AIPNO

Second Research Showcase 2014

CITY OF CLEVELAND
Mayor Frank G. Jackson

November 1, 2014

Dear AAPI Members:

On behalf of the people of Cleveland, I am honored to welcome you to Cleveland for the annual AAPI dinner, in which it is always a pleasure to participate.

Cleveland serves as a leader in the health industry from the biomedical field to world-renowned hospitals and health care, making it the perfect location to host the 2017 National Convention of AAPI. I am certain that the Global Center for Health Innovation and the Cleveland Convention Center's successful event management combined with our state-of-the-art facilities and amenities will meet the needs of the members of your national convention. Cleveland has the best cost structure compared to larger cities and provides all the amenities of a major metropolitan area. The Local Chapter, Association of Indian Physicians of Northern Ohio, is very active in helping the community and its leadership is committed to hosting the AAPI convention in Cleveland.

The City's Health Tech Corridor is the first of its kind nation-wide and is home to major institutions like Cleveland Clinic Foundation, University Hospitals, and the Case Western Reserve Lerner School of Medicine as well as small start-up medical tech and innovation companies. Cleveland is also home to other major hospitals, such as MetroHealth System and Sisters of Charity Health System.

Located on the beautiful shores of Lake Erie, Cleveland is a vibrant, diverse and growing city with a rich history and world-class attractions. There are several conveniently located hotels and tourist attractions such as the Rock and Roll Hall of Fame, Science Center, Cleveland Horseshoe Casino and several museums in the vicinity of the Convention Center. These venues are sure to provide entertainment for the members of the convention and their guests. Cleveland also has the second largest theater district in the country and boasts the world famous Cleveland Orchestra. Our fine dining in unique neighborhoods like Little Italy and Ohio City and wonderful nightlife of East 4th Street and the Warehouse District will provide something for everyone to enjoy.

On behalf of the City of Cleveland, I would again like to welcome you here for this event as well as encourage you to host the 2017 Convention of AAPI in Cleveland. I hope you are drawn to all that we have to offer and will share in the experiences that are uniquely Cleveland.

Sincerely,

Frank G. Jackson, Mayor

ABSTRACT and POSTER RESEARCH

Iodide mumps: A rare case of contrast induced sialadenitis after fistulogram in an end stage renal disease patient

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Introduction:

Iodide mumps or contrast induced acute sialadenitis is characterized by the rapid, painless enlargement of the parotid and submandibular glands following the use of iodinated compounds. The pathogenesis of this adverse reaction remains unclear. It may be due to an idiosyncratic reaction or related to toxic accumulation of iodide in the ductal systems of the salivary glands.[1] The onset of symptoms can start within a few minutes to five days after contrast administration.[2] The course of iodine-induced sialadenitis is usually benign, and rapid resolution of symptoms is expected without definite treatment. The symptomatic management includes parenteral non steroidal anti-inflammatory drugs (NSAIDs), steroids and dialysis.[3]

Case:

We report a case of 65 years old African American female, end stage renal disease on hemodialysis 3 times/ week, presented in the emergency room with complaint of facial and upper neck swelling, one day after fistulogram.

The past medical history was significant for increasing right arm swelling for last 2-3 weeks and inability to access right arm AV fistula for dialysis. A dialysis permacath was placed in left subclavian vein for access. A fistulogram was performed to check the patency of the AV fistula with visipaque® (Iodixanol), a non-ionic iodine containing contrasts media. It showed stenosis at the junction of right subclavian and superior venacava (SVC). Balloon angioplasty was performed and repeat fistulogram showed good resolution of stenosis with less than 10% remaining. The patient was stable in PACU post procedure and went home without immediate complication.

The next day she woke up with lower facial and upper neck swelling. The patient did not have any signs of SVC obstruction including superficial venous prominence on chest, arm edema, cyanosis and plethoric face. She also denied any hoarseness of voice, difficulties in breathing but complained of pain during mouth opening. Nifedipine was stopped for suspicion of drug induced angioedema.

Bilateral tender submandibular glands were noted on examination (Images 1&2). CT of the neck and face showed enlarged bilateral submandibular glands with infiltration of adjacent fat planes and diffuse soft tissue swelling in submandibular region and upper neck (Image 3&4, CT scan).

Initial labs including CBCD, CMP, electrolytes and acid-base were essentially normal except elevated WBC count of 11,000 but no bandemia. BUN and Cr values were also high commensurate with ESRD. The patient was started on unasyn on day 1 for a possible infective cause of sialadenitis. It was stopped next day as there were no signs of infection including fever, chill, tachycardia and no pus discharge from submadibular duct.

A diagnosis of contrast induced sialadenitis was made and patient was started on IV ketorolac, decadron, fluid and pain management. Emergency intubation kit was prepared at bedside for possible airway compromise which was not required. Hemodialysis was done within 24 hours of admission and the submandibular swelling improved significantly in next 2-3 days. The patient was discharged in a stable condition on oral tapering dose of prednisone for 2 weeks.

