ST. VINCENT CHARITY MEDICAL CENTER

JOURNAL

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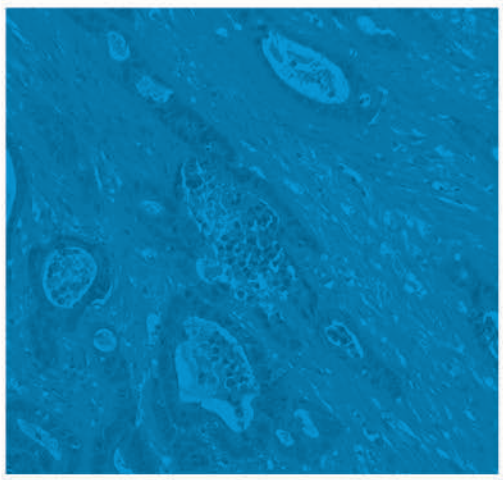

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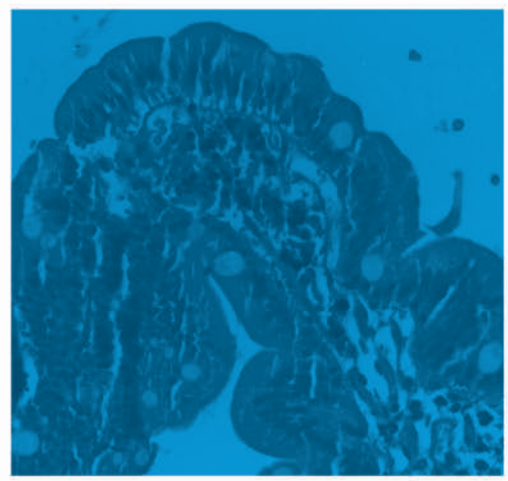

ST. VINCENT CHARITY MEDICAL CENTER JOURNAL
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ST. VINCENT CHARITY
MEDICAL CENTER

The St. Vincent Charity Medical Center family is committed to the healing mission of Jesus. We serve with: a deep respect for the dignity and value of all persons; our practice of quality care; our dedication to the poor; and, our commitment to education. St. Vincent Charity Medical Center, with the commitment of its Caregivers and physicians, will be a leading model for healthcare delivery in Northeast Ohio based on its faith-based mission, dedication to education, commitment to the communities it serves, excellence in the patient experience it provides, focus on surgical services, and partnerships with physicians and other constituencies.

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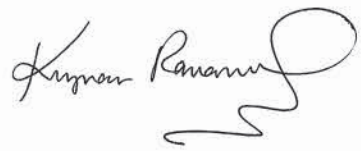
A MESSAGE FROM THE EDITOR

I was suffering from chronic shoulder pain so I saw a physician who I trusted and knew was competent and knowledgeable. She needed an image of my shoulder to make the diagnosis. She offered CT or MRI. It was a no-brainer, MRI was the answer. I did not want to expose myself to radiation. It causes cancer. I have been preaching about it, discouraging my patients from unnecessary exposures. As a matter of fact we recently reviewed articles on radiation and cancer relationship.

Then I asked myself, why do we have these CT machines every where? Why do we offer them to our patients? Do we really need a CT machine in every ED, urgent care center, and outpatient and inpatient facilities? I am aware, we can argue that for a few diagnoses, here and there, CT is better than other modalities, but do we ask our patients if they want to take a significant risk and jeopardize their safety? I doubt so and I doubt if they would have gone with the test if they knew the risk-benefit ratio.

Ok, you want to talk about the cost! MRI is much more expensive, but why? Who determined the price? It is not a new technology anymore. A flat-screen, 60-inch TV is $700 today compared to $10,000 10 years ago. How come MRI machine and the tests prices are not dropping?

A Miami children's hospital will soon list the price of their services, some not all, since insurance company contracts prohibit them from listing. Regardless, maybe this is a beginning for us to ask these questions and help to change our healthcare ourselves.



Keyvan Ravakhah, MD, MBA, FACP
Editor in Chief

We want to hear from you. Send your feedback to researchjournal@stvincentcharity.com

Immediate Post-Operative Results of Total Ankle Replacement using the S.T.A.R. at St. Vincent Charity Medical Center

By **Michael B. Canales, DPM, FACFAS and Duane J. Ehredt Jr, DPM**

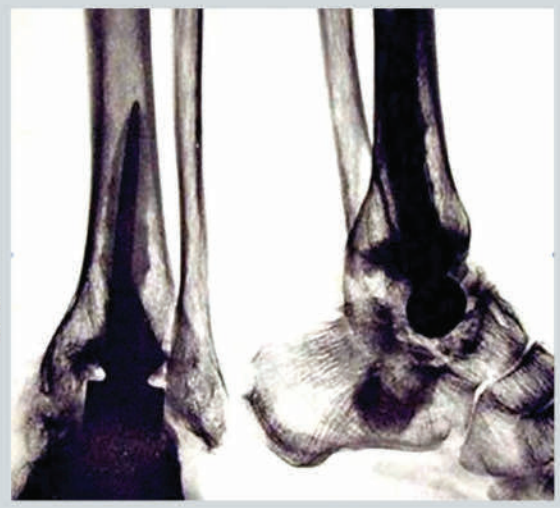


Figure 1: Radiographic imaging of the first total ankle arthroplasty utilizing an inverted hip prosthesis in 1970.

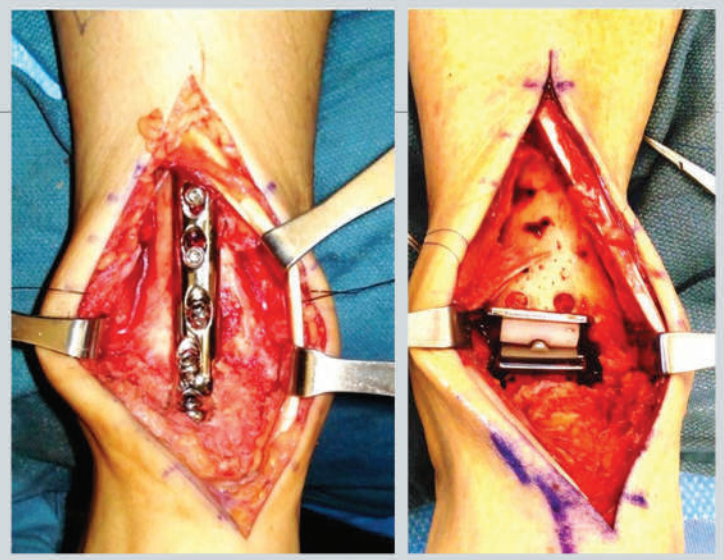
LEARNING OBJECTIVES

1. To introduce and review total ankle replacement as a treatment option for the painful arthritic ankle
2. To become familiar with the radiographic parameters for proper prosthetic implantation

ABSTRACT

End-stage ankle arthritis is a debilitating condition that is frequently treated at our hospital. Total ankle replacement is considered an acceptable alternative to ankle arthrodesis for patients suffering from symptoms of ankle arthritis. Numerous studies have been completed on the Scandinavian Total Ankle Replacement (S.T.A.R.) (Small Bone Innovations, Inc., Morrisville, PA), with favorable mid- and long-term results. Immediate post-operative implant placement parameters have been established. Five consecutive patients have undergone total ankle replacement with the S.T.A.R. system at St. Vincent Charity Medical Center (SVCMC). The angular parameters of our patient cohort have been compared to the published biomechanical angles indicating proper placement. To date, all cases performed at our institution are in line with the acceptable range for proper prosthetic placement, thus suggestive of probable long-term success.

