PSOH Annual Meeting

THE EVOLUTION OF PRACTICE IN 2021

October 1, 2021 | 7:45 AM–5:30 PM | VIRTUAL

Attendee Guide

PSOH | ASCO® State/Regional Affiliate Program
Pennsylvania Society of Oncology & Hematology

This program has been awarded AMA PRA Category 1 Credit ™ by the Pennsylvania Medical Society.

AIRMEET PLATFORM

This year's meeting is being held virtually via the AirMeet platform. Here's some information to ensure you have a seamless virtual experience.

How do I access the event?

You will be sent an email from AirMeet with a unique link to login. When you click on the unique link, you'll be able to enter the meeting.

Can I chat with others during the meeting?

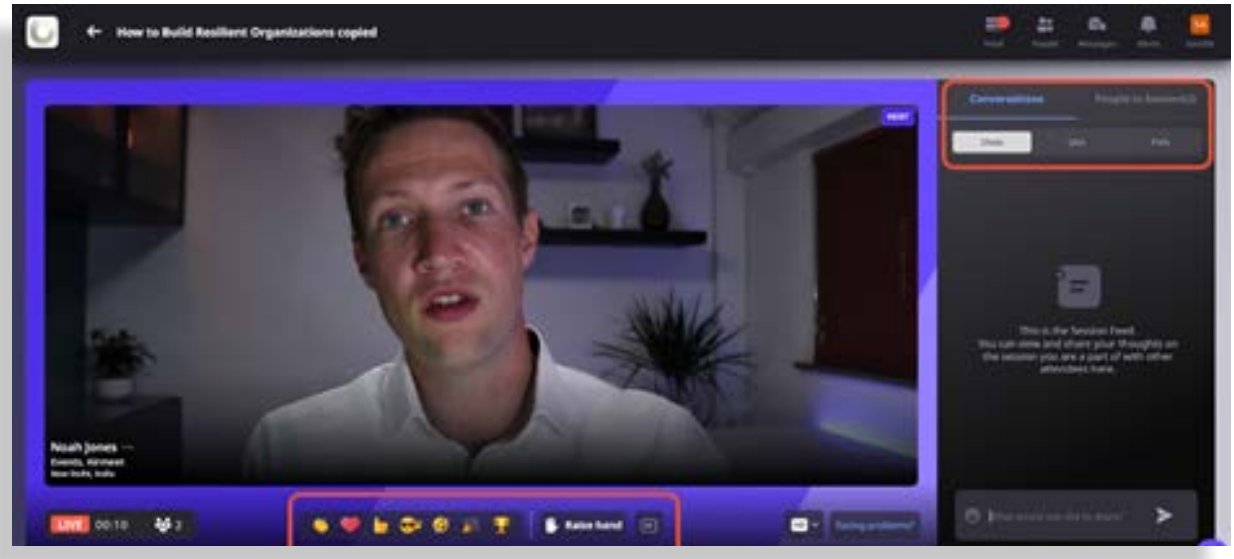
Yes! There is a "Feed" in the upper right-hand corner of the screen that you'll be able to chat with others throughout the meeting. Alternatively, you can chat one-on-one with other attendees by clicking on "People" in the same area, finding the individual you wish to chat with, and clicking on their name. You can either send them a message or schedule a meeting with them.

How do I see the agenda?

Simply click on the Schedule tab at the top of the screen.

Can I interact during the sessions?

Yes! You can raise your hand, ask a question, react with emojis, chat with others and participate in polls.



AIRMEET PLATFORM

What is the lounge?

This area allows you to interact with other participants attending the event and hop between tables to meet new people and have conversations.

Is there a virtual exhibit hall?

Yes! You can access the hall by clicking on the "Booths" tab at the top of the screen. Use the video chat feature in the booth lounge to meet-up with booth representatives in real time or click on the "Register Interest" button to send you contact details to exhibitors.

You can find Exhibitor's resources like marketing collateral, social media plugins, and videos inside the exhibitor booth.

What if I need assistance with the AirMeet platform?

The "Help" button on the bottom right takes you to the 24*7 Support Lounge or Chat support along with FAQs to assist you in case you face any issues during the event.

Can I access the meeting on my phone or tablet?

Yes! Simply download the AirMeet application from the app store. You will then have to enter the event link (https://www.airmeet.com/e/26de0e60-e0c8-11eb-9f20-bddf06f1c951) and register to join.

Note: Virtual booths are not available on the mobile app and can only be viewed via laptop/desktop.

Quick Tips

For a flawless visual experience on AirMeet, keep the following in mind:

- Use a laptop/desktop and Google Chrome to join.
- Have a stable and good internet connection.
- If you have difficulty seeing the speaker's feed, refresh the page/restart browser, and ensure that you close any other video conferencing tool you may have used recently.
- If using any VPNs or anti-viruses, please turn them off for a smooth experience.

CONTINUING EDUCATION

This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of the Pennsylvania Medical Society and the Pennsylvania Society of Oncology and Hematology. The Pennsylvania Medical Society is accredited by the ACCME to provide continuing medical education for physicians.

The Pennsylvania Medical Society designates this live activity for a maximum of ***7.0 AMA PRA Category 1 Credit(s)™***. Physicians should only claim credit commensurate with the extent of their participation in the educational activity.

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To obtain a CME certificate, please use the link provided below to view and complete the online post-course survey which is available through our learning management system.

You will need to create a web account for the PAMED website if you don't already have one. Membership in PAMED is not required for a Web account. The information required to create a web account includes first and last names, date of birth, and an email address (cannot be a shared email address – each learner profile must have a distinct email address of record). Entering your license number is optional but is helpful in establishing your learner profile.

Once you have created your account/logged in, you will be redirected to the course and able to view and complete the survey. A CME certificate will be available to download, print, or email after you have completed the survey.

CME Evaluation Link

Please note that you cannot use Internet Explorer to access our learning management system as it is not supported by the platform. You must use Google Chrome or another browser.

If you have any questions about the process to claim CME, please feel free to contact PSOH Meeting Manager, Lauren Klinedinst (lklinedinst@pamedsoc.org), at your convenience. If you need assistance creating a website account, please contact the Knowledge Center at 855-PAMED4U (855-726-3348) or KnowledgeCenter@pamedsoc.org.

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In accordance with the Accreditation Council for Continuing Medical Education (ACCME) Standards, the following presenters of this course have indicated that they either do or do not have a relationship which, in the context of their presentation, could be perceived by some as a real or apparent conflict of interest, (e.g., ownership of stock, or honoraria or consulting fees). Those presenters having such relationships do not consider that it will influence their presentation.

Financial relationships reported by members of the Scientific Meeting Planning Committee are provided below. During all phases of planning for the Pennsylvania Society of Oncology a ology 2021 Annual Meeting, areas of conflict were managed through a peer-review process and/or through individual recusal when appropriate.

The Meeting Planning Committee has reviewed all presenter disclosure reports, identified potential conflicts of interest, and implemented strategies to manage those areas of conflict, where they exist.