Discussion:

Visipaque® (Iodixanol) is a non-ionic iodine containing contrast media favoured for its iso-molar properties. With normal renal function, 97% is excreted unchanged in urine within 24 h.[2,3] The risk for sialadenitis is directly related to serum iodide levels (> 10 mg/100 mL) and inversely related to normal renal function.[2,3] With increasing renal dysfunction, the elimination half-life is prolonged. Our patient was at an increased risk because of her end-stage renal failure. The delay in dialysis for the first 24 h after fistulogram might have contributed further in pathogenesis. There are also a few published case reports of pancreatic mumps and transient thyroid dysfunction; whose etiology thought to be similar to iodide induced sialadenitis. Our patient did not have any of these symptoms including thyroid swelling, abdominal pain, back pain and nausea and vomiting. Amylase, lipase, TSH and free T4, T3 were essentially normal.

Role of steroids in the management of contrast induced sialadenitis has been found to be controversial in published case reports. Usual prophylactic regimens for iodide allergy were also ineffective in a previous case report proving it more idiosyncriatic reaction than hypersensitivity.[4] The reaction is probably a class effect, because substituting one form of low-osmolar nonionic contrast media for another did not prevent recurrences of the condition. The way to prevent recurrence of iodide mumps is to avoid using intravenous iodinated contrast in those patients again or urgent dialysis within 24 hours if the use of iodinated dye is absolutely essential.[5] There is absolutely no role of antibiotic in the management of iodide mumps as the elevated WBC count is always reactive in nature.

References

1. Shacham Y[1], Havakuk O, Roth A. A rare case of acute contrast-induced sialadenitis after percutaneous coronary intervention. Isr Med Assoc J. 2013;15:652-3.
2. Alkaied H, Harris K, Azab B, Odaimi M. A complete resolution of sialadenitis induced by iodine containing contrast with intravenous dexamethasone infusion. Clin Med Insights Gastroenterol. 2012;5:61-3.
3. Christensen J.Iodide mumps after intravascular administration of a non-ionic contrast medium. Case report and review of the literature. Acta Radiol 1995;36:82-84.
4. St Amour TE, McLennan BC, Glazer HS. Pancreatic mumps: a transient reaction to IV contrast media (Case report). Am J Roentgenol 1986;147:188-189.
5. Moisey RS[1], McPherson S, Wright M, Orme SM. Thyroiditis and iodide mumps following an angioplasty. Nephrol Dial Transplant. 2007;22:1250-2.

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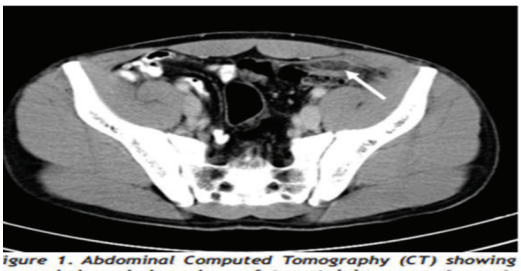
Epiploic appendigitis a rare case of abdominal pain

A 54 years old female with a background history of hypertension, SVT, frequent UTI, and thyroid dysfunction on levothyroxine presented to the emergency department with 3 days history of LUQ abdominal pain, and worsening low back and left flank pain. It came on suddenly and was sharp stabbing, non-radiating, non-migratory pain 8/10 in severity , getting worse couple hours after eating food. No other symptoms. review of systems otherwise unremarkable. On physical examination she was overweight with central obesity (BMI of 32), appeared uncomfortable and grimacing in pain. She was afebrile and hemodynamically stable. Her abdomen did not show signs of localized peritonism except mild left upper and mid abdomen tenderness on deep palpation. She complained of dull ache around the left lower lumbar area over the erector spine, but no muscle or bony tenderness.

Blood test did not show leukocytosis, except mild elevation of monocyte, normal electrolyte. Liver and renal function tests were within normal limits. Chest and abdominal radiograph were performed, which did not show any evidence of infection , pneumoperitoneum, or bowel obstruction . Further radiological investigation was performed with a computed tomography (CT) scan of the abdomen and pelvis with and without contrast showed a focal area of fat stranding surrounding the mid descending colon compatible with epiploic appendagitis. There was a normal appendix. She was admitted for overnight observation and treated nonoperatively with analgesia, intravenous fluids and bowel rest. She was discharged home with an oral analgesia and anti-inflammatory agent.

Epiploic appendagitis is a self-limited condition secondary to torsion or thrombosis of the epiploic appendages, usually followed by inflammation. The clinical findings are non-specific, leading to frequent misdiagnosis situations. On the other hand, the Computed Tomography (CT) features of epiploic appendagitis are quite typical and well described. Therefore, physicians should consider the diagnostic role of CT in this under diagnosed challenging disease.



igure 1. Abdominal Computed Tomography (CT) showing n oval-shaped, hypodense fat-containing mass (arrow), ith surrounding fat stranding, suggesting epiploic ap-endagitis.

Reference

http://www.gastrores.org/index.php/Gastrores/article/viewFile/422/475

http://www.ejgm.org/upload/sayi/20/EJGM-00443.pdf

Uptodate.com

Extramedullary Hematopoiesis in a patient with Myelodysplastic Syndrome

Introduction :
Extramedullary hematopoiesis (EMH) is the formation of hematopoietic tissue outside the bone marrow as a compensation of bone marrow dysfunction. It has been seen in conditions such as myelofibrosis, thalassemia, hereditary spherocytosis, polycythemia rubra vera, multiple myeloma and certain other malignancies. EMH in patients with myelodysplastic syndrome is a very rare association. We present a rare case of an 85 years old man with a history of myelodyplastic syndrome/myeloproliferative Neoplasm (MDS/MPN) as per WHO (World health organization) classification who presented with an asymptomatic right sided abdominal mass which was later found to be EMH on biopsy.