Figure 2: Intra-operative perspective of ankle arthrodesis (left) versus total ankle arthroplasty (right).



INTRODUCTION

Osteoarthritis of the ankle joint is a debilitating condition that is familiar to the experienced foot and ankle surgeon. Arthritis of the ankle negatively impacts an individual's quality of life as much as arthritis of the hip (1) and congestive heart failure (2). It is estimated that by age 47, 8% of the American population will have evidence of this painful condition, and by age 76, 20% of the American population will suffer of this ailment (3). The prevalence of painful ankle arthritis is considerably less than the prevalence of those who suffer from hip and knee arthritis. The hip and knee are prone to primary osteoarthritis. In contrast, the ankle typically develops arthritis secondary to a traumatic event such as a fracture of the ankle. Consequently, ankle arthritis is predominantly post-traumatic in nature (4).

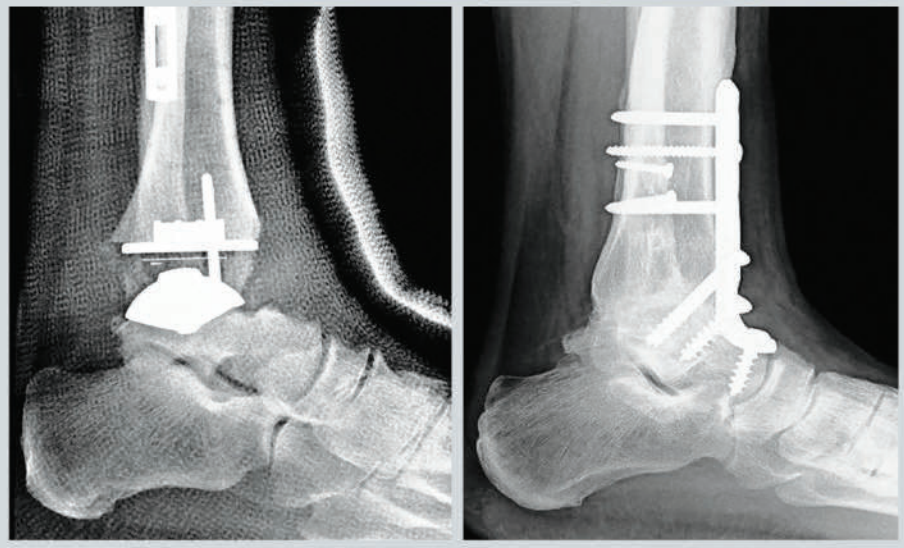


Figure 3: Post-operative plain film radiographs of ankle arthrodesis (left) versus total ankle arthroplasty (right).

Traditionally, the mainstay of treatment | continued on p.10

Pseudomelanosis Duodeni

A Rare Finding from Upper Gastrointestinal Endoscopy

By **Abdelle Ferdinand, MD; James Boyle, MD; and Carrie Bassett, DO**

LEARNING OBJECTIVES

1. Recognize the endoscopic characteristics of pseudomelanosis duodeni
2. Recognize the associated clinical conditions related to pseudomelanosis duodeni

INTRODUCTION

Melanosis of colon is a commonly encountered entity in routine screening colonoscopy. However, pseudomelanosis duodeni (PD) is a very rare condition, in which dark pigment accumulates in the duodenal mucosa. It has been found to be associated with systemic diseases, such as hypertension, chronic renal failure and diabetes mellitus. Medications have also been commonly associated, with the most frequent being anti-hypertensives. Endoscopically, it is manifested as peppery speckles in the duodenal mucosa. We present a case of pseudomelanosis duodeni found incidentally during esophagogastroduodenoscopy (EGD).

CASE PRESENTATION

A 69-year-old African American female patient was admitted and being treated for an acute chronic obstructive pulmonary disease exacerbation. After having a CT scan of abdomen for an unrelated reason, she was referred for evaluation of a 1.5cm mass abutting the head of the pancreas and the duodenum. She denied having any abdominal pain, jaundice, pruritis, steatorrhea, hematochezia, melena or weight loss. Her past medical history was significant for chronic obstructive pulmonary disease, coronary artery disease, hypertension, Type II diabetes, peripheral vascular disease, Stage III chronic kidney disease, seizure disorder, depression and osteoarthritis. She was a chronic smoker of 1 pack per day for 53 years. Her daily medications included claritin, advair, clonazepam, imdur, nitroglycerin, cardura, plavix, spiriva, lantus insulin, norvasc, zocar, dilantin, clonidine, oscal, prozac, and hydralazine. Her family history was significant for leukemia in her father, melanoma in her mother, gastric cancer in her grandfather and multiple female relatives with breast cancer.

Vital signs revealed a blood pressure 162/62mmHg; pulse 84 beats per minute; temperature 37°F; respiratory rate 18 breaths per minute; pulse oximetry 93% on room air. There was periorbial edema but no scleral icterus. There was no palpable lymphadenopathy. Abdominal examination revealed an obese abdomen with a healed open cholecystectomy scar; it was soft, non-tender, non-distended, with no organomegaly or palpable masses. The laboratory findings revealed hemoglobin of 10.2 g/dL and hematocrit of 32.7%; MCV was within normal limits; BUN was 21 and creatinine was 1.2 with a GFR of 52; liver function tests were within normal limits with the exception for albumin of 2.8.

The patient underwent an EGD, as well as a colonoscopy for further evaluation. EGD revealed a small hiatal hernia and uniform speckling of dark brown pigment throughout the duodenum (Figure 1). Colonoscopy revealed mild diverticulosis and internal hemorrhoids; colonic mucosa had normal pink color without any melanosis.

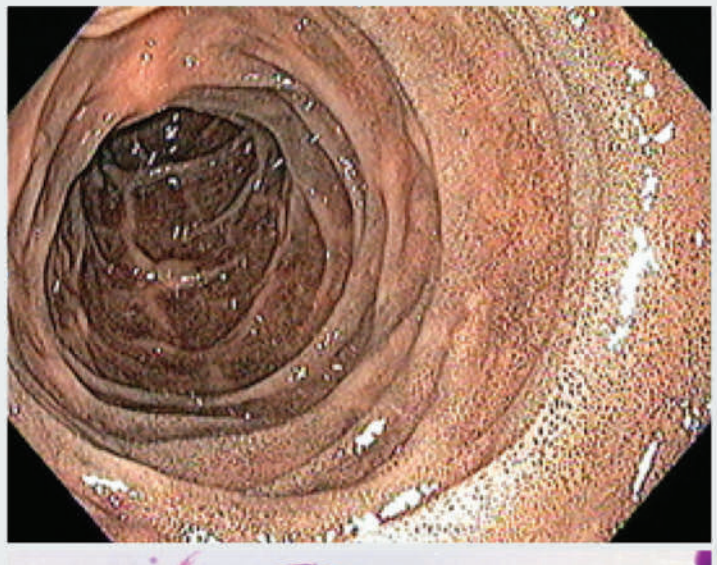


Figure 1: Endoscopic view of the proximal duodenum shows fine dark spots typical of pseudomelanosis duodeni