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Charu Aggarwal, MD, MPH	AstraZeneca Blueprint Celgene Daichii Sankyo Eli Lilly Merck Roche	Consultant/Advisory Board Consultant/Advisory Board Consultant/Advisory Board Consultant/Advisory Board Consultant/Advisory Board Consultant/Advisory Board Consultant/Advisory Board
Nathan Bahary, MD, PhD	AstraZeneca Bristol-Myers Squibb	Consultant Consultant
David Bartlett, MD		Nothing to Disclose
Crystal Denlinger, MD	Beigene Study Bristol-Myers Squibb Exelixis Merck Taiho Oncology Zymeworks	Committee Member Advisory Board Advisory Board Advisory Board Consultant/Advisory Board DSMB Member
Allison Hirschorn		Nothing to Disclose
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Heath Mackley, MD, MBA, FACRO		Nothing to Disclose
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Heather Rocha, MS		Nothing to Disclose
Rajiv Panikkar, MD		Nothing to Disclose

Planning Committee	Company Name	Nature of Relationship
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Steven Cohen, MD		Nothing to Disclose
Arturo Loaiza-Bonilla, MD, MSEd, FACP		Nothing to Disclose

Oral Abstract Presenter	Company Name	Nature of Relationship
Benjamin Miron, MD		Nothing to Disclose
Hirsch Matani, FACP		
Yan Leyfman		Nothing to Disclose

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AGENDA

Time	Session
7:45 a.m. - 8:00 a.m.	**Welcome & Annual Business Meeting**
8:00 a.m. – 8:45 a.m.	**Cancer Genetics in Rural Pennsylvania** Rajiv Panikkar, MD Heather Rocha, MS
8:45 a.m. – 9:00 a.m.	**Oral Abstract** **Influence of First-line Chemotherapy Regimen on Survival Outcomes of Patients with Advanced Urothelial Carcinoma Who Receive Second-line Immunotherapy** Benjamin Miron, MD
9:00 a.m. – 9:45 a.m.	**State Legislative Update & Award Presentation** Heath Mackley, MD, MBA, FACRO Representative Bridget Kosierowski
9:45 a.m. – 10:15 a.m.	**Break with Exhibitors**
10:15 a.m. – 11:00 a.m.	**Recent Developments in Targeted Therapies and Genomics for Thoracic Malignancies** Charu Aggarwal, MD, MPH
11:00 a.m. – 11:45 a.m.	**Immunotherapy Ddvances and Toxicity Considerations for the Clinician** Anthony Olszanski, MD
11:45 a.m. – 1:00 p.m.	**Lunch & Visit with Exhibitors**
11:45 a.m. – 12:45 p.m.	**Non-CME Product Showcase presented by BeiGene, USA**
1:00 p.m. – 2:00 p.m.	**Biliary Roundtable** Nathan Bahary, MD, PhD David Bartlett, MD
2:00 p.m. – 2:15 p.m.	**Oral Abstract** **Novel Predictive and Prognostic Gene Signatures for Chemoradiotherapy in Locally Advanced Esophageal Adenocarcinoma** Hirsch Matani, MD
2:15 p.m. – 2:45 p.m.	**Visit with Exhibitors**
2:45 p.m. – 3:30 p.m.	**Evaluation and Management Services in 2021** Allison Hirschorn
3:30 p.m. – 3:45 p.m.	**Oral Abstract** **A Mechanistic Interplay for Cancer and COVID-19 with a Therapeutic Intervention** Yan Leyfman
3:45 p.m. – 4:30 p.m.	**Virtual Health in Oncology** Chevon Rariy, MD
4:30 p.m. – 5:15 p.m.	**NCCN Overview & Community Programs** Crystal Denlinger, MD
5:15 p.m. – 5:30 p.m.	**Awards & Wrap Up**

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BeiGene USA
EMD Serono
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Tempus

NON-CME PRODUCT SHOWCASE

Presented by BeiGene, USA

Discussion of Brukinsa for Adult Patients with Waldenstrom's Macroglobulinemia

Speaker:

Dr. Kasra Karamlou

Assistant Clinical Professor of MedicineCleveland Clinic,
Taussig Cancer Institute, North Coast Cancer Center

*Visit the Lounge in the virtual platform to take part in this session.

WITH OUR APPRECIATION

Thank you to our PSOH 2021 Program Planning Committee

Steven Cohen, MD, *Program Chair*

Moshe Chasky, MD

Arturo Loaiza-Bonilla, MD, MSEd, FACP

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POSTERS

AV nodal dissociation and facial droop: an atypical presentation of lymphoma
James Dreer, DO • Penn State Health

A rare case of EBV-associated HLH with spontaneous resolution
Ian Garrahy, DO • Tower Health System

A rare case of IgM Multiple Myeloma presenting with hyperviscosity syndrome
Ian Garrahy, DO • Tower Health System

HES: A Rare Infiltrative Hematological Disorder with Catastrophic Manifestations
Keerthy Joseph, DO • Mercy Catholic Medical Center

Significant lipid and neutrophil accumulation and active inflammasome in high BMI tumor regions of human pancreatic ductal adenocarcinoma
Ahmed Khattab, MD • Allegheny Health Network

MABs for TMAs: When Plasma Exchange Is Not Enough
Shoja Rahimian, DO • Tower Health System

Recurrent Squamous Cell Carcinoma of the Skin - a Rare Side Effect of nilotinib
Ali Rizvi, DO • Allegheny Health Network

Swelling of the Preauricular Area: An Atypical Presentation of T-Cell Lymphoma
Manpreet Sidhu, DO • UPMC Pinnacle

Tumor Lysis Syndrome: Inpatient Outcomes amongst NHL patients
Muhammad Usman Zafar • Lehigh Valley Health Network

Outcomes in patients with malignant pleural effusions from Lung Cancer
Muhammad Usman Zafar • Lehigh Valley Health Network

Impact of venous thromboembolism in patients with Hepatocellular Carcinoma
Muhammad Usman Zafar • Lehigh Valley Health Network

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AV nodal dissociation and facial droop: An atypical presentation of lymphoma

James Dreer, DO, Kevin Rakszawski, MD

Penn State Milton S. Hershey Medical Center

Introduction

Diffuse large B cell lymphoma is the most common lymphoid malignancy. [1]

Symptoms commonly consist of lymphadenopathy and constitutional symptoms at diagnosis.

Extra-nodal symptoms occur in 20-40% patients at initial diagnosis.

Cardiac conduction abnormalities and neurologic deficits are rarely the presenting symptoms of DLBCL. [2]

Case

50-year-old female with initial presentation of shortness of breath and chest pain was found to be bradycardic with hypotension (HR: 40, BP: 92/51).

She was treated in an ICU with atropine injections and a dopamine infusion for symptomatic bradycardia.

Electrocardiogram revealed a junctional bradycardia (HR: 40). Ischemic workup was pursued for lower extremity swelling, dyspnea on exertion, and elevated troponin (46ng/L). Transthoracic echocardiogram revealed a normal ejection fraction (60%) and no valvular abnormalities. A left heart catheterization was unrevealing.

Additionally, the patient had an associated left sided facial droop that developed early during her clinical course. Differential included Lyme disease or Ramsay Hunt Syndrome. Head CT showed no evidence of intracranial abnormality.

Case (cont.)