Case Description :
A 85-year-old man diagnosed with MDS/MPN eight years ago and being managed with erythropoietin (EPO) injections presented with a large asymptomatic abdominal mass on the right side which was incidentally found by his wife. Imaging studies were done to further investigate the mass. Abdominal positron emission tomography (PET) scan showed a hypermetabolic 17 x 13 x 11 cm mass in the right retroperitoneal region along with multiple moderately hypermetabolic soft tissue masses in the left and right paraspinal regions in the thoracic cavity; findings that were suspicious for primary abdominal malignancy. Computed tomography (CT) scan guided biopsy of the mass was done which showed a mixture of hematopoietic cells with scattered megakaryocytes consistent with EMH. Due to concern that the main production of red blood cells in the body was coming from the mass and that radiating it could cause harm to the patient by removing the source of production, it was decided to not radiate the mass. Instead, the patient is being managed conservatively with treatment focused on MDS. EPO injections are being continued.

Conclusion :
MDS/MPN are clonal myeloid disorders that possess both dysplastic and proliferative features but are not classified as either MDS or chronic myeloproliferative disorders (CMPD). EMH is the formation and maturation of blood cells occurring outside the medulla of the bone marrow, commonly in the liver, spleen and lymph nodes, but may occur in unusual locations such as retroperitoneal region as in this case. To the best of our knowledge, only 2 cases(1) have been reported of patients with MDS on EPO injections developing EMH. Furthermore, in these cases the EMH resolved completely after withdrawal of EPO. Other treatments include low dose radiation(3), frequent blood transfusions(3) and hydroxyurea(2). Surgery is generally avoided due to the risk of massive bleeding and high recurrence rates. We decided not to treat the mass aggressively and instead followed the patient with current medical management; the patient continued to do well at his 6 month follow up visit. On clinical exam, the mass had significantly reduced in size. It is important to know that EMH need not always be aggressively treated, in certain cases it can be followed and managed conservatively especially in patients who are asymptomatic.

Inter-professional Evidence Based Care of Hospitalized Patients with and at Risk for Sleep Apnea Improves Care Quality

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Purpose:
The project goal was to enhance healthcare outcomes for hospitalized patients with and at-risk for sleep apnea (SA) by increasing the ability of hospital nurses to asses for known SA, identify SA risk, and design appropriate nursing care management using an inter-professional care guideline.

Background/Significance
Hospital prevalence of SA is estimated to be 80%, yet only 6.8% are reported, and 5.8% of patients on home therapy continue treatment during hospitalization. Adverse hospital outcomes including increased length of stay, cardio-respiratory failure, and death are associated with untreated SA. Validated SA screening tools and care guidelines are available but have not been widely adopted. Educating nurses on SA assessment, screening, and evidence-based care guidelines can improve patient outcomes.

Methods
An educational intervention to the care team of a monitored care unit at a community hospital consisted of an a)overview of SA diagnosis, treatment, impact on patients' health, and hospitalized patient outcomes, b)rationale for screening for SA diagnosis and continued hospital use of home PAP, c) use of the STOP-Bang questionnaire, and d) use of an inter-professional evidence-based SA care management guideline. The Obstructive Sleep Apnea Knowledge and Attitude (OSAKA) assessment was administered to the care team pre/post intervention and 30-days post implementation of the care guideline. Patient length of stay, unplanned transfer, death, and 30-day readmission were monitored for 90-days.

Results
The intervention was attended by 41 care team members, 3o completed the Pre/Post OSAKA. Paired t-test showed significant increase in OSAKA scores post educational intervention for knowledge, attitude and confidence that was retained 30-days post implementation of the care guideline. One-way ANOVA showed no correlation between staff type, years of practice or education level and OSAKA scores. Of the 104 patients screened, 67.8% were identified as high SA risk, (21% with known SA), and 32% low SA risk . PAP therapy was received by 100% of those identified on home PAP compared to 5.5% prior to the intervention. The ALOS was shortest for the SA group (2.6 days), compared to 3.28 days (high risk) and 2.74 days (low risk). The 30-day readmission rate for the SA group was 0%, high risk/10%, and low risk 14%. No unplanned transfers to higher acuity of care or death occurred during the 90-day pilot. Identification of known SA pre-intervention was 5.5% and 21% post.

Conclusions and Implications for Practice:
Implementing and sustaining quality improvement changes designed to improve SA patient outcomes will require inter-professional collaboration led by the hospital nurse. Education provides a means to bridge the current care gap and enhance healthcare outcomes in this vulnerable patient population. National and local policy directing the care of this vulnerable population is recommended.

Title:
Inter-professional Evidence Based Care of Hospitalized Patients with and at Risk for Sleep Apnea Improves Care Quality

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Severe and Prolonged Hypocalcemia Following Zoledronic Acid Therapy In Patient With Malignant Hypercalcemia.

Introduction: Zoledronic acid (ZA) is a new long-acting bisphosphonate that has been shown to be more effective than other bisphosphonates in treating hypercalcemia of malignancy. It is important to be aware of its ability to induce prolonged and severe hypocalcemia following administration, which can be difficult to control despite aggressive calcium replacement. We report a patient with metastatic breast cancer who presented with severe symptomatic hypocalcemia after receiving ZA for hypercalcemia of malignancy.