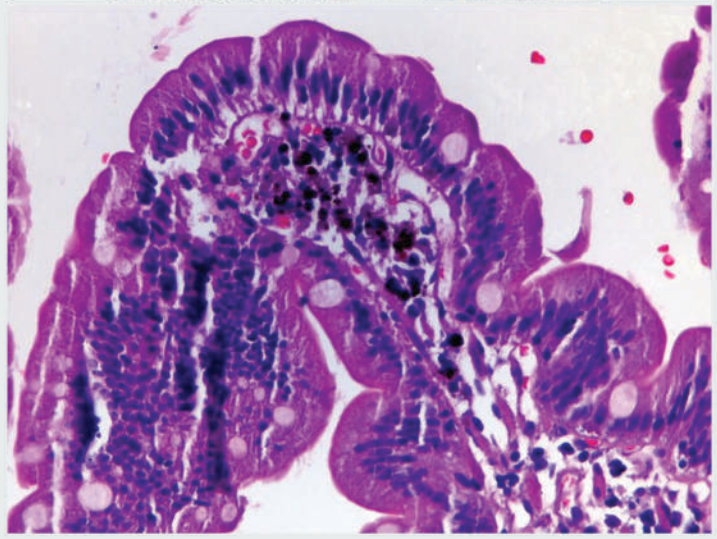


Figure 2: Duodenal villi showing brownish-black pigment located within the apical portion of the villi

DISCUSSION

Pseudomelanosis duodeni is an extremely rare, benign condition in which the duodenum has multiple, flat, discrete, black, brown or slate gray pigmented spots that are usually <2mm. Bisordi and Kleinman first described the phenomenon in 1976 [1]. The term pseudomelanosis is a bit of a misnomer, as the pigment is not produced by melanocytes, which are not found in the gastrointestinal tract. The source of the pigment and the mechanism by which the duodenal mucosa is selectively susceptible to pig-

| continued on p.12

Gastric Perforation in a Patient with Non-Small Cell Lung Cancer Treated with Bevacizumab

By **Fazel Dinary, MD; Basel Altaqi, MD; and Keyvan Ravakhah, MD**

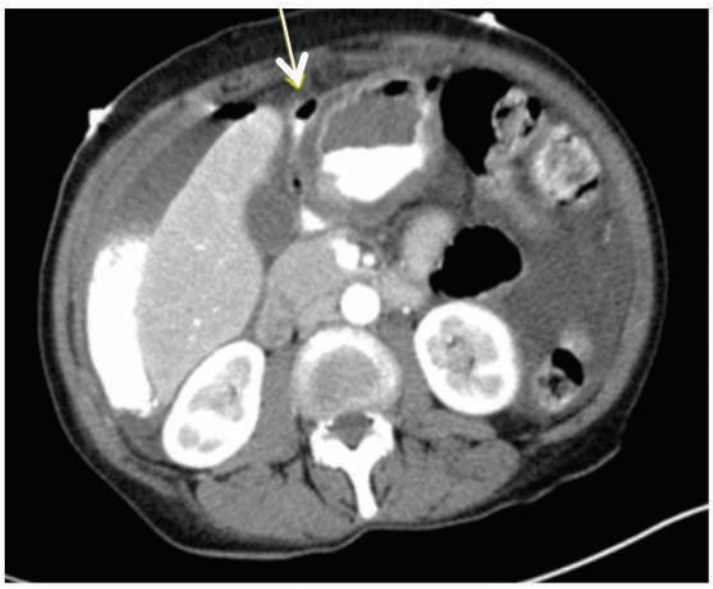


Figure 1: CT Abdomen/ pelvis with oral and IV contrast: Demonstrating anterior air-fluid level involving free fluid and free air anterolateral to the liver.

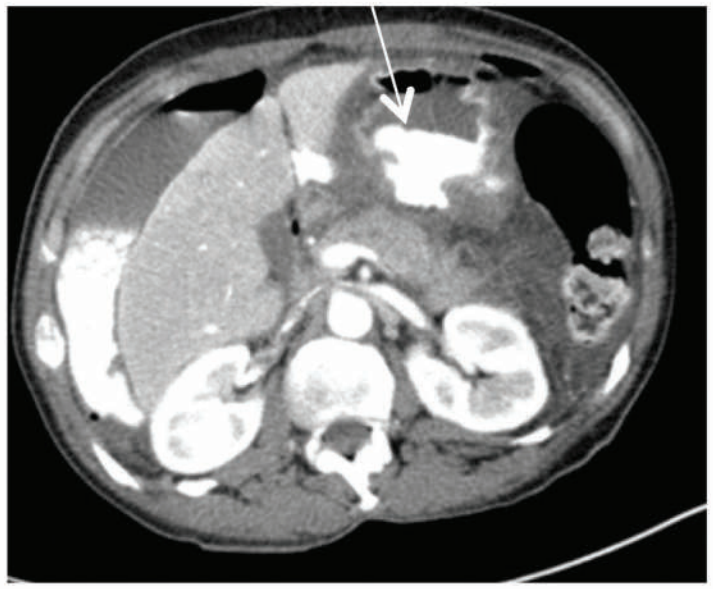


Figure 2: Extraluminal Contrast leak from Stomach presented immediately posterior to the lateral Segment of the left lobe of liver.

LEARNING OBJECTIVES

1. To recognize the life-threatening complications associated with Bevacizumab use
2. To introduce and review the associated clinical conditions and risk factors for gastrointestinal perforation related to Bevacizumab

INTRODUCTION

GI metastasis and perforation in patients with non-small cell lung cancer is rare. Bevacizumab has emerged as new therapy in the treatment of metastatic non-small cell lung cancer. Viscous perforation associated with its use has been described in colon and ovarian cancers. The exact mechanism by which perforation occurs is under debate, and many theories exist. In this report, we present the first known case of stomach perforation in a patient with metastatic non-small cell lung cancer after treatment with Bevacizumab.

CASE PRESENTATION

Six months ago, a 53-year-old female was diagnosed with metastatic non-small cell lung cancer (NSCLC) involving the hilum and upper lobe of the left lung, T12 vertebral body, right hip, and lower back soft tissue. She initially presented with cough, hemoptysis, and a 30-pound weight loss.The patient's medical history was significant for chronic obstructive lung disease, hypertension, and hypercholesterolemia. She was a lifetime smoker. Her family history was significant for a mother with lung cancer.

Bronchoscopy with transbronchial biopsy confirmed moderate to poorly differentiated adenocarcinoma. Immunohistochemistry stains were positive for EGFR mutation. A bone scan demonstrated area of increased tracer uptake within the sternum, posterior aspect of the calvarium, thoracic spine, involving T8 and T12, lumbar spine at L2 and L3, acetabular regions of the pelvis bilaterally. These activities were seen diffusely throughout the diaphysis of the left tibia and the medial malleolus in the right ankle. There was no evidence of cord compression on magnetic resonance imaging of the spine, and magnetic resonance imaging of the brain was negative for metastatic disease. Because of the clinical, radiographic, and pathologic findings, the patient was thought to have an undifferentiated NSCLC.

