8 and GATA3.

Discussion: Tumour-to-tumour metastasis is a rare phenomenon and few case reports exist that describe tumour-to-tumour metastases to and from clear cell renal cell carcinoma (*J Otolaryngol Head Neck Surg* 2017; 46: 17). In order for metastases to become established, tumour cells must be shed, survive in circulation, and implant, grow, and establish vascularity in a distant site - which in our case was within another primary tumour (*Nat Rev Cancer* 2002; 2: 563-572). Tumours are, by definition, environments that promote growth of neoplastic cells. Clear cell renal cell carcinoma, in particular, provides a unique pro-tumour environment, in part due to its molecular characteristics, affording metastatic tumours the opportunity to survive and grow (*Nat Rev Cancer* 2002; 2: 563-572). Further, this case illustrates the potential for sampling errors with percutaneous biopsies of renal masses and highlights the need for pathologists to consider the rare possibility of tumour-to-tumour metastasis when confronted with tumours showing striking morphologic heterogeneity.

References:

1. Song J, Taylor S, Trites J, Rigby M, Bullock M, Merrimen J, Rendon R, Hart R. Tumor-to-tumor metastases: papillary thyroid carcinoma into a clear cell renal cell carcinoma. *J Otolaryngol Head Neck Surg* 2017; 46: 17.
2. Chambers A, Groom A, MacDonald I. Dissemination and growth of cancer cells in metastatic sites. *Nat Rev Cancer* 2002; 2: 563-572.

Disclosure: This has not been previously presented, although it has been accepted by *Diagnostic Histopathology* as a Short Case.

Neuronal intranuclear rods in the human substantia nigra across the age spectrum

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Background: Parkinson's disease (PD) is a neurodegenerative disease characterized by a depletion of dopaminergic neurons in the substantia nigra (SN). Loss of SN neurons occurs at a rate of up to 10% per decade in non-pathological ageing. Other age-related changes in nigral neurons include accumulation of intranuclear inclusions called Marinesco Bodies (MBs). MBs have been shown to associate with a distinct type of neuronal intranuclear body called the intranuclear rod (INR). **Objective:** Characterize morphologic changes of INR in the SN across the human age spectrum. **Materials and Methods:** The laboratory information system was searched for hospital and forensic autopsy conducted from 2010-2017 that had midbrain sections taken. Ten slides were cut from each of 11 age groups from ages ranging from 1 month to 80 years. Sections were immunostained with glucocorticoid receptor (GR) to identify INRs. **Results:** There was a progressive age-associated transition in INR morphology from long, linear intranuclear structures in the youngest age groups (infants), to shorter linear structures at middle ages, culminating in small, dot-like juxtannucleolar structures in elderly subjects. A proportion of short INRs displayed contact with MBs in the middle age groups. **Conclusions:** We demonstrated a striking progressive, age-dependent alteration in INR morphology. These results suggest that INRs give rise to MBs in the SN during the middle ages. Ultimately, we plan to expand our cases for the creation of a human SN tissue microarray which we hope will shed light on the cellular mechanisms of neuronal ageing and degeneration in the SN.

This abstract has not been presented before.

Breakdown of diagnostic categories in voided versus non-voided urine: a study on the impact of the Paris system for reporting urinary cytology (PSRUC) in a large academic institution
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Objectives: The appearance of urothelial cells vary depending on collection method (voided versus non-voided). Voided (V) urothelial cells tend to exhibit degeneration, whereas non-voided (NV) urothelial cells tend to have higher nuclear-to-cytoplasmic (N/C) ratio, which may cause over-interpretation as atypical. The PSRUC includes four main cytological categories: negative for high grade urothelial carcinoma (NHGUC), "atypical" (AUC), "suspicious for high grade urothelial carcinoma" (SHGUC) and "high grade urothelial carcinoma" (HGUC). We evaluated the impact of the PSRUC on the breakdown of different cytological diagnostic categories in both V and NV urine.

Design and Methods: A comparative study was conducted over a 6 month period in 2013 (pre-PSRUC), including 1653 patients and 2,371 specimens, versus a 6 month period in 2016 (post-PSRUC), including 1478 patients and 2,392 specimens.

Results: Significant changes were observed within V urine: NHGUC increased by 6.5% (74.5% vs. 81%, P<0.001), whereas AUC decreased by 5.5% (20% vs. 14.5%, P<0.001). A reverse trend was seen in NV specimen, although not statistically significant (see table below).

CYTO	2013 V (2039)	2016 V (2113)	P-value
NHGUC	1520 (74.5%)	1706 (81%)	<0.0001
ATYP	409 (20%)	307 (14.5%)	<0.0001
S	57 (2.8%)	44 (2%)	0.1581
HGUC	53 (2.5%)	56 (2.5%)	0.9231
CYTO	2013 NV (332)	2016 NV (279)	P-value
NHGUC	268 (81%)	211 (75.6%)	0.1392
ATYP	34 (10.2%)	38 (13.6%)	0.5325
S	13 (4%)	13 (4.6%)	0.6908
HGUC	17 (5%)	17 (6%)	0.6011

Conclusions: It is more difficult to apply the diagnostic criterion of N/C ratio >0.5 in NV than V specimens because a high NC ratio is intrinsic to instrumentation effects. Our results raise the question as to whether the PSRUC's criteria for AUC (especially the criteria for N/C>0.5) should be different between N and NV urine specimens.