Case Presentation: A 51-year-old female with recently diagnosed stage-IV breast cancer with metastases to axial skeleton and liver, presented with polyuria and was found to have hypercalcemia of malignancy with a calcium (ca) level of 22 mg/dl. Her surgical history was significant for parathyroidectomy for primary hyperparathyroidism. Her other laboratory values included elevated PTHrp of 14 pmol/L (<2pmol/L) and low PTH of 10 pg/ml (15-65pg/ml). She was treated with intravenous (IV) fluids and was given a 3.3 mg dose of IV ZA. 6 weeks following ZA treatment, the patient presented with tingling, numbness all over the body and carpopedal spasm of her upper extremities. Her labs were significant for Ca of 5.2 mg/dl, ionized Ca of 0.74 mmol/L, magnesium of 1.1 mg/dl, and potassium of 2 mmol/L. Serum 25 (OH) D level was very low (5.9 ng/ml) consistent with vitamin D deficiency; PTHrp was 2.2 pmol/L and PTH of 180 pg/ml suggestive of secondary hyperparathyroidism due to vitamin D deficiency and hypocalcemia. She was started on a slow continuous calcium infusion after being given 2 grams of IV calcium and was monitored in the intensive care. She required 6-12 grams of IV calcium daily in addition to high doses of oral calcium (up to 3.375 grams), despite potassium and magnesium repletion for 10days. Following this she was discharged home on 5g IV calcium, 100 mEq of Kcl and 2 grams of magnesium daily for 4 weeks along with Vitamin D 50,000 units three times a week. Subsequently after 4 weeks off of calcium and vitamin D supplementation, she presented again with hypercalcemia of malignancy (Ca of 16.6mg/dl) with PTHrP of 44pmol/L. She was given pamidronic acid 60 mg IV; this time she did not develop hypocalcemia as vitamin D levels were replete.

Discussion: This case illustrates the importance of identifying and treating vitamin D deficiency in patients with metastatic cancer. In this case, vitamin D deficiency together with administration of ZA, lead to severe life threatening hypocalcemia. Physicians managing hypercalcemia of malignancy should be aware of the severe side effect profile of ZA, and screen all patients for vitamin D deficiency prior to initiating therapy. We also recommend using a lower potency bisphosphonate such as pamidronic acid, especially in patients who previously developed severe hypocalcemia with ZA.

Title: Role of hormonal manipulations in delaying the progression of LAM. A 16-years follow-up report after oophorectomy.

INTRODUCTION: Lymphangioleiomyomatosis (LAM) is a slowly progressive lung disease that leads to respiratory failure over one to two decades. It is exclusively seen in women and is characterized by progressive proliferation of smooth muscle-like cells (LAM cells) in lung parenchyma and causes cystic destruction, chylous pleural effusions and recurrent pnuemothoraxes. LAM has historically been considered an estrogen dependent tumor and was treated with hormonal manipulation strategies such as antiestrogens, antiprogesterones and oophorectomy. Current insights into the pathophysiology of LAM have provided new treatment drugs such as sirolimus, a mTOR inhibitor, that is effective in stabilizing lung function. Since the advent of novel therapies, hormonal manipulation strategies have become less popular. We describe a case of LAM in a young woman who underwent oophorectomy and was followed closely for 16 years without worsening of her lung function.

PRESENTATION: A 49-year-old female was referred to our institution in 1996 for recurrent pneumothoraxes. Computed tomography of the chest demonstrated (Figure 1) numerous cystic lesions uniformly scattered throughout the lung. A subsequent lung biopsy confirmed the histologic diagnosis of LAM (Figure 2). Pulmonary function tests showed FEV1 of 2.68 L, FVC of 4.56 L, TLC of 6.18 L and a DLCO of 21.3. She had a 15 yr history of smoking and her other comorbitities included asthma and uterine leiomyoma. She was subsequently treated with hysterectomy and oophorectomy. Sixteen years following the surgery, she remained asymptomatic and serial PFTs done over the same time period interestingly did not show progressive worsening of her lung function. Her most recent PFTs in 2013 showed FEV1 of 2.25 L. She did not receive any targeted therapy and is not requiring supplemental oxygen at rest or during exertion.

DISCUSSION: LAM is a rare multisystem disease of women that targets the lung. There are several features of LAM that suggests its estrogen dependency such as its propensity to affect females, occurrence before menopause, and worsening respiratory function during pregnancy[1]. Estrogen and progesterone receptors expression is seen in LAM cells[2,3].
Although novel agents have shown promise in controlling symptoms[4], they are associated with drug toxicity and development of resistance, and never been tested in RCTs in direct comparison with hormonal manipulation. In this report we hope to demonstrate that oophorectomy might still be beneficial in certain subset of patients with LAM.

References

1.Li C, Zhou X, Sun Y, et al. Faslodex inhibits estradiol-induced extracellular matrix dynamics and lung metastasis in a model of lymphangioleiomyomatosis. AmJ Respir Cell Mol Biol. 2013 Jul;49(1):135-42.

2. Baldi BG, Medeiros Junior P, Pimenta SP, et al. Evolution of pulmonary function after treatment with goserelin in patients with lymphangioleiomyomatosis. J Bras Pneumol. 2011 May- Jun;37(3):375-9.

3. Yu JJ, Robb VA, Morrison TA, et al. Estrogen promotes the survival and pulmonary metastasis of tuberin-null cells. Proc Natl Acad Sci USA. 2009 Feb 24;106(8):2635-40.