The bone lesions were asymptomatic, therefore radiotherapy was not begun. Two weeks after diagnosis, chemotherapy with Carboplatin, Paclitaxel (200 mg/m2), and Bevacizumab (15 mg/kg) was initiated on a 3-weekly schedule. Zoledronic acid was given monthly. CT scans after the second cycle demonstrated stable disease. Bevacizumab 15mg/kg every 3 weeks was continued. After 9 weeks of therapy, the patient developed severe abdominal pain, nausea and vomiting. On physical examination, she was febrile (temperature of 102° F) with abdominal tenderness. Radiography demonstrated free intraabdominal air (Figure 1-2). She underwent laparoscopic procedure which revealed a 2 cm perforated ulcer near the incisures along the lesser curve. Postoperatively, the patient recovered on broad spectrum | continued on p.12

Lipomatous Hypertrophy of Interatrial Septum (LHIS) presenting with Atrial Arrhythmias

By **Sushruth Edla, MD; Ahmed Elsherbiny, MD; Raktim Ghosh, MD; Keyvan Ravakhah, MD**

INTRODUCTION

Lipomatous Hypertrophy of the Interatrial Septum is a rare but increasingly recognized lesion in the heart.It is usually a benign condition where surgical resection is generally not recommended. Occasionally, LHIS may present with atrial arrhythmias or right atrial obstruction where surgical resection may become necessary.

CASE DESCRIPTION

A 60-year-old Caucasian woman with past medical history of chronic obstructive pulmonary disease (COPD) and diabetes mellitus presented to the emergency room complaining of shortness of breath and productive cough for the last five days. Her vital signs on admission were a temperature of 36.9 °c, blood pressure of 115/64 mmHg, Pulse Rate of 100 and Respiratory Rate of 20. On physical examination she was alert and oriented, had prolonged expiration, decreased breath sounds and mild rhonchi bilateral, her heart was irregularly irregular and pulses were full and equal.

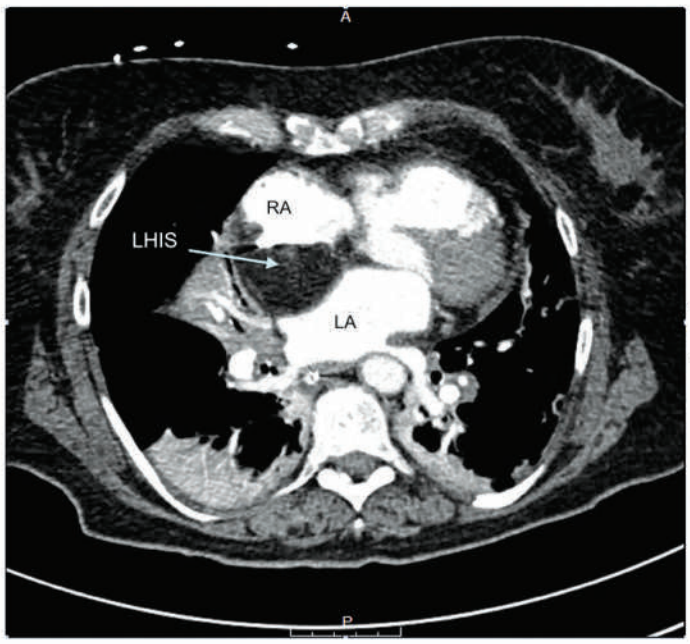
During the patient's stay in the ER she suddenly became very hypoxic. Her ABG showed O2 saturation 70%, PO2 38, PCo2 64. She was in severe respiratory distress that required intubation; she also had an episode of transient asystole less than 60 seconds requiring ACLS. She was resuscitated and had a Computed Tomography (CT) angiogram to rule out pulmonary embolism.

There was no evidence of embolism but the angiogram showed a large interatrial septal mass 4.5 x 3.5 cm encroaching more on to the right side. Patient was admitted to the intensive care unit and treated for severe chronic obstructive pulmonary disease (COPD) exacerbation. Patient was also managed as a case of new onset atrial fibrillation since there was no previous documentation indicative of this and was started on diltiazem drip. Initially a Transthoracic echocardiogram (TTE) was done to assess her cardiac mass which confirmed the presence of severe lipomatous hypertrophy of the interatrial septum with no evidence of PFO.

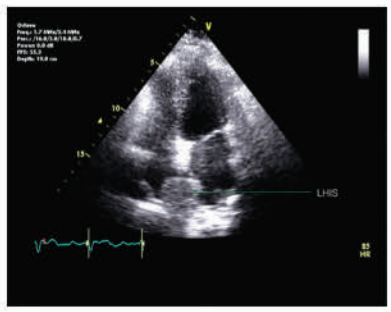
Better visualization of the left atrial appendage as well as right atrial filling was sought with a Transesophageal Echocardiogram (TEE) which showed a dramatic lipomatous hypertrophy of the interatrial septum, diameter of about 5 cm in its greatest dimension and restriction of right atrial filling. We felt the arrhythmias and the hemodynamic instability were secondary to the cardiac mass and that surgical resection would be the best approach. Patient had a cardiac catheterization prior to the intended open heart procedure, which showed mild coronary artery disease and a normal ejection fraction.

Surgery was eventually called off due to her worsening respiratory condition as it was felt that she was too high risk a candidate for open heart surgery in case the patient required cardioplegia during the procedure. The patient remained on mechanical ventilation and continued to require high levels of respiratory support. She was difficult to wean off the ventilator or the pressors. Ethics committee was consulted; the decision was made to change her code status to comfort care. Life support was withdrawn and the patient expired.

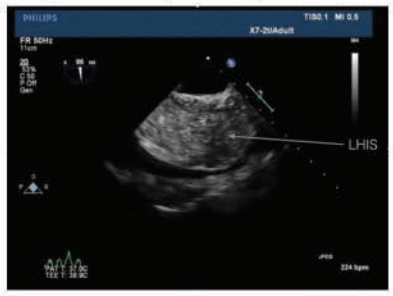
TEE image (Bi-caval view):



CT image



TTE (4-chamber apical view)



DISCUSSION

Lipomatous Hypertrophy of the Interatrial Septum was first described in 1964 in a postmortem examination. [1] It is not a true tumor. It has been defined as a > 2cm thick fatty infiltration of the atrial septum [2]. It is being more frequently reported with the advancement of imaging modalities like TEE, CT and MRI. This has led to an

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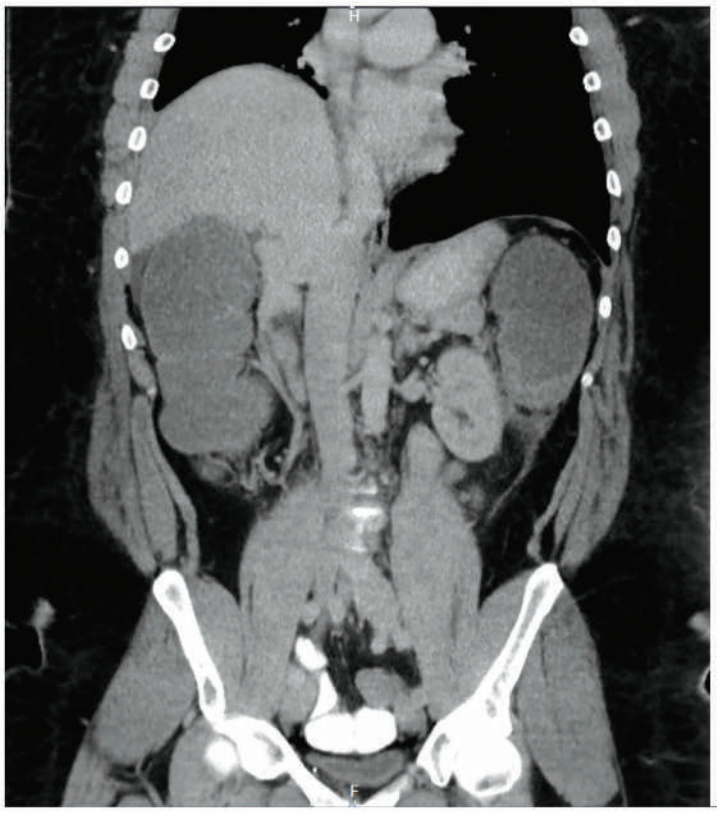
::: A CASE REPORT :::



Composite Carcinoid Adenocarcinoma of Colon; Unusual Cause of Large Bowel Obstruction

By **Ali Ziaolhagh, MD; Suresh Balasubramanian, MD; and Srivinas Merugu, M.D.**

LEARNING OBJECTIVES

1. To present an uncommon histo-pathologic type of large bowel tumors
2. To discuss clinical manifestations and imaging of large bowel obstruction
3. To discuss suggested hypotheses about existence of this type of neoplasm

INTRODUCTION

Mixed carcinoid adenocarcinoma is one of the very diverse tumors found in the Gastrointestinal (GI) Tract. These tumors consist of a glandular and neuroendocrine component. Depending on the position of the two components in cells, these lesions are divided into three categories: mixed, collision, and composite tumors 1, 2, 3.