Given her presentation of symptomatic bradycardia, Lyme disease was suspected. She was treated with ceftriaxone and later pacemaker placement after Lyme titers returned negative. She was also started on antivirals for facial droop due to concern for Ramsay Hunt Syndrome. With negative titers and neurologic abnormalities, a more systemic disease was considered.

A left renal lesion was identified after performing a CT scan of her pelvis for leg pain. Described as area of enhancement concerning for infiltrative malignancy, it was biopsied.

Her presenting symptoms continued, including lower extremity edema while awaiting biopsy results and she was again admitted. She also developed atrial flutter.

Labs & Imaging

WBC: 26k/uL **Hgb**: 10.9g/dL **Plt**: 198k/uL
Differential: neutrophilia

Peripheral smear: no blasts
Lyme titers: negative

Lactate: 2.1 **CRP**: 4.52 **ESR**: 10 **LDH**: 778

ALT: 342 **AST**: 176 **ALP**:86 **Tbili**: 0.4

CT body: Enhancing densities most significant at lateral aspect of the left kidney measuring 2.5cm thick with bilateral urethral thickening. Findings consistent with infiltrative malignancy.

Left renal lesion biopsy: aggressive B-cell lymphoma

FISH: high-grade B-cell lymphoma; double hit (C-Myc, BCL-6 rearrangements on FISH)

CSF: Lymphoma cells.

Bone marrow: Negative for lymphoma.

PET/CT: Consistent with bony lesions, pericardial disease and abdominal organ infiltration

MRI: leptomeningeal & cranial nerve enhancement of CNS and spinal cord consistent with CNS involvement

Clinical Course

Left kidney biopsy **revealed high-grade B-cell double-hit DLBCL**, and treatment was initiated during her hospitalization.

Ramp-up therapy: R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone)

Definitive induction therapy: DA-R-EPOCH (rituximab, etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin)

CNS prophylaxis: via Ommaya reservoir: etoposide, cytarabine, methotrexate, gemcitabine, rituximab.

Despite optimal treatment, her DLBCL progressed, and she experienced complications including pain related to osteolytic lesions, Ommaya reservoir infection, adrenal insufficiency, and debilitating neurologic symptoms including cranial deficits, dysphagia, recurrent aspiration, headaches, and neuropathic pain.

Conclusions

Cardiac conduction and cranial nerve abnormalities are a marker of late and aggressive disease if associated with DLBCL. [3]

Cardiac conduction abnormalities as a marker of CNS involvement is a unique presentation of DLBCL.

Myocardial involvement is more often asymptomatic and identified on autopsy.[1,4]

Cardiac MRI is the best test to identify specific lesions of the cardiac conduction system. [3]

Maintain a broad differential diagnosis. This patient's signs and symptoms are a marker of systemic disease resulting in a diagnosis of a high-grade lymphoma.

References

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3. Al-Mehisen R, Al-Mohaissen M, Yousef H. Cardiac involvement in disseminated diffuse large B-cell lymphoma, successful management with chemotherapy dose reduction guided by cardiac imaging: A case report and review of literature. *World J Clin Cases*. 2019;7(2):191-202.

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PennState Cancer Institute

A rare case of EBV-associated HLH with spontaneous resolution

Ian Garrahy, DO, PGY5
Department of Hematology-Medical Oncology, Reading Hospital, West Reading, PA

BACKGROUND

- Hemophagocytic lymphohistiocytosis (HLH) is a life-threatening syndrome of excessive immune activation.
- It often manifests as a persistent fever, splenomegaly, pancytopenia, and hemophagocytosis in the bone marrow.
- HLH can be familial or acquired, both of which are triggered by an event that disrupts immune homeostasis.
- Acquired HLH is mostly caused by infection, malignancy, and autoimmune disease.
- Epstein-Barr virus-associated HLH is the most common type of infection-associated HLH.

CASE PRESENTATION

- History:

34-year-old female with a prior history of EBV-associated HLH who presented to the hospital with a fall preceded by a week of generalized body aches, fever, and fatigue. Pancytopenia developed during the hospitalization.

- PE:

Temperature 39.5C, spleen palpable 1 cm below costal margin

- Labs:

White blood cell count 1.5E3/uL, absolute neutrophil count 830, hemoglobin 8.2 g/dL, platelet count 58E3/uL, soluble IL-2 receptor 4,611 U/mL, EBV blood PCR 672,000 cpy/mL, fibrinogen 89 mg/dL, ferritin 2133 ng/mL, LDH 1,139 IU/L, AST 290 IU/L, alkaline phosphatase 354 IU/L

- Imaging:

CT chest/abd/pelvis: enlarged liver and enlarged spleen 14.7 cm.

- Pathology

Bone marrow biopsy: hemophagocytic lymphohistiocytosis is present and prominent. The is hypercellularity and trilineage hematopoiesis.

DIAGNOSIS AND TREATMENT

- A clinical diagnosis is consistent with HLH if 5/8 of the following are met: fever > 38.5C, splenomegaly, cytopenias, hypertriglyceridemia and/or hypofibinogenemia, hemophagocytosis, low or absent NK cell activity, ferritin > 500 ng/mL, and elevated soluble IL-2 receptor >2,400 U/mL.
- Prompt treatment is typically required for this highly fatal condition.
- Our patient's pancytopenia, inflammatory markers, and EBV blood PCR slowly returned to normal without treatment.

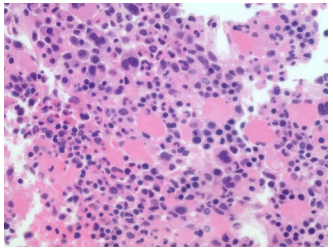

Figure 1: bone marrow biopsy at 40x magnification with prominent hemophagocytosis.

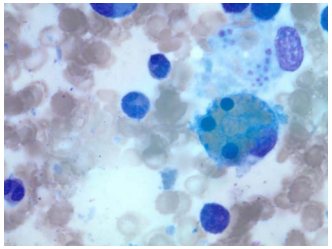

Figure 2: bone marrow aspirate at 100x magnification with reactive histiocytes and phagocytosis of nucleated red blood cells.

DISCUSSION

- Our patient met 7/8 criteria for HLH with hemophagocytosis in bone marrow, fever, cytopenias, splenomegaly, hypofibrinogenemia, elevated ferritin, and elevated soluble IL-2R.
- To distinguish between familial and acquired HLH, an HLH genetic panel was performed and was negative.
- A regimen of dexamethasone and etoposide has been the mainstay of treatment based on the HLH-1994 and HLH-2004 studies.
- In patients with EBV-associated HLH, the addition of rituximab can be useful to deplete the reservoir of EBV in B cells.
- The distinction between HLH and primary EBV infection can be very difficult, as patients with primary EBV may develop some of the hallmark signs of HLH as part of natural infection.
- During the patient's hospitalization, her pancytopenia, inflammatory markers, fever, transaminitis, and EBV PCR all slowly resolved.
- A literature review was performed. Our cause is the first case published of a patient with EBV-associated HLH with spontaneous resolution.