4. McCormack FX, Inoue Y, Moss J, et al. Efficacy and safety of sirolimus in lymphangioleiomyomatosis. N Engl J Med. 2011 Apr 28;364(17):1595-606.

Cleveland Clinic

An interesting case of a large gastric polyp removal

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CASE

- A 75-year-old female with persistent nausea and vomiting along with abdominal pain was referred from an outside hospital on an endoscopy finding of a large gastric polyp.
- Past medical history was significant for hypertension, coronary artery disease, hypothyroidism and hyperlipidemia.
- The medications included metoprolol, lisinopril, furosemide, levothyroxine and pravastatin.
- We repeated an upper endoscopy at the Beth Israel Deaconess Medical Center and noticed a pedunculated polyp which appeared to be 9 cms in size and was prolapsed into the duodenum.
- We used a grasping forceps to pull the polyp into the stomach.
- We injected 4 cc of 1:10,000 epinephrine into the polyp.
- A 25 mm hard snare was used to resect the pedunculated polyp. The settings were zero cut and 18 coag.
- Three resolution clips were placed prophylactically on the base of the polyp.
- The resected polyp was retrieved using an endoscopic net.
- On pathology, the polyp was noted to be an inflammatory fibroid polyp.
- The patient did well. There were no complications and there was no recurrence of the polyp one year later.

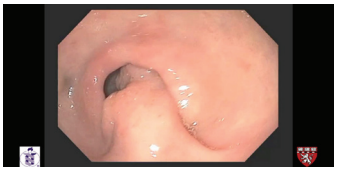
Image 1 – Gastric Polyp

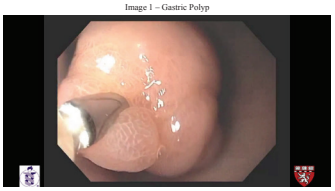
Image 2 – Grasping Forceps used to grasp the polyp

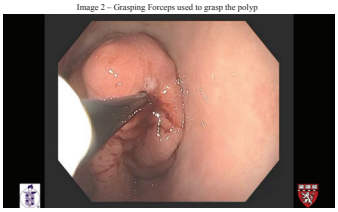
Image 3 – Injection of 1:10,000 Epinehprine

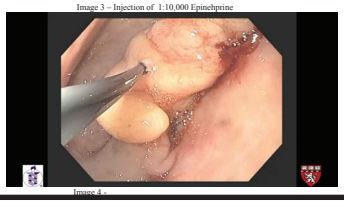
Image 4 –

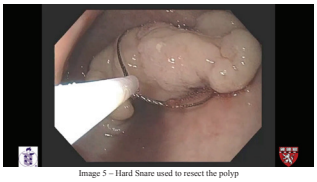
Image 5 – Hard Snare used to resect the polyp

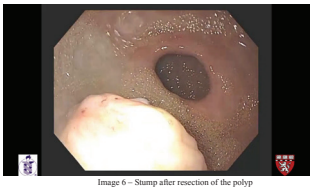
Image 6 – Stump after resection of the polyp

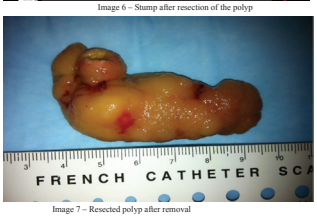

Image 7 – Resected polyp after removal

Pro-angiogenic remodeling of extracellular matrix by TGF-beta

Muppala S, Frolova EG, Krukovets I, Plow EF, Stenina-Adognravi O

Extracellular matrix (ECM) plays an important role in cardiovascular functions, including angiogenesis. TGF-β induces angiogenesis and is known as an important regulator of ECM in tissue remodeling. However, specific molecular mechanisms controlling ECM composition and angiogenesis in response to TGF-β are still poorly understood. We report a novel molecular mechanism that controls remodeling of the extracellular matrix and angiogenesis in response to TGF-β.

We discovered for the first time that TGF-β stimulation dramatically increases TSP4 production (up to 10 fold) in cultured microvascular endothelial cells (EC). Thrombospondin 4 (TSP4), an ECM protein, regulates cell-cell and cell-matrix interactions. Recent reports highlight the importance of TSP4 in cardiovascular tissue remodeling and inflammatory responses, but specific stimuli leading to its upregulation still remain unknown.

Our functional *in vitro* assays revealed that microvascular EC from WT mice had increased migration (up to 80% increase), adhesion (up to 40% increase) and proliferation (up to 40% increase) in response to TGF-β stimulation compared to unstimulated cells, but TSP-4 KO (*Thbs4*$^{-/-}$) cells did not have any increase in the migratory, adhesive and proliferative capacity in response to TGF-β stimulation when compared to unstimulated cells. These data suggest that increased TSP4 levels mediate the effects of TGF-β on angiogenesis. *Thbs4*$^{-/-}$ cells demonstrated significantly reduced migration (90% of WT cell migration, p=0.00008), adhesion (30% of WT cells adhesion, p=0.01), and proliferation (80% of WT cell proliferation, p=0.000005), highlighting the role of TSP4 in these processes. Consistent with the *in vitro* data, *in vivo* experimental results demonstrated that TSP4 is pro-angiogenic: TSP4 KO mice had decreased angiogenesis (65% decrease, p=0.025) compared to WT mice in the Matrigel plug angiogenesis assay.