In mixed tumors, the two components combine together with some transitional areas. The carcinoid component should compose one third of the tumor cell population in a composite tumor. In collision tumors, the two elements should be in intimate contact without intermixture. In amphicrine tumors, endocrine and nonendocrine elements are present within the same cell 1,2,3.

Mixed composite tumors are uncommon and they are described in different parts of the GI tract. We describe a unique case of mixed composite carcinoid adenocarcinoma that was found in the mid-descending colon.

CASE PRESENTATION

A 41-year-old male patient was admitted with the diagnosis of partial large intestine obstruction. He presented with complaints of progressively worsening abdominal pain, which was mainly located in the left lower quadrant and periumbilical area. His abdominal pain exacerbated two nights before presentation, which prompted him to seek medical attention. He also had nausea, several episodes of vomiting, and abdominal distension. His past medical history was significant for hypertension for which he had been taking Amlodipine, Hydrochlorothiazide, and Losartan.

His vital signs included a temperature of 97.9 °F, blood pressure of 176/102 mmHg, pulse rate of 91 beats per minute and respiratory rate of 18 breaths per minute. On physical examination, the patient had mild distended abdomen with sluggish bowel sounds. His abdomen was soft but tender to palpation in the periumbilical and left lower quadrant. Rectal examination revealed some stool in the rectal vault and hemoccult was negative. Routine hematologic and biochemical investigations were within normal limits.

An abdominal CT scan with and without contrast showed obstructing lesion in the mid-descending colon with pericolonic fat infiltration (figure 1).

Colonoscopic evaluation revealed a 5.5 cm apple core, a partial obstruction circumferential mass with central necrosis. The descending colon was found to be dilated proximal to the lesion, and collapsed distal to the lesion. Tissue samples were taken for pathology. The patient underwent an exploratory laparotomy with left hemicolectomy and low pelvic colorectal anastomosis. During the procedure, the abdomen was inspected and several internal organs were palpated for gross abnormalities and had no obvious metastatic disease.

The specimen was sent for histopathological investigations. The mucosa was remarkable for a circumferential neoplasm that measured 5.5 cm in length. Grossly, the neoplasm invaded through the muscularis propria to the subserosa. Multiple lymph nodes were dissected from the attached pericolonic adipose tissue. Metastatic carcinomas were found in 42 out of 50 lymph nodes. Pathologically, the tumor was staged T3, N2b, Mx.

Immunoperoxidase stains were positive for synaptophysin and negative for chromogranin. The investigation shows adenocarcinoma with 'necrosis.' These changes are consistent with a composite carcinoid adenocarcinoma with extensive mucinous differentiation (figure 2).

DISCUSSION

The origins of adenocarcinomatous and endocrine tumors are different. Adenocarcinomas are derived from endodermal cells and endocrine tumors from neural crest [4]. In general finding a tumor with two different origins is not common. In 1924, Cordier for the first time described a GI tumor with a

| continued on p.14

Non Resolving infiltrates – think of the zebras!

By **Suresh Balasubramanian, MD; Anna Affan, MD; and Mukul Pandit, MD**

LEARNING OBJECTIVE

To recognize potential complications of Sirolimus therapy.

INTRODUCTION

Sirolimus (Rapamycin) is a macrocyclic triene immunosuppressive agent. It is primarily used in organ transplant for induction and long-term maintenance therapy. The growing use of Sirolimus over the last decade has increased the probability of patients on Sirolimus being seen by transplant physicians and internists alike. In this regard, it is important for physicians to be acquainted with the clinical manifestations and management of its side effects. Most noteworthy, may be the potentially devastating but treatable pulmonary toxicity, mainly because of its close resemblance to more common lung disorders.

Early recognition of drug-induced lung disease is important because it can be easily reversed if the drug is discontinued soon after the onset of symptoms.

CASE PRESENTATION

A 61-year-old Caucasian male with past medical history of stage 3 chronic kidney disease and hepatitis C status post liver transplant in 1997 was transferred to our Long Term Acute Care facility (LTAC) after chronic extubation protocol. Two months prior, he was admitted in Florida for acute on-set chronic kidney disease resulting in intermittent hemodialysis. The acute renal failure was biopsy proven to be secondary to Calcineurin inhibitor (Cyclosporine) induced nephrotoxicity. At that time Cyclosporine was promptly discontinued and he was started on Sirolimus 3 mg for maintenance immunosuppressive therapy. In Florida he also developed respiratory failure during the same stay requiring prolonged mechanical ventilation with failure of several weaning attempts. He was transferred to our LTAC facility after a successful chronic weaning protocol. His medication on admission was notable for Sirolimus 3 mg daily as part of maintenance immunosuppression for his liver transplant and trimethoprim-sulfamethoxazole with voriconazole to prevent opportunistic infection.

While in LTAC he had an episode of massive GI bleed which was self-limiting, and thereafter, thought to be due to an ulcer on the right side of the colon found on colonoscopy prior to his admission to LTAC. The earlier colonoscopy was done to investigate a drop in hemoglobin while he was an inpatient in Florida. The patient had been progressing well without major complaint apart from some generalized fatigue which was attributed to the anemia and prolonged hospital stay.

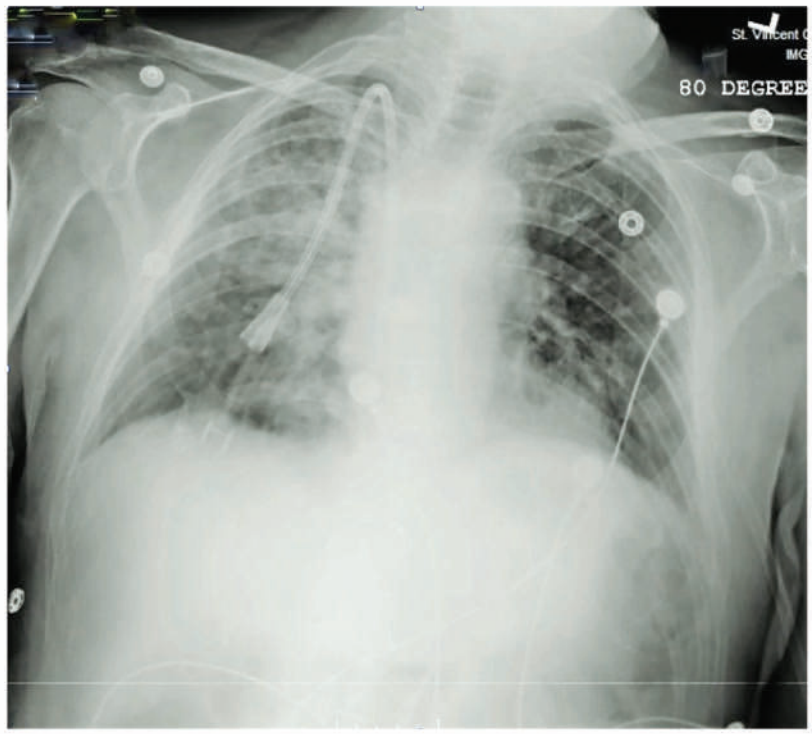


Figure 1: PA chest radiograph showing venous congestion with bilateral infiltrates increased on the right. Heart size is normal. There are low lung volumes. Dialysis catheter tip overlies the right atrial superior vena cava junction