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A rare case of IgM Multiple Myeloma presenting with hyperviscosity syndrome

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BACKGROUND

- Multiple Myeloma (MM) is characterized by the neoplastic proliferation of immunoglobulin-producing plasma cells and has various subtypes, the rarest of which is IgM.
- Common presentations of MM are related to the plasma cell infiltration of the bone marrow or to kidney damage from excess light chains.
- These include anemia, bone pain, elevated creatinine, fatigue, and hypercalcemia.
- Hyperviscosity syndrome is a much more common presentation in Waldenstrom macroglobulinemia (WM) but can very rarely occur in patients with IgM MM.

CASE PRESENTATION

- History:

A 74-year-old female with no significant past medical history presented to the hospital with 2 weeks of blurry vision and lightheadedness.

- PE:

Afebrile, hemodynamically stable.
Ophthalmic evaluation noted bilateral central retinal vein occlusions.

- Labs:

CBC - anemia with hemoglobin of 8.0 g/dL.
SPEP/IFE – elevated IgM kappa monoclonal protein 5.02 g/dL.
UPEP/IFE – 335 mg/d paraprotein excretion.
IgM > 5,000 mg/dL, Kappa FLC 147.5 mg/L, K/L ratio 22.5.
Beta-2 macroglobulin 6.7 mg/L
Serum viscosity elevated 5.22 centipoise
MYD88 L265P mutation was not detected.

- Pathology

Bone marrow biopsy: significant for IgM multiple myeloma. CD138 stain showed plasma cells to account for approximately 30% of cellularity. No B-cell proliferation identified by morphology or by flow cytometry.

DIAGNOSIS AND TREATMENT

- Patient met criteria for IgM kappa MM with 30% bone marrow plasma cells and anemia with hemoglobin 8 g/dL.
- FISH panel did not demonstrate any high-risk features such as del(17p), t(4;14), t(14;16), t(14;20), or gain(1q).
- Patient received daily therapeutic plasma exchange until the IgM level improved to 2,618 mg/dL.
- When blurry vision and hyperviscosity syndrome improved, she was started on myeloma-directed therapy with bortezomib, lenalidomide, and dexamethasone.

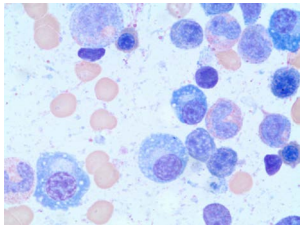

Figure 1:
Touch preparation from core bone marrow biopsy at 100x magnification showing the plasma cells with eccentric nuclei and perinuclear hof.

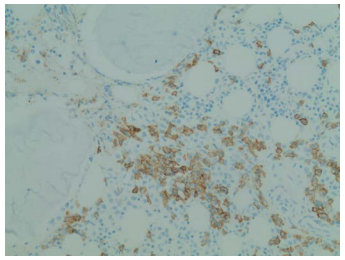

Figure 2:
CD138 immunohistochemical stain at 20x magnification.

DISCUSSION

- WM is a distinct clinicopathologic entity demonstrating lymphoplasmacytic lymphoma (LPL) in the bone marrow with an IgM monoclonal gammopathy in the blood.
- While the presence of an IgM monoclonal protein is more typical of lymphoplasmacytic lymphoma, the absence of MYD88 L265P mutation and presence of bone marrow infiltration with clonal plasma cells are suggestive of Multiple Myeloma.
- IgM MM is an extremely rare subtype, comprising only 0.5% of patients with MM.
- When there is hyperviscosity syndrome due to high serum IgM levels, it is important to consider IgM MM as the etiology.
- Therapeutic plasma exchange relieves the symptoms of hyperviscosity syndrome and should be performed regardless of the serum viscosity level.
- Myeloma-directed therapy can be commenced when IgM levels improve to 4000 mg/dL.

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HES: A Rare Infiltrative Hematological Disorder with Catastrophic Manifestations

Keerthy Joseph DO[1], Navyamani Kagita MD[1], Samia Hossain MD[1], Aisha Shaik MD[1], Robert Borden DO[2], Rajesh Thirumaran MD[3]

[1]Mercy Catholic Medical Center Department of Medicine, [2]Mercy Catholic Medical Center Department of Radiology, [3]Mercy Catholic Medical Center Department of Hematology & Oncology

Case

A 68 year old woman with underlying hypertension and diabetes presented with chest pressure and exertional dyspnea for 2 days, along with progressively worsening dysphagia for 1 week. Labs showed elevated troponin of 6.73 ng/mL (peaked at 13 ng/mL), and leukocytosis with 36,000 WBCs and 52% eosinophils. EKG showed ST depressions in leads V2-V5 (Figure 1). CT chest revealed circumferential thickening of the esophagus. Heparin drip was started for NSTEMI. Cardiac catheterization did not reveal CAD. Patient developed a left sided facial droop on second day of hospitalization; brain MRI (Figure 2) showed multiple areas of restricted diffusion, concerning for embolic stroke versus vasculitis. Telemetry did not reveal any arrhythmias.

To assess for intracardiac thrombus, cardiac MRI was obtained, which revealed diffuse subendocardial hypoperfusion involving the left ventricular and papillary muscles, consistent with ischemia (Figure 3). Hypercoagulable and vasculitis workup was negative. Bone marrow biopsy showed hypercellular bone marrow with marked increase in eosinophils (Figure 4); flow cytometry revealed 45% eosinophils without an increase in other cell lineages. JAK2 V617 mutation and PDGFRA/PDGFRB/FGFR1 rearrangements were not detected. Idiopathic hypereosinophilic syndrome (HES) was deemed to be the etiology of her multi-organ damage with eosinophilic infiltration causing myocarditis, stroke, and esophagitis.

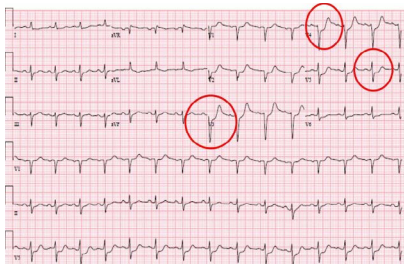

Figure 1: EKG showing ST depressions in V2-V5.

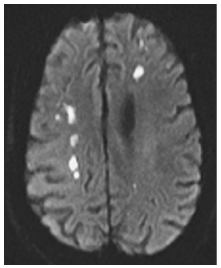

Figure 2: Brain MRI showing multiple areas of restricted diffusion.

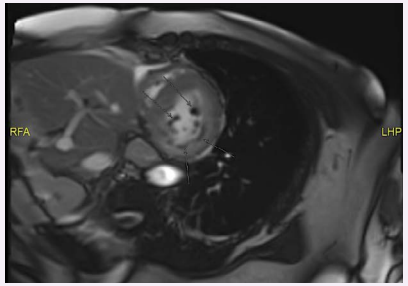

Figure 3: Cardiac MRI showing diffuse subendocardial hypoperfusion and delayed enhancement in multiple vascular territories involving the left ventricular wall and papillary muscles.

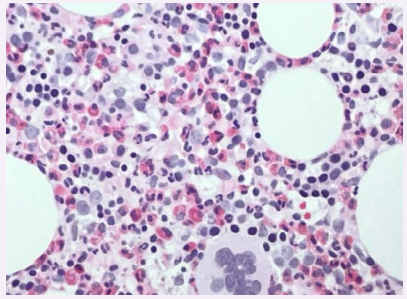

Figure 4: Bone marrow biopsy showing hypercellular marrow with hypereosinophilia.