DISCLOSURE STATEMENT: this poster was also presented at the 2018 USCAP Conference in Vancouver, BC, Canada.

Title: Phosphorylated STAT3 expression in primary colorectal carcinomas and paired liver metastases.

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Objectives: In colorectal carcinoma (CRC), activated STAT3 (pSTAT3) overexpression by immunohistochemistry (IHC) is associated with poor survival. STAT3-targeted therapies are being widely explored in the treatment of metastatic CRC (mCRC). However, the concordance between pSTAT3 IHC expression in the primary tumor and metastasis has not been studied. We examined the concordance of pSTAT3 IHC expression between paired primary CRC tumor and liver metastases (LM).

Design and Methods: We included all mCRC patients treated with colon resection and liver metastectomy at The Ottawa Hospital from 2001-2012. Using tissue microarrays, pSTAT3 intensity was evaluated by two independent pathologists as 0 (absent), 1-2 (low), or 3 (high).

Results: Ninety-one patients with CRC and LM were evaluated. Expression of pSTAT3 in primary tumors was 23% high, 47% low, and 30% absent, compared to 29% high, 50% low, and 21% absent in LM. In 32 (35%) of patients, pSTAT3 expression from the primary was retained in paired metastatic samples. Its expression increased in 26% and decreased in 38%. In LM the median survival of those with positive pSTAT3 expression was 2 years more than those with negative pSTAT3 expression; HR 0.6 (95%CI 0.1-1.1), p-value 0.07.

Conclusions: In this selective population, we found no correlation between pSTAT3 IHC expression in primary CRC and LM. Our study, albeit small, underlines the importance of concordance studies when developing a biomarker.

Higher level of neuroendocrine differentiation and aggressive clinical behavior in basaloid predominant squamous cell carcinomas of the lung

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Background/Objective:

Basaloid Squamous Cell Carcinoma (B-SqCC) is an uncommon entity that exhibits histological overlaps with small cell carcinoma (SCLC) including neuroendocrine differentiation (NE-d). Our objective was to assess the NE-d in B-SqCC and its prognostic impact comparing with poorly-differentiated SqCCs (PD-SqCC).

Methods:

Patients: 40 B-SqCC, 9 peripheral SCLC, 21 PD-SqCCs; institutional resections 2005-2016. After review of 40 B-SqCCs by two thoracic pathologists, 20 cases were identified as basaloid predominant (BP)-SqCC (10 pure basaloid and 10 with >50% basaloid differentiation). Two blocks per case were used for immunohistochemical stains.

Results:

NE-d was identified in 65% (13/20) of BP-SqCCs, demonstrated by >10% cell positivity with one NE marker while 40% (8/20) demonstrated >one NE marker positivity. In comparison, only 19% of PD-SqCCs (4/21) showed >10% cell positivity with one NE marker ($p < 0.01$) and none showed >one NE marker positivity. Interestingly, 30% of pure B-SqCC tumors showed >10% TTF1 positivity.

Clinically, 50% (5/10) of pure B-SqCC cases presented with stage T3 or higher compared to 14% (3/21) of PD-SqCC ($p = 0.02$). Moreover, 50% (10/20) of BP-SqCCs experienced <2 years disease-free survival (DFS) compared to 23% (4/17) of PD-SqCC ($p = 0.031$). A lower 2-year DFS trend was seen in BP-SqCCs with NE-d compared to BP-SqCCs without NE-d (54% (7/13) vs. 43% (3/7), respectively).

Conclusions:

Our study demonstrates that NE-d in B-SqCC tumors can pose a diagnostic challenge especially in biopsy specimens. Although currently managed similar to SqCC, B-SqCCs exhibit higher NE-d, present at higher T-stage and have shorter DFS. Therefore, further molecular and management studies are required.

Keywords: basaloid squamous cell carcinoma, neuroendocrine differentiation, small cell carcinoma

* Please note that this study will be presented in CAP-ACP 2018 annual meeting.

Abstract Title:

MyPathologyReport.ca: an online pathology education resource for patients

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Keywords: website, online, patient education

Word Count: 248 words

Introduction:

Patients are receiving increasing access to their electronic medical record (EMR) and laboratory results, including pathology reports, are amongst the most frequently accessed pieces of information. MyPathologyReport.ca is a novel website exclusively providing pathology education to patients, designed to help patients understand the language of pathology and to effectively navigate their pathology report. Feedback on this free online tool was solicited from healthcare providers to determine whether MyPathologyReport.ca would serve the needs of their patient population.