In conclusion, we have identified TSP4 as a novel regulator of angiogenesis and found the first stimulus upregulating TSP4 production - TGF-β. The novel TGF-β/TSP4 pathway that regulates angiogenesis connects TGF-β and TSP4, suggests new therapeutic targets for regulation of TGF-β-induced angiogenesis, provides new insights into mechanisms of regulation of angiogenesis by ECM, and emphasizes the role of an ECM protein, TSP4, in angiogenesis.

Propofol versus traditional sedative agents for Advanced Endoscopic Procedures: A Meta-analysis

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BACKGROUND

- The optimum method for sedation for advanced endoscopic procedures (EUS, ERCP and Small Bowel Enteroscopy) is not known.
- Propofol sedation [PS] has a faster recovery time than conscious sedation, but may be associated with increased complication rates.
- Several studies have compared the efficacy and safety of MAC with conscious sedation; however, the results of these individual studies have been inconclusive.

AIMS

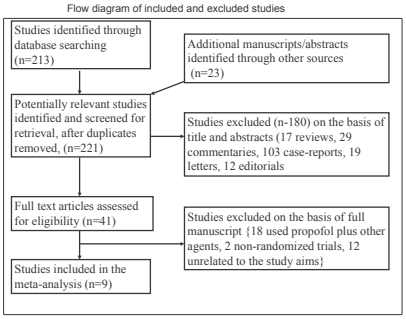
- To systematically pool all available studies to compare the efficacy and safety of PS with traditional sedative agents (TSA) for advanced endoscopic procedures

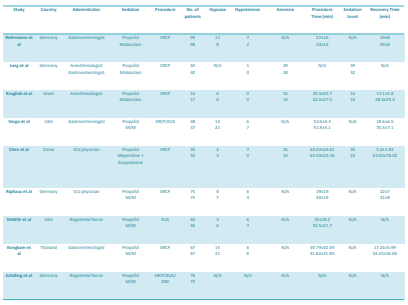
METHODS

- SEARCH STRATEGY:
  - EMBASE, PUBMED, Cochrane Central Register of Controlled Trials
  - Search terms: Propofol, traditional sedative agents, endoscopic ultrasonography, small bowel enteroscopy, randomized controlled trials
- ELIGIBILITY:
  - RCTs in patients>= 18 years who underwent small bowel enteroscopy, published as full articles or meeting abstracts in peer-reviewed journals
  - Studies that examined the efficacy and safety of PS and TSA for advanced endoscopic procedures;
  - Studies in humans; and
  - Data not duplicated in another manuscript.
- STATISTICAL ANALYSIS:
  - Review Manager (RevMan version 5.1).
  - Fixed or random-effect methods, depending on the absence or presence of significant heterogeneity.
  - $\chi 2$ test and I^2 to assess heterogeneity
  - $P < 0.1$ or $I2 > 50\%$ - significant heterogeneity.
  - Results expressed as odds ratios or mean differences with 95% CI. $P < 0.05$-statistically significant.

RESULTS

Flow diagram of included and excluded studies





RESULTS

FIGURE 1: Forest plot of meta-analysis comparing procedure time during PS and TSA for Advanced Endoscopy Procedures

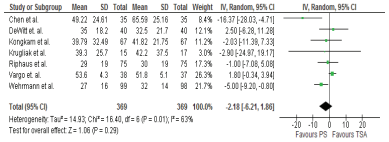


FIGURE 2: Forest plot of meta-analysis comparing recovery time during PS and TSA for Advanced Endoscopy Procedures

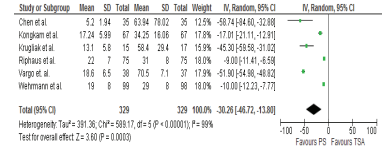
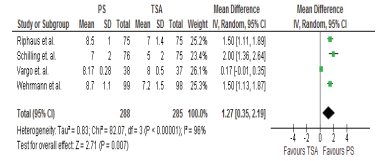
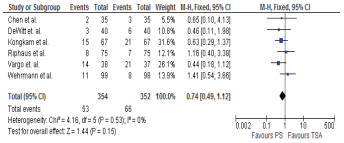


FIGURE 3: Forest plot of meta-analysis comparing patient cooperation during PS and TSA for Advanced Endoscopy Procedures

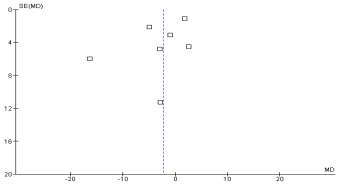


RESULTS

FIGURE 4 : Forest plot of meta-analysis comparing hypoxia during PS and TSA for Advanced Endoscopy Procedures



Funnel plot of trials of propofol sedation and traditional sedative agents for Advanced Endoscopy Procedures



CONCLUSIONS

- **MAC for advanced endoscopic procedures is associated with shorter recovery time, better sedation and amnesia level without an increase in risk of cardiopulmonary complications.**
- **The overall patient cooperation is also improved with propofol sedation**

Temporal trends in endoscopic retrograde cholangio-pancreatography (ERCP) in USA over the last 18 years

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BACKGROUND

- The introduction of non-invasive imaging for biliary and pancreatic diseases has changed the indications and volumes of endoscopic retrograde cholangiopancreatography (ERCP) over time.

AIMS

- The aim of this study was to evaluate nationwide trends in the utilization of diagnostic and therapeutic ERCP over the last 18 years.