Discussion and Conclusion

HES is a very rare clinical entity; its estimated prevalence in US is between 0.3 and 6.3 cases per 100,000 person-years. HES is characterized by elevated eosinophil count >1500 cells/microL in peripheral blood and subsequent organ damage, mediated by rapid monoclonal proliferation of eosinophils and excessive production of eosinophilopoetic cytokines, such as IL-5. HES has several variants. Myeloid variants are often secondary to PDGFRA/PDGFRB/FGFR1 rearrangements or JAK2 mutations. T cell lymphocytic variants are secondary to aberrant IL-5 producing T cells. Additionally, there are idiopathic HES, familial HES, and organ-restricted HES.

Initial studies comprise blood chemistries, IgE levels, LDH, serum tryptase, and stool testing for parasites. Further workup with echocardiogram, chest/abdominal CT, and tissue biopsies is recommended to evaluate for end-organ damage. Bone marrow aspirate and biopsy should be assessed for morphology and cellularity, followed by molecular testing for gene mutations and rearrangements. Initial therapy depends mainly on the variant of HES and manifested clinical symptoms. Myeloid variants with PDGFR mutations are initially treated with imatinib mesylate, while systemic steroids are the initial therapy for all other types of HES. Second line agents include IL-5 monoclonal antibodies (i.e., mepolizumab) to downregulate eosinophilic maturation and activation and hydroxyurea to suppress eosinophilopoiesis. Hematopoietic cell transplantation is utilized for refractory cases.

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Trinity Health Mid-Atlantic | Mercy Catholic Medical Center

Significant lipid and neutrophil accumulation and active inflammasome in high BMI tumor regions of human pancreatic ductal adenocarcinoma

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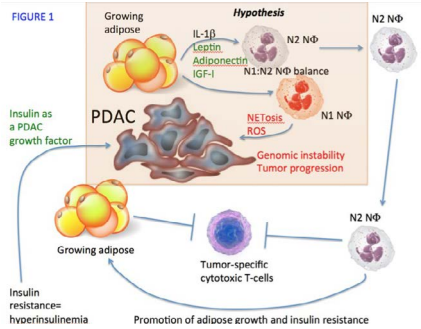
BACKGROUND

- Obesity is an established risk factor for cancer and cancer-related mortality. Adipocytes may act as a "damage" signal resulting in the accumulation of innate immune cells, or tumor-associated neutrophils (TANs), which fuel an inflammatory micro-environment.
- Obesity-driven adipose may fuel the progression of PDAC in a TAN and inflammasome-facilitated manner via several mechanisms, including genomic instability of aggressive PDAC clonal populations.



METHODS

- Tissue from resected tumors of PDAC patients (n=44) with a body-mass index (BMI) > 27 (obese [n=21]) and BMI< 22 (normal [n=23]) were incubated with anti-human CD66b and LipidTox antibodies and detected using standard immunofluorescent microscopy techniques

- There is a significantly greater density of adipocytes in the tumor environment, suggesting that these cells are acting as a damage signal
- High BMI results in a significantly higher neutrophil count in tumor specific tissue, suggesting an association between BMI and inflammasome accumulation in the tumor environment

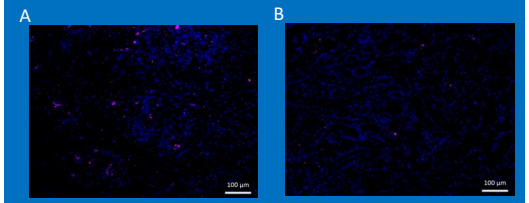
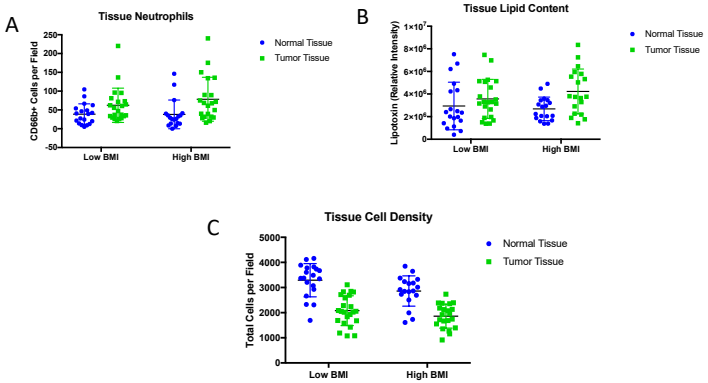


Fig 1: CD66b in Tumor (A) and Control (B) tissue

This study was made possible through a Johns Hopkins AHN Grant

RESULTS



A: Comparison of neutrophil accumulation by tissue type (p=0.0020)
B: Comparison of lipid accumulation by tissue type (p=0.0086)
C: Comparison of total cell count by tissue type (p=0.0001)

FUTURE DIRECTIONS FOR RESEARCH

- We are currently obtaining tissue from a novel PDAC mouse model to decipher the mechanism by which obesity-driven adipose tissue inside PDAC modulates the neutrophil phenotype to potentially drive tumor progression

MABs for TMAs: When Plasma Exchange Is Not Enough

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INTRODUCTION

Thrombotic microangiopathies (TMA) consist of syndromes with microangiopathic hemolytic anemia (MAHA) with shistocytes, thrombocytopenia, and microvascular thrombi.

TMA can have multiple etiologies including thrombotic thrombocytopenic purpura (TTP) or hemolytic uremic syndrome (HUS) which can be typical (*E. coli*-associated), secondary (malignancy, hypertension, drugs, autoimmune diseases), or complement-mediated.

Therapeutic plasma exchange (TPE) is often an early intervention while its ability can be limited in some cases.

This case series highlights the life-saving potential of various monoclonal antibody (mAb)-based therapies therapies in two different cases of TMA at our institution.

CASE 1

A 32-year-old woman presented with hematuria.

Thrombocytopenia with 5,000 platelets, anemic with hemoglobin of 8.3 g/dL along with frequent shistocytes on smear (Fig. 2a).

TPE was initiated and diagnosis of thrombotic thrombocytopenic purpura (TTP) made when ADAMTS13 returned <5%.

She appeared refractory after TPE, steroids, and rituximab (Fig. 3). Rituximab was continued weekly while addition of Caplacizumab led to resolution of MAHA and normal ADAMTS13 activity in 4 days.

She was continued on daily caplacizumab until one month after her last TPE date and remained without TTP recurrences at time of annual follow-up.

CASE 2

A 28-year-old woman presented with hypertensive emergency and transient stroke-like symptoms of right-sided weakness and expressive aphasia.

She was found to have microangiopathic hemolytic anemia with platelet nadir of 56,000. Few shistocytes were found on smear (Fig 2b).

A creatinine of 2.32 at presentation reached plateau of 4.20 mg/dL during her admission. Renal biopsy revealed evidence of thrombotic microangiopathy. Renal function was unchanged after two days of TPE.

Diagnosis of complement-mediated hemolytic uremic syndrome (atypical HUS) was suggested when other causes such as TTP and scleroderma were deemed unlikely. She received 2 days of TPE.