On the fifth day of stay in LTAC he developed progressive shortness of breath with oxygen saturation dropping into the 80s. Physical examination at that time revealed an elderly man who was alert and oriented but appeared to be in moderate respiratory distress. He was able to complete short sentences and was not using accessory muscles for respiration. His oxygen saturation was 85% which improved to 99% on 100% FiO2. Blood pressure was 119/83 with a heart rate of 102 and a respiratory rate of 35. No fever was documented. Laboratory investigation showed a white cell count of 12.6 with 82% neutrophils and no bandemia, hemoglobin 7.9 which was stable, platelets of 229. ABGs were consistent with hypoxemic respiratory failure. The biochemical profile showed serum sodium of 142, potassium 3.7, chloride 103, bicarbonate 25, BUN 20, creatinine 2.5 with anion gap 18. Chest x-ray showed bilateral infiltrates more prominent on the right (Figure 1).

The patient subsequently underwent dialysis in view of possible volume overload but there was no improvement of the hypoxia nor the infiltrates post dialysis. He was intubated due to increasing oxygen requirements. Differentials at that

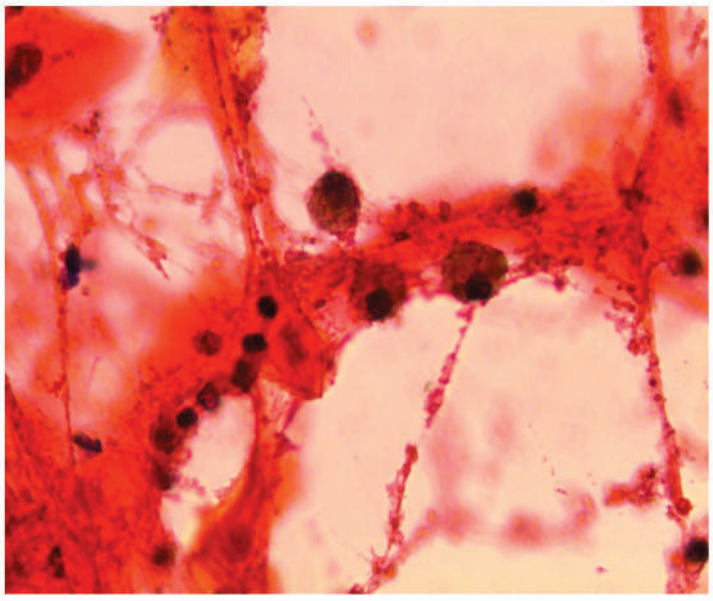


Figure 2a: PAP stain of right middle lobe bronchoalveolar lavage showing moderate hemosiderin-laden macrophages

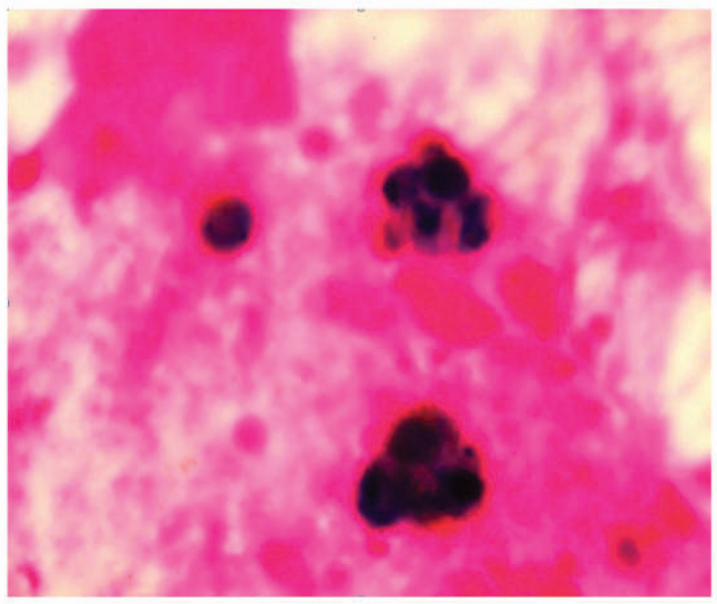


Figure 2b: Prussian stain of bronchoalveolar lavage showing moderate hemosiderin-laden macrophage

time included acute pneumonia with possible opportunistic infection keeping in mind he had been on immunosuppressive therapy. Antibiotics were started with aztreonam, linezolid and levofloxacin. Sirolimus was still continued. With no improvement in the course, bronchoscopy was done which revealed a blood-tinged lavage. Microbiology analysis of the fluid was unremarkable excluding tuberculosis, pneumonitis and CMV infection; however, cytology revealed hemosiderin-laden macrophages in the bronchoalveolar lavage (Figure 2 (a) and (b)). A diagnosis of diffuse alveolar hemorrhage as the underlying cause for acute hypoxemic respiratory failure was made. Sirolimus was promptly discontinued. He was started on high dose steroids and a decision was made to transfer him to a transplant center. Unfortunately he succumbed to a recurrent lower GI bleed despite attempts to embolize the bleeding ulcer.

DISCUSSION

Pulmonary drug toxicity is increasingly recognized as a cause of acute and chronic lung disease [1]. Early recognition of drug-induced lung disease is important because it can be easily reversed if the drug is discontinued soon after the onset of symptoms. The main challenge, especially in immune-compromised patients, is differentiating drug-related injury from opportunistic infections.

Sirolimus belongs to a class of drugs called proliferation signal inhibitors (PSIs), also known as mammalian target of rapamycin inhibitors (mTOR), a drug class being increasingly used in solid-organ transplantation[2,3]. Pulmonary toxicity has been reported in up to 11% of patients receiving high-dose Sirolimus. More than 70 cases of SRL-associated lung toxicity have been described in solid organ transplant (SOT) patients. Usually it is reversible, with a 4.8% mortality rate. High SRL levels (>15 ng/dl), late drug exposure (that is, switch in therapy) and male gender are the risk factors [4].

Several distinct types of pulmonary damage have been recognized, including lymphocytic interstitial pneumonitis, lymphocytic alveolitis, bronchiolitis obliterans with organizing pneumonia, focal pulmonary fibrosis, or a combination of these entities [5,6].

The pathogenic mechanism of PSI-associated pulmonary toxicity is not well understood. Both a direct, dose-dependent toxicity and an autoimmune response or delayed hypersensitivity reaction triggered by exposure to PSI with or without a cryptic pulmonary antigen have been postulated as possible underlying pathogenetic mechanisms [5,6]. It is also postulated that Sirolimus induces podocyte dysfunction.