METHODS

- Retrospective cohort study.
- Nationwide Inpatient Sample (NIS) database was used to calculate the rate for ERCPs performed from 1993 to 2010.
- .NIS is the largest publicly available all-payer inpatient care database in the United States.
- It contains data from approx. 8 million hospital stays each year.
- Statistical significance of the difference in the number of hospital discharges, length of stay and hospital costs over the study period was determined by chi-square test for trend.
- The specific ICD-9-CM codes utilized are as follows: ERCP (51.10, 51.11, 52.13, 52.92), ERCP with placement of a nasobiliary or nasopancreatic tube (51.86, 52.97), ERCP with stone extraction (51.88, 52.94), ERCP with dilation of the ampulla, biliary, or pancreatic duct (51.84, 52.98), ERCP with stent placement in either the biliary or pancreatic duct (51.87, 52.93), ERCP with sphincterotomy and papillotomy (51.85), ERCP with brushings and/or biopsies (51.14, 52.14), ERCP with excision of a lesion within the biliary or pancreatic duct (51.64, 52.21, 51.69), and ERCP with manometry (51.15).
- Diagnostic ERCPs were defined as ERCP (51.10, 51.11, 52.13, 52.92), ERCP with brushings and/or biopsies (51.14, 52.14), and ERCP with manometry (51.15).
- Therapeutic ERCPs were designated as all other diagnostic codes listed above.

RESULTS

FIGURE 1:

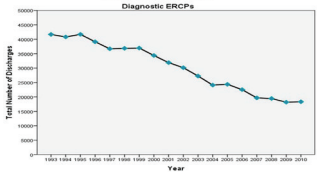


FIGURE 2:

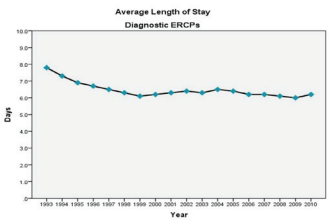
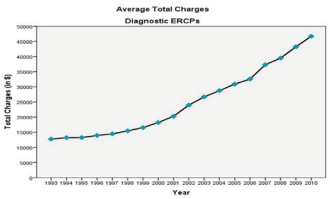


FIGURE 3:



RESULTS

FIGURE 4:

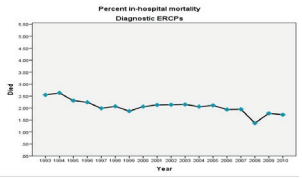


FIGURE 5:

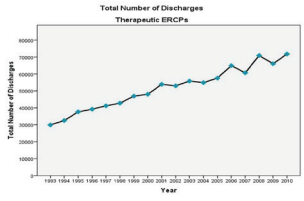
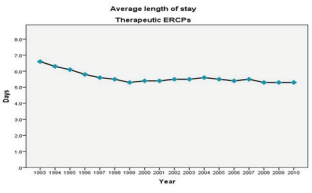


FIGURE 6:



RESULTS

FIGURE 7 :

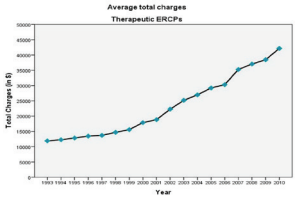
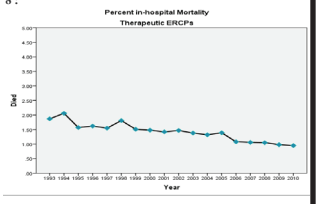


FIGURE 8 :



CONCLUSIONS

- **There has been a steady decline in the utilization of diagnostic ERCPs from 1993 to 2010.**
- **However, the number of therapeutic ERCPs has increased over the same time duration**
- **The cost associated with both diagnostic and therapeutic ERCPs has increased significantly.**
- **The mean length of hospital stay was higher for diagnostic ERCP c.f. therapeutic ERCP in 2010 (6.2 cf. 5.3 days)**
- **The inpatient mortality rate has decreased for both diagnostic and therapeutic ERCP but was higher for diagnostic ERCP as compared from therapeutic in 2010 (1.72 vs 0.95 %)**

Bilateral Renal Infarction Associated to Oxaliplatin-based chemotherapy for Colon carcinoma: A Case Report

Introduction:

Renal infarction (RI) is an uncommon condition resulting from a sudden disruption of blood flow in the renal artery. RI is frequently misdiagnosed or diagnosed late because of its rarity and frequently nonspecific clinical presentation, which may result in irreversible damage to the renal parenchyma or an increase in the risk of other embolic events affecting other organs. Several reports investigating its clinical effects have suggested that most patients have atrial fibrillation, valvular heart disease and risk factors for thromboembolic events including protein C&S deficiency[1]. Oxaliplatin has been associated with renal failure/toxicity but till date, there has been no reported case of bilateral renal infarction in a patient treated with oxaliplatin. The only study that remotely mentioned of a cause and effect relation was by Khushalani et al[2]. In this study oxaliplatin in addition to a protracted-infusion of fluorouracil was used in the treatment of esophageal cancer,a patient who was not able to continue with oxaliplatin therapy because he developed renal arterial infarction. We report an unusual case of bilateral renal infarction in a patient receiving oxaliplatin.