Eculizumab was administered and then continued as gene testing further supported aHUS (Fig 4). Functional and inhibitor complement studies were unremarkable.

Following six treatments, creatinine improved to 1.59 mg/dL, with plan to continue therapy using the long-acting ravulizumab.

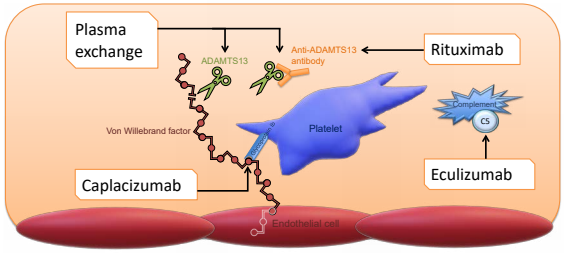

Figure 1. Sites of action of several treatment modalities as it relates to pathophysiology of TTP and CM-TMA

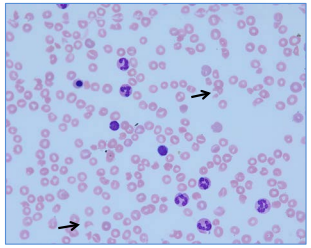

Figure 2a. Case 1 peripheral smear, noting frequent shistocytes/fragments among polychromatic and nucleated red blood cell forms.

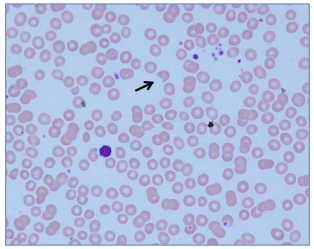

Figure 2b. Case 2 peripheral smear, noting few shistocytes

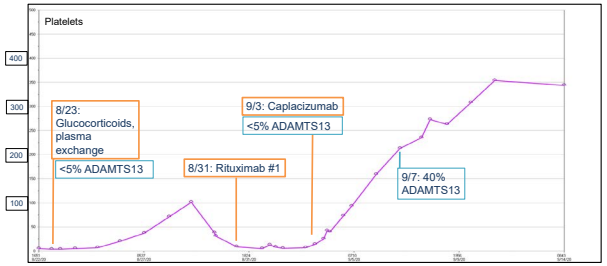

Figure 3. Platelet counts in relation to therapy and ADAMTS13 activity in Case 1

- Heterozygous missense exon 20 CFH (c.3143G>T, p.Cys1048Phe)
- Heterozygous missense exon 20 CFH (c.3004G>C, p.Gly1002Arg)
- Heterozygous missense exon 6 MASP2 (c.881C>T, p.Thr294Met)
- Heterozygous missense exon 7 CFHR5 (c.1067G>A, p.Arg356His)
- 3 polymorphisms in CFH
- 5 polymorphisms MCP/CD46 gene

Figure 4. The complement genetic findings for case 2

DISCUSSION

Therapeutic plasma exchange (TPE)

- TPE continues to have a role in the treatment of TTP, but limited in other causes such as complement-mediated (CM-)TMA[1]
- Even with TTP, patients can prove refractory to TPE as seen in case 1

Case 1 demonstrates successful and life-saving use of **rituximab** and **caplacizumab** for TTP

- When given early for an initial episode of TTP, rituximab has been found to reduce ICU stay by 7 days.[2]
- Caplacizumab lowered recurrence rate by 67% compared to placebo in the HERCULES trial.[3]
- The 2020 TTP guidelines by the International Society on Thrombosis and Hemostasis gives rituximab and caplacizumab a conditional (rather than strong) recommendation for use in first episode of TTP based on available evidence and cost of the medications. Caplacizumab can amount to $270,000 for an acute case of TTP.
- Most experts recommend early use of rituximab while reserving caplacizumab for high-risk TTP (based on PLASMIC score).[4]

Case 2 shows utility of **eculizumab** to improve and maintain renal function for CM-TMA

- Most patients with CM-TMA have been found to respond to eculizumab use, altering the historical 60-70% development of end-stage renal disease to 10%.
- Discontinuation of C5 complement inhibiting agents led to recurrence in about 50% in one of the larger studies.[1]
- Complement genetics may be utilized to identify those at higher risk for recurrence of CM-TMA, where variants of CFH and MCP had highest risk in one study (50%).[5] Given her higher risk, the patient in case 2 was transitioned to ravulizumab with long-term therapy plan.

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Recurrent Squamous Cell Carcinoma of the Skin – a Rare Side Effect of nilotinib

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Introduction

- Chronic myeloid leukemia (CML) is a type of myeloproliferative neoplasm and linked to translocation between chromosomes 9 and 22 resulting in the over expression of BCR-ABL gene, which increases cell proliferation
- Tyrosine kinase inhibitors (TKI) are the treatment of choice for CML as it selectively inhibits BCR-ABL
- Patients on TKIs have been shown to be at higher risk for secondary malignancies

Methodology

- Case review through electronic medical record
- Extensive literature review

Case Presentation

- 79-year-old male with CML who was on imatinib therapy for 10 years experienced disease progression to accelerated phase with WBC > 150,000 (7% blasts)
- Patient required hospitalization and therapy transition to dasatinib then subsequently to nilotinib due to dasatinib's cardiopulmonary side effects
- Bone marrow biopsy showed hypercellular marrow with myeloid hyperplasia
- Fluorescent in situ hybridization (FISH) confirmed BCR/ABL gene in 52.6% of cells
- Patient developed multiple skin lesions that were confirmed as squamous cell carcinoma (5 lesions over 7 months), requiring removal via Mohs microsurgery
- Current disease status is complete cytogenic response (CCyR) with major molecular response (MMR)

Discussion

- Nilotinib is a 2nd generation TKI that is known to have adverse reactions including vascular events (especially in patients with increased risk for cardiovascular disease) (1), psoriasis (2), thrombocytopenia, myalgia, headache (3), QT prolongation and hyperbilirubinemia (5)
- Development of secondary malignancies (SM) while on TKI over a 10-year period found that gastrointestinal, nose and throat cancers were more common in these patients (6)
- Interestingly, the most common nonhematologic adverse reaction with TKI involves the skin. These have been documented as skin pruritis and rash as well as occasional benign papillomas and panniculitis (4).
- The association of nonmelanotic skin cancers with nilotinib is rare as seen in this case and two others (see table 1 below)

Authors	Skin cancer history	Primary cancer	Duration of therapy before diagnosis	SCC characteristic	# of lesions	Treatment of SCC	Recurrence	Outcome
Crain, et al.	Nonmelanoma (SCC/BCC?)	CML (PHL +)	1 week	Keratoacanthoma-type SCC Well differentiated SCC	10	Electrodessication & curettage	Yes, after 1 month; repeat electrodessication & curettage	Good; Alternative CML therapy
Peters, et al.	Intraepithelial carcinoma; BCC (excised 2 years prior to Nilotinib)	CML (PHL +)	6 months	Well differentiated SCC	9	Systemic retinoid	None	Good; continued Nilotinib
Our paper	SCC BCC	CML (PHL +)	7 months	Well differentiated SCC	5	Mohs micrographic surgery/shaving	None	Good; continued Nilotinib