Four diagnostic criteria have been proposed by Morelon et al .[7]for the diagnosis of SRL-associated lung toxicity: (1) SRL exposure before the onset of pulmonary symptoms; (2) exclusion of infection and other possible causal agents; (3) resolution of symptoms and radiological findings within 3 months after discontinuing or reducing SRL doses; and (4) lymphocytotoxic alveolar cell profile and pathological findings.

The common radiological findings related to diffuse alveolar hemorrhage (DAH) include bilateral, patchy infiltrates without mediastinal or pleural abnormalities [8]. Clinical suspicion of DAH and lung injury is usually confirmed by lung biopsy or autopsy. BAL will help exclude infectious etiologies.

It is therefore prudent to look for unusual causes of pulmonary infiltrates from the beginning of presentation in patients who are on immunosuppressants and frame a differential diagnosis beyond opportunistic infection, especially drug induced pulmonary toxicity as in this case here.

Prompt discontinuation of Sirolimus and initiation of high dose corticosteroid therapy can prevent a patient from succumbing to this potentially lethal manifestation. This case, in combination with the extant literature suggests that any patient taking the drug who may have developed unexplained pulmonary symptoms, should be considered for Sirolimus induced pulmonary toxicity, and managed accordingly.

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Total Ankle Replacement

(cont. from p.3)

for end-stage ankle arthritis has been arthrodesis of the ankle joint. The first attempt at ankle joint replacement was performed by Lord and Marotte in 1970, by utilizing an inverted hip prosthesis (Figure 1) (5). The results were disappointing. Since 1970 various prosthetic designs have been introduced for replacement of the ankle joint. Of note, one of the first generation ankle implants was developed here at SVCMC. The Conaxial (Beck-Steffee) Ankle (DePuy, Warsaw, IN) was designed by the innovative orthopedic surgeon Arthur Steffee, MD, former chief of orthopedic surgery at SVCMC. Regrettably, the Conaxial Ankle like many first generation implants performed poorly in mid- and long-term results. Failure rates up to 90% were reported, and recommendations were made against implant arthroplasty of the ankle (6). Historically, total ankle arthroplasty was largely abandoned due to poor survivorship, principally caused by loss of bone support (7). High complication rates were reported, and ultimately a vast majority of surgeons disregarded total ankle arthroplasty as a surgical strategy to address ankle arthritis.

Although ankle arthrodesis has proven to be an effective, reproducible and predictable treatment for end stage ankle arthritis, negative consequences of ankle fusion remain. The long-term effects of ipsilateral adjacent joint arthrosis following ankle arthrodesis have been studied. Most notably the harmful effects on the subtalar joint and knee joint have been observed. It is clear the gait pattern after ankle arthrodesis is abnormal. Gait analysis has shown decrease in stride length, gait velocity, and cadence (4). Many patients find it arduous to walk without a limp, and stair climbing can be challenging. Owing to the disappointing long-term sequelae associated with ankle arthrodesis, in addition to the continued success of hip and knee arthroplasty, the pursuit for a reliable ankle prosthesis has heightened over the last 10-15 years. Figures 2 and 3 demonstrate the intra-operative clinical and post-operative radiographic appearance of ankle arthrodesis versus ankle replacement.

Over the last decade, noteworthy advances have been made in implant research, design, materials, surgical technique, and patient selection. The second and third generations of ankle prostheses have revolved around the concept of decreasing constraints at the joint interface. Recent prospective controlled trials and meta-analyses have suggested that modern implants offer comparable pain relief and perhaps better function than ankle arthrodesis (8). The S.T.A.R. is the only three-part, mobile-bearing, un-cemented prosthesis available for use in the United States (Figure 4). At the time of this publication, the S.T.A.R. is the most studied ankle prosthesis in the world (9). Median and long-term survivability results have been favorable with five and 10-year survival rates being reported in the ranges of 80% to 98% and 70.7% to 95%, respectively (10, 11, 8, 12).

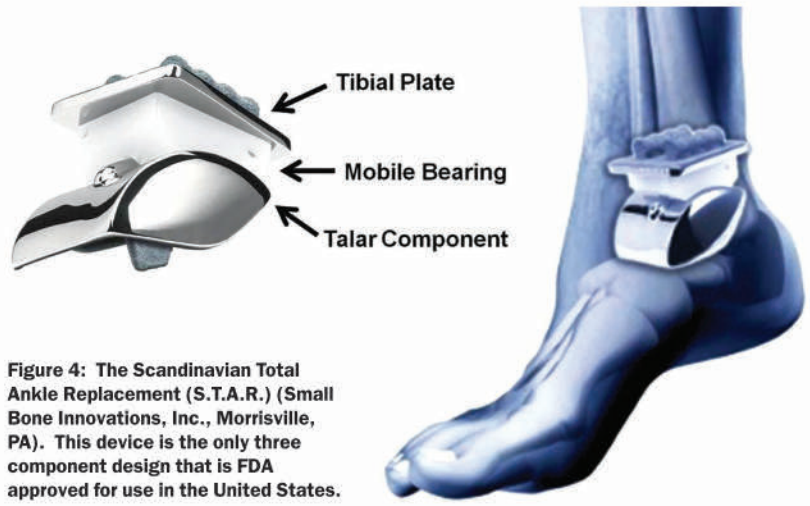

Figure 4: The Scandinavian Total Ankle Replacement (S.T.A.R.) (Small Bone Innovations, Inc., Morrisville, PA). This device is the only three component design that is FDA approved for use in the United States.

In 2003, Wood and Deakin illustrated the need for corrected biomechanics of the ankle joint after total ankle arthroplasty (10). The biomechanical angles illustrated in Figure 5 have been shown to lead to more favorable outcomes in the immediate post-operative period. Attainment of these angles intra-operatively will assure the surgeon that all deformities including: ankle varus, ankle valgus, tibial procurvatum, tibial recurvatum, and anterior dislocation of the talus, have been corrected. The purpose of our study was to evaluate our ability to achieve the immediate post-operative alignment necessary for joint survivability.

METHODS

From April 3, 2012 through January 14, 2014, five un-cemented mobile bearing total ankle replacements employing the S.T.A.R. design were implanted in five consecutive patients at SVCMC. Demographic and descriptive data is presented in Table 1. The procedure was offered to patients with a diagnosis of end-stage ankle arthritis. All surgical procedures were performed by the senior author (MBC) utilizing the recommended manufacture's technique. Radiographic measurements were performed by one author (DJE), as per the guidelines established by Wood and Deakin (10). A standard description of our quantitative data was performed using Microsoft Excel (Microsoft Corp., Redmond, WA). The mean, standard deviation and range were calculated for each biomechanical angle, and compared to the standards of previously published data (10).