Case Report:

A 62 year old male presented to emergency department after developing right flank pain at the time of 6th cycle of oxaliplatin infusion. He was diagnosed with colon cancer with liver metastasis in November 2012 and completed 12 cycles of FOLFOX (Folinic acid, Fluorouracil, Oxaliplatin) without Bevazizumab from cycle 8 because of exploratory laparotomy, subtotal colectomy, intraoperative ultrasound and partial liver resection. He was restarted again on FOLFOX every 3 weeks because of positive margins after 6 weeks of initial 12 cycles of FOLFOX. His past medical history included left breast carcinoma on tamoxifen since November 2012 and left lower extremity DVT (deep vein thrombosis) being treated with coumadin since January 2013. He had a similar episode of right flank pain 3 weeks ago while he was receiving 5th cycle of oxaliplatin infusion. During previous admission, his INR was 2.3, urine analysis was only positive for minimal red blood cells. Computer tomography (CT) of abdomen showed bilateral renal infarction (Figure 1). EKG (Electro cardiogram) revealed sinus rhythm. He was discharged home on coumadin, and no identifiable cause for renal infarction was found. He remained pain free until current admission with 6 th cycle of oxaliplatin infusion. During the current admission, his vitals were noted; pulse rate - 57, blood pressure - 168/92, temperature - 98 F. Physical examination was unremarkable except for right costovertebral angle tenderness. His INR was 1.8. He had no intracardiac thrombus by transesophageal echocardiogram. He had negative lower extremity DVT and renal artery duplex. CT abdomen with contrast showed new wedge shaped infarct in upper pole of right kidney infarcts involved 25% right renal parenchyma and 10% of left renal parenchyma (Figure 2). His creatinine was 0.9 mg/dl with GFR more than 60. FOLFOX was discontinued. Subsequently, He was started on FOLFIRI (folinic acid, 5-flurouracil, Irinocetan)/Bevacizumab for new liver lesion without developing any further flank pain. He remained free from flank pain during last 8 months of follow up visits.

Discussion:

Oxaliplatin a platinum derived alkylating agent**,** is approved by FDA only for colorectal cancer. However, it is used in other cancers as well. It is highly protein bound and metabolized non-enzymatically into active and inactive metabolites excreted primarily through the kidneys[3]. Like most chemotherapy agents, oxaliplatin causes common side effects like, nausea, vomiting, diarrhea, neutropenia and thrombocytopenia[4,5]. Dose limiting toxicity includes neurotoxicity, gastrointestinal toxicity, hematologic toxicity[5,6]. Cisplatin, also a platinum based chemotherapy drug, has been associated with increased arterial thromboembolic events. However, this association is based on case reports and retrospective studies[7]. The mechanisms by which cisplatin triggered vascular events is unknown, but endothelial damage seemed to play a major role[7,8].

Cases of oxaliplatin causing renal toxicity have been reported[9,10] even though they are rare. Possible causes of renal failure from oxaliplatin include dehydration, high doses, acute tubular necrosis and induced intravascular hemolysis[9,11]. Our patient was treated with FOLFOX. During cycle 6, oxaliplatin therapy was stopped because the patient developed second episode of severe flank pain which was confirmed as bilateral renal infarction by CT scan of abdomen. He had two similar episode of bilateral renal infarction during oxaliplatin infusion and no further episode for more than 8 months after discontinuation of oxaliplatin, this support a possible cause effect relation between oxaliplatin and renal infarction.Bevacizumab is less likely to be the cause of renal infarction in this case,as the patient tolerated FOLFIRI/Bevacizumab without recurrence of renal infarction.Physicians should be aware of this potential complication of oxaliplatin.

References:

1. Chung SD, Yu HJ, Huang KH. Bilateral Renal Infarction. Urology. 2009 Feb;73(2):273-4
2. Khushalani NI, Leichman CG, Proulx G, et al. Oxaliplatin in combination with protracted-infusion fluorouracil and radiation: report of a clinical trial for patients with esophageal cancer. J Clin Oncol. 2002 Jun 15;20(12):2844-50.
3. Koutras AK, Makatsoris T, Paliogianni F, et al. Oxaliplatin-induced acute-onset thrombocytopenia, hemorrhage and hemolysis. Oncology. 2004, 67(2):179-182.
4. Taleghani BM, Meyer O, Fontana S, et al. Oxaliplatin induced immune pancytopenia. Tranfusion. 2005 May;45(5):704-8
5. Saif MW, The A, Ledbetter L. Oxaliplatin-mediated autoimmune thrombocytopenia.Clinical Colorectal Cancer. 2009 Jan;8(1):61-2.
6. Oxaliplatin. Lexi-Comp, Inc. (Lexi-Drugs). Lexi-Comp, Inc.; April 14, 2013.
7. FERNANDES, D. D. et al. Acute aortic thrombosis in patients receiving cisplatin-based chemotherapy. Current Oncology, [S.l.], v. 18, n. 2, p. e97-e100, Apr. 2011. ISSN 1718-7729.
8. Dieckmann KP, Gehrckens R. Thrombosis of abdominal aorta during cisplatin-based chemotherapy of testicular seminoma—a case report. *BMC Cancer* 2009;9:459.
9. Pinotti G, Martinelli B. A case of acute tubular necrosis due to oxaliplatin. Ann Oncol. 2002; 13: 1951–1952
10. Abaye J, Sarret D, Duvic C, et al. Renal toxicity of oxaliplatin. Nephrol Dial Transplant. 2005; 20:1275-1276.
11. Ulusakarya A, Misra S, Haydar M, et al. Acute renal failure related to oxaliplatin-induced intravascular hemolysis. Med Oncol. 2010; 27:1425-1426.

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