Conclusion

It is proposed that nilotinib induced BRAF inhibition may cause paradoxical activation of oncogenic Ras pathway in pre-disposed patients as ours, however further clinical investigation is recommended

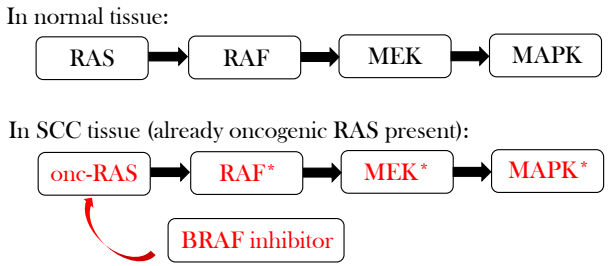

Figure 1. Outlining the pathway of activation of MAPK in normal tissue and SCC tissue

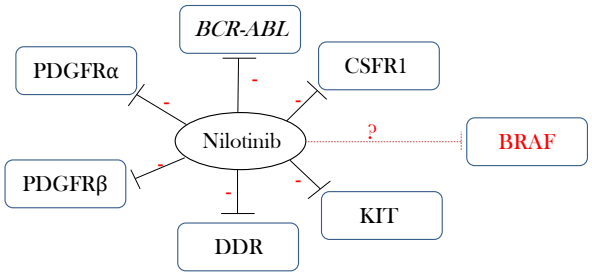

Figure 2. Mechanism of action of nilotinib

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Swelling of the Preauricular Area: An Unusual Case of T Cell Lymphoma

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Introduction

- T Cell Lymphoma or Peripheral T cell lymphoma is a type of aggressive non- Hodgkins lymphoma. Peripheral T cell lymphoma is the most common subtype.
- The lymphoma is characterized by an abnormal proliferation of malignant T cells.
- The most common extra nodular sites are the skin and gastrointestinal system. Patient can present with systemic B symptoms such as fever, night sweats, and weight loss.
- The purpose of this study is to look at an unusual presentation of T cell lymphoma and demonstrate a different take of diagnosis of this aggressive lymphoma.

Case Presentation

- **A 60 year old male with history of BPH and COPD presented to UPMC Carlisle with a 6 week history of induration and swelling to the preauricular area.**

Hospital Course

- The patient was transferred to UPMC Harrisburg for further work-up. At UPMC Harrisburg the patient's hospital course was complicated by persistent pancytopenia and febrile episodes while on broad spectrum antibiotics.
- Hematology-Oncology was consulted, and started the patient on Neupogen with resolution. IV antibiotics were discontinued as an infectious etiology was thought to be unlikely.
- Further areas of induration and swelling were noted on the left and right chest walls, which were similar to those seen on the preauricular area.
- Several biopsies were obtained and revealed subcutaneous panniculitis as would be seen in T-cell Lymphoma.
- Outpatient bone marrow biopsy confirmed diagnosis of T cell Lymphoma.
- Staging PET-CT was obtained to aid in prognostication and staging, revealing significant activity in the subcutaneous tissues and lymph nodes above the diaphragm.
- The patient was started on CHOP therapy and referred to Johns Hopkins University for eventual allogeneic stem cell transplant from the patient's biological

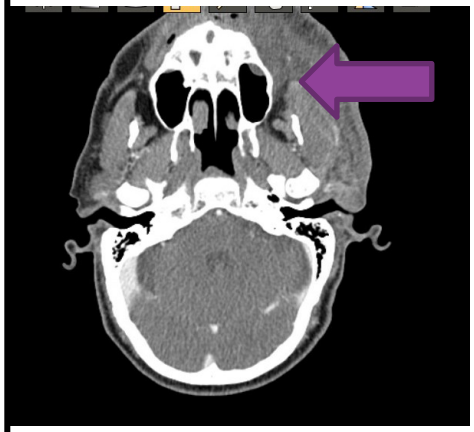

Figure 1: CT scan of the neck showing extensive skin thickening of the left side of the neck with inflammation of the parotid gland

Discussion

- T cell lymphoma commonly presents with lymph nodes in the skin and GI system
- Thereis no characteristic immunophenotype associated with this T cell lymphoma however T cell antigens (CD3, CD2, CD5, CD7) can be expressed.
- This atypical presentation highlights an unusual presentation and treatment of T cell lymphoma. This case identifies the importance of early evaluation and treatment in aggressive malignancies such as T cell lymphoma

Take Home Points

- T cell lymphoma may not always present with typical symptoms of night sweats, fever, and weight loss
- As this case demonstrates preauricular area swelling that is not otherwise explained may be a presenting sign.

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UPMC Pinnacle

Tumor Lysis Syndrome: Inpatient Outcomes amongst Non-Hodgkin Lymphoma patients

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Introduction

-Tumor lysis syndrome (TLS) occurs when tumor cells release their contents into the bloodstream either spontaneously or in response to therapy.

-causes hyperuricemia, hyperkalemia, hyperphosphatemia, and hypocalcemia

-more frequent in high-grade Non-Hodgkin Lymphoma (NHL) and acute leukemia

-less frequent in chronic leukemia and multiple myeloma

-We analyze inpatient outcomes, utilizing National Inpatient Sample, among patients with NHL that have been affected by TLS.

Methods

•ICD-10 codes for TLS and NHL queried in National Inpatient Database for 2017 – 18.

•Multivariate logistic regression performed STATA MP 16.1

•Confounding variables included in analysis – chemotherapy, stem cell therapy, neutropenia

•Primary outcome was inpatient mortality. Secondary outcomes were hospital length of stay and cost utilization.

Table 1 - Mortality

Inpatient Mortality	Odds Ratio	P Value	95% Confidence	Interval
Tumor Lysis Syndrome	2.729	0.000	2.354	3.162
Charlson Comorbidity Index	1.122	0.000	1.102	1.141
Hx of Smoking	0.771	0.000	0.706	0.842
Hx of Stem Cell Transplant	1.415	0.000	1.178	1.701
Hx of Neutropenia	1.326	0.000	1.156	1.521
Hx of Chemotherapy	1.006	0.924	0.891	1.136
Age	1.022	0.000	1.020	1.025
Gender (Female)	0.842	0.000	0.782	0.908

Table 2 – Length of Stay

Length of Stay	Coef.	P Value	95% Confidence	Interval
Tumor Lysis Syndrome	4.558	0.000	3.826	5.290
Charlson Comorbidity Index	0.298	0.000	0.261	0.335
Hx of Smoking	-0.648	0.000	-0.763	-0.533
Hx of stem cell transplant	0.897	0.000	0.432	1.362
Hx of neutropenia	4.011	0.000	3.592	4.429
Hx of chemotherapy	-0.799	0.000	-0.971	-0.628
Age	-0.014	0.000	-0.020	-0.009
Hospital Teaching Status	1.249	0.000	1.099	1.398

Table 3 – Total Hospital Charge

Total Charge ($)	Coef.	P Value	95% Confidence	Interval
Tumor Lysis Syndrome	90427.000	0.000	76027.660	104826.300
Charlson Comorbidity Index	2588.639	0.000	1899.282	3277.995
Hx of Smoking	-9068.683	0.000	-11351.740	-6785.630
Hx of Stem Cell Transplant	32004.440	0.000	17369.260	46639.620
Hx of Neutropenia	58776.370	0.000	48610.330	68942.410
Hx of Chemotherapy	-11506.220	0.000	-15748.580	-7263.848
AGE	-569.181	0.000	-677.651	-460.711
Gender (Female)	-4268.410	0.000	-6219.687	-2317.134
Hospital Teaching Status	22917.710	0.000	18850.750	26984.670

Results

•Total NHL patients – 7540; 34% female; mean age for patients with TLS – 62.5 years and mean LOS – 13 days. Mean LOS in NHL without TLS – 7 days.

•NHL patient with TLS had higher odds of mortality – (Odds Ratio (OR) 2.73, 95% Confidence Intervals – 2.35 – 3.16) (Table 1).

•NHL patients with TLS had higher LOS by 5 days (4.6, 95% CI 4.39 – 5.20) (Table 2).

•NHL patients with TLS also had a higher total charge - $90,427 (95% CI 76027 – 104826) (Table 3).

Conclusions

- TLS affects outcomes in NHL patients admitted in the hospital.
- This includes an increase in inpatient mortality, hospital length of stay and total hospital charge.

Outcomes of malignant pleural effusions in patients with Lung Cancer

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Introduction

- Malignant pleural effusion is present in more than 15% patients at time of diagnosis of lung cancer.
- Median survival - 4.3 months.
- Management - mostly palliative but helps lower hospital stay and inpatient mortality.
- Aim of this study is to identify inpatient mortality in patients with malignant pleural effusion

Methods

- ICD-10 codes for Lung cancer and malignant pleural effusions (MPE) identified from the NIS database (2016-2018).
- Multivariate logistic regression performed in STATA MP 16.1.
- Confounding variables accounted for in the analysis - previous chemotherapy, history of weight loss, smoking and neutropenia.
- In addition, Charlson-comorbidity index was also utilized.
- Primary outcome was inpatient mortality. Secondary outcomes were hospital length of stay and cost utilization.

Table 1 – Factors affecting Inpatient Mortality

Inpatient Mortality	Odds Ratio	P Value	95% Confidence	Intervals
Malignant Pleural Effusion	2.014	0.000	1.900	2.136
Charlson Comorbidity Index	1.077	0.000	1.068	1.085
History of Coronary Artery Disease	0.815	0.000	0.780	0.852
History of Congestive Heart Failure	1.129	0.000	1.075	1.187
Diabetes Mellitus	0.763	0.000	0.730	0.798
Hypertension	0.910	0.000	0.876	0.945
Smoking History	0.794	0.000	0.766	0.823
Obesity	0.715	0.000	0.661	0.773
Acute Kidney Injury	3.117	0.000	2.994	3.245
History of Chemotherapy	0.843	0.000	0.795	0.895
Neutropenia	1.159	0.003	1.053	1.275
Weight Loss	0.738	0.000	0.632	0.861
Weekend Admission	1.184	0.000	1.137	1.233
Age	1.002	0.050	1.000	1.003
Gender (Female)	0.860	0.000	0.830	0.891

Table 2 – Factors affecting Hospital Length of Stay

Length of Stay	Coefficient	P Value	95% Confidence	Intervals
Malignant Pleural Effusion	1.262	0.000	1.120	1.404
Charlson Comorbidity Index	0.169	0.000	0.155	0.183
History of Heart Failure	0.567	0.000	0.470	0.665
Obesity	0.612	0.000	0.495	0.728
Acute Kidney Injury	1.804	0.000	1.701	1.906
Neutropenia	0.878	0.000	0.682	1.074

Results

- Total patients with MPE – 51,747, 48% female. Mean age – 69 years and mean LOS - ~7 days
- Hospitalizations in year 2016 – 15950, 8.7% mortality rate
- Hospitalizations in year 2017 – 17100, 8.4% mortality rate
- Hospitalizations in year 2018 – 18620, 8.6% mortality rate
- Patients with MPE had higher odds of mortality among patients with lung cancer [Odds Ratio (OR) 2.01 (1.90 – 2.14)]
- Additional factors contributing to mortality include – increasing Charslon-comorbidity index, history of heart failure, acute kidney injury, history of neutropenia, increasing age and weekend admissions.
- Patients with MPE had higher hospital length of stay by 1.3 days [1.26 (1.12 – 1.4)]
- Patients with MPE had higher hospitalization charge by $14,111 (12,012 – 16,210)

Conclusion

Patients with a history of lung cancer that present to the hospital with malignant pleural effusion have higher odds of inpatient mortality, hospital length of stay and total cost. Efforts need to be put to manage these patients in a timely and effective manner to improve outcomes.

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Impact of venous thromboembolism in patients with Hepatocellular Carcinoma

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Introduction:

- Patients with cancer are prone to thromboembolism (VTE). In hepatocellular carcinoma (HCC) VTE rates are increased due to a hypercoagulable state from malignancy and cirrhosis.
- We analyzed National Inpatient Sample (NIS) to understand the burden of VTE in patients with HCC.

Results:

- 73,600 patients with HCC also had VTE; 38% were females. Mean age was 65 years.
- Average hospital length of stay was 9 days for patients with VTE and 6 days for those without VTE.
- HCC patients with VTE had higher odds of mortality [1.51, 95% Confidence Interval (1.28 – 1.77)]; patients with concomitant AKI had higher odds of mortality [5.08 (4.73 – 5.45)].
- VTE patients had higher length of stay - ~3 days [2.7, (2.2 – 3.3)].
- VTE patients also had a higher total hospital charge [$50967 (31204 – 70731)].

Methods

- Data obtained from NIS Database (2016 – 18).
- ICD-10 codes for diagnosis of HCC and VTE utilized.
- STATA MP 16.1 used for multivariate regression analysis
- Primary outcome was inpatient mortality. Secondary outcome was hospital length of stay and total hospital charge.
- Data was considered statistically significant if p-value was <0.05.

Inpatient Mortality	Odds Ratio	P Value	95% Confidence	Intervals
Venous Thromboembolism	1.507	0.000	1.280	1.775
Acute Kidney Injury	5.078	0.000	4.730	5.452
Gender (Female)	0.865	0.000	0.805	0.929
Teaching Hospital Status	0.768	0.000	0.708	0.833
Length of Stay	**Coef.**	**P Value**	**95% Confidence**	**Intervals**
Venous Thromboembolism	2.770	0.000	2.212	3.330
Acute Kidney Injury	2.853	0.000	2.666	3.041
Gender (Female)	0.275	0.000	0.139	0.411
Teaching Hospital Status	0.987	0.000	0.846	1.128
Total Charge	**Coef.**	**P Value**	**95% Confidence**	**Intervals**
Venous Thromboembolism	50967.99	0.000	31204.47	70731.51
Acute Kidney Injury	48517.72	0.000	43804.05	53231.39
Teaching Hospital Status	26046.93	0.000	22526.23	29567.62

Conclusion:

- Patients with hepatocellular carcinoma that develop venous thromboembolism have higher odds of inpatient mortality, increased length of stay and subsequent total hospital cost.
- It is important to consider these patients for prophylaxis for thromboembolism.