Patient Diagnosis	Age	Sex	Limb	Weight (kg)	DOS	'a'	'b'	'c'
Primary Osteoarthritis	56	M	R	96	04/03/2012	90	84	30
Post Traumatic Arthritis	58	M	R	104	08/21/2012	90	88	15
Post Traumatic Arthritis	68	M	R	56	05/28/2013	90	88	25
Post Traumatic Arthritis	67	M	L	75	08/06/2013	89	84	20
Post Traumatic Arthritis	59	M	R	100	01/14/2014	90	89	24
Averages	61.6			86.2		89.8	86.6	22.8

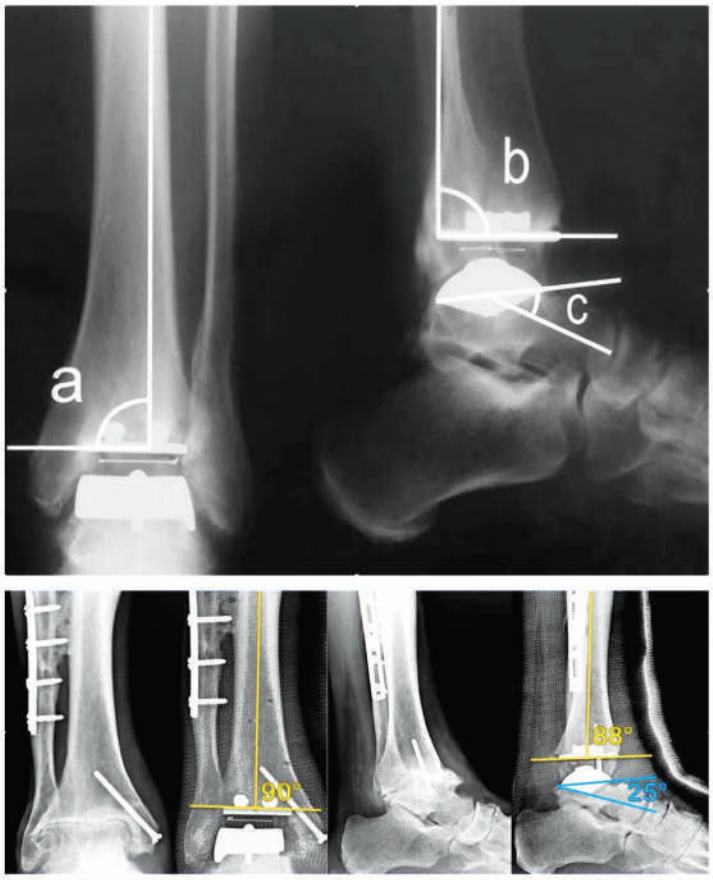

Figure 5: The positioning of implants as illustrated by Wood and Deakin (10). The 'a' angle is measured between the anatomical axis of the tibia and the articular surface of the tibial component on an AP film. A value of 90° is considered normal, and deviation of greater than 5° is considered malalignment. The 'b' angle is measured between the anatomical axis of the tibia and the articular surface of the tibial component on a lateral film. A value of 85° is considered normal, and deviation of greater than 5° is considered malalignment. The 'c' angle is measured between a line joining the posterior and anterior margins of the articular surface of the talar implant and a line drawn along the center of the talar neck. 20° is considered normal, and variation of more than 10° is considered malalignment.

Figure 6: A sample of our patient population with the pre and post-operative results.

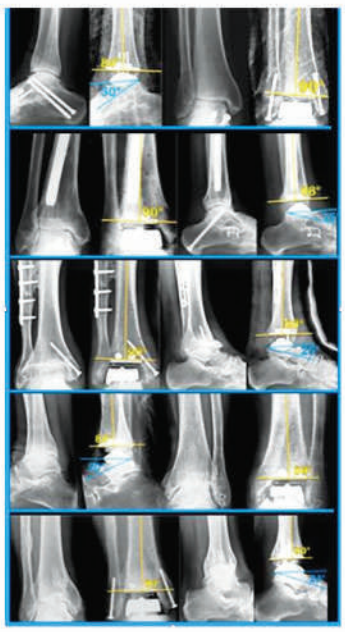

Figure 7: Our entire patient population with both pre and post-operative plain film radiographs

RESULTS

The positioning of the implants was measured by angles 'a', 'b', and 'c' on the immediate post-operative radiographs (Figures 6 and 7). An angle 'a' between 85° and 95° was achieved in all five cases. The mean was 89.8° ffi 0.45 with a range of 89°- 90°. An angle 'b' between 80° and 90° was achieved in all six cases. The mean was 86.6° ffi 2.41 with a range of 84° - 89°. An angle 'c' between 10° and 30° was achieved in all six cases. The mean was 22.8° ffi 5.63 with a range of 15° - 30°.

DISCUSSION

Our study has demonstrated that the technical dexterity necessary to achieve proper S.T.A.R. prosthesis implantation is currently present at SVCMC based upon the standards of published data. The purpose of this study was not designed to investigate the mid- to long-term results of either radiographic or clinical outcomes. It has been demonstrated that utilization of the S.T.A.R. technique has a prolonged learning curve (13). Peri-operative complications tend to decrease as a surgeon becomes more familiar with the technical requirements necessary to execute the procedure. Anecdotally, our complications have decreased with experience. Our first case was complicated by an intra-operative malleolar fracture which was addressed with open reduction and internal fixation at the time of implantation. The patient progressed well through the initial post operative period, but suffered from a symptomatic valgus deformity of the hindfoot. A corrective osteotomy of the calcaneus was performed. The second patient in our series developed a superficial wound dehiscence which was treated with local wound care and oral antibiotics with no significant sequelae. Since the second total ankle replacement in the series has been performed, no peri-operative complications have been observed. In summary total ankle arthroplasty is a reemerging treatment for end stage ankle arthritis. The Scandinavian Total Ankle Replacement is a new generation implant with a well-studied record of success. The implantation of this prosthesis is currently performed at SVCMC. The immediate results are favorable according to published guidelines and suggest that the prosthesis can be implanted with the prediction of long-term success at our hospital.

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Pseudomelanosis Duodeni

(cont. from p.4)

ment deposition are unknown.

PD typically occurs in the sixth and seventh decade with a female predominance of 2:1. It has been shown to be associated with systemic diseases such as chronic renal failure, hypertension, and diabetes mellitus [2]. Upon analysis of previous case reports, hypertension was found in the vast majority of patients. Medications have also been implicated in the association of PD. The most common medications found during the review of literature were ferrous sulfate, hydralazine, propanolol, hydrochlorothiazide and furosemide.2

It has been postulated that the ferrous sulfide pigment that is present in PD is derived from iron deposition secondary to intramucosal hemorrhage or impaired intramucosal iron transport after oral ferrous sulfate supplementation [3, 4]. It is postulated that iron sulfide storage can also be a product of an acquired inherent defect in macrophage metabolism. However, review of case reports has shown that PD can occur in the absence of a history of oral iron supplementation [5].

There is also strong evidence that sulfur is also found in the lysosomes of the macrophages. Even though iron is the main pigment compound, varying amounts of sulfur, calcium, potassium, aluminum, magnesium and silver can also be detected4. Some authors have proposed that antihypertensive medications may be the source of the sulfur since some of the medications, such as hydrochlorothiazide and furosemide, contain a sulfur moiety [2]. However, many patients noted to have PD were on medications that did not contain a sulfur moiety so the clinical significance of this is unclear.

Histology demonstrates the accumulation pigment-laden macrophages of the lamina propria in the tips of duodenal villi (Figure 2). There are no cases where endoscopic hyperpigmentation was not supported by histological evidence of PD. However, there have been cases in which biopsies of normal appearing duodenum identified histological evidence of PD. Because of this, it is impossible to establish a temporal association between disease onset and endoscopic manifestation.2 One of the largest series (Giusto, et al.) that reviewed 17 adult patients with histologically confirmed PD showed that only 35% had endoscopically apparent pigment spots[2]. In four case reports, patients diagnosed with PD were noted to have previous normal EGDs [5]. Because of this, it can be said that PD is an acquired rather than congenital condition.

The diagnostic and prognostic significance of PD has yet to be determined and appropriate follow up, if any, is unclear. It has not been documented to cause fibroinflammatory reactions such as stricture formation, fibrosis or erosive duodenitis. It also is not associated with duodenal malignancy. Upon reviewing the literature, no therapeutic