Methods:

An online questionnaire was distributed to targeted healthcare providers at the Ottawa Hospital, the Children's Hospital of Eastern Ontario, and select community practices. Respondents were required to navigate MyPathologyReport.ca and complete a 15-question survey regarding their use of pathology reports and whether MyPathologyReport.ca provided useful information for their patients.

Results:

There were 22 respondents across six specialties, including multiple surgical subspecialties, pediatrics, medical genetics, and family medicine. Over 80% reported that all features of MyPathologyReport.ca were either very useful or extremely useful, including: i) how to read a pathology report; ii) an illustrated pathology dictionary; and iii) articles outlining the most common pathological diagnoses. 72% of respondents stated they were somewhat likely or very likely to recommend MyPathologyReport.ca to a patient.

Conclusion:

An informed patient is an active member of the healthcare team. Our feedback questionnaire demonstrates that clinicians find MyPathologyReport.ca to be a useful patient resource. Next steps involve longitudinal assessment of MyPathologyReport.ca from non-medical community members and evaluation of patient satisfaction and knowledge with access to this resource.

Disclosure of Previous Presentations:

USCAP - March 2018 (Poster)

CAP - July 2018 (Platform)

Title: A proposal for standardized sampling of reduction mammoplasty specimens

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Objectives. There are no standardized protocols for reduction mammoplasty specimens (RMS). However, incidence of clinically important pathologic findings (CIPF) ranges 0.06-12.8%. The goals of our study were to identify the incidence of CIPF at our institution, to evaluate the existing approach to RMS, and propose a protocol for further tissue sampling once CIPF were found in the initial blocks. **Design:** This is a prospective study over a four-year period (1.01.2012-31.12.2016) including 1383 patients without any prior history of breast pathology. Patients had 2 (Group A (younger than 40) or 4 sections per breast (Group B (older than 40 years) initially submitted. We recorded data on number of blocks submitted after initial CIPF were identified, pathology that triggered the submission of additional tissue. **Results.** The incidence of CIPF in our institution was 3.6% (Table 1). Group B showed higher incidence rate of CIPF than Group A ($p < 0.01$). On average 13 additional sections were submitted after initial CIPF were identified in Group B which resulted in an upgrade in diagnosis in 9 cases (average block 11). **Conclusions.** We recommend submission of additional 20 sections (in 10 cassettes) after initial CIPF identified which would allow detection of 89% of the potential upgrade in CIPF.

Table 1

Age group	%	Mean age \pm SD	All CIPF (%)	ALH (N/age \pm SD)	ADH (N/age \pm SD)	LCIS (N/age \pm SD)	DCIS (N/age \pm SD)	Invasive Carcinoma (N/age \pm SD)
Younger than 40 (541)	39	29 \pm 7	5(1%)	2/37 \pm 0	1/28	1/33	1/31	0
40 and older (842)	61	53 \pm 8	45(5%)	16/52 \pm 7	13/53 \pm 8	7/50 \pm 4	6/55 \pm 11	3/55 \pm 8
Total (1383)	100	44 \pm 14	50(3.6%)	18/50 \pm 8	14/52 \pm 10	8/48 \pm 7	7/51 \pm 14	3/55 \pm 8

Disclosure: This abstract was presented at USCAP meeting on March 18, 2018.

Ewing's Sarcoma of the Small Intestine with EWSR1 Gene Fusion: Case Report

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Introduction: Extraskkeletal Ewing's sarcoma is a rare primary soft tissue malignant tumor which mainly affects adolescents and young adults. It occurs mostly in the trunk, extremities, retroperitoneum, and head and neck regions and is more common in males than in females. This report describes a rare case of Ewing's sarcoma of the small intestine in a 41-year-old female. Cytogenetic study confirmed the EWSR1 gene rearrangement.

Case Presentation: The patient presented with 3-day progressive right flank pain migrating to the umbilical area. CT scan showed a single 5.5 x 4.2 x 3.2 cm complex enhancing soft tissue mass in the proximal jejunum. Examination of the resected specimen revealed a 3.5 x 3.0 x 3.0 cm tumor in the wall of the jejunum with extension to the overlying mucosa, perienteric adipose tissue and the serosa. The tumor showed typical histologic features for a small round cell tumor. Immunohistochemically, tumor cells positive for BCL2, CD99, CD56, and FLI-1; negative for CD20, CD3, CD10, CD45, CKAE1/AE3, CK5/6, CK7, CKHMW, CK19, CK20, EMA, CD31, CD34, chromogranin, synaptophysin, CDX-2, TTF-1, desmin, SMA, MSA, CD117, DOG1, S100, melan A, SOX10, CD10, calretinin, WT1, inhibin, mammaglobin, GCDFP-15, ER, and PR. Nuclear fluorescence in situ hybridization revealed EWSR1 gene rearrangement in 57% of tumor cell nuclei. A diagnosis of extraskkeletal Ewing's sarcoma was established. The patient underwent chemotherapy.

Disclosure Statement: This case report has not been presented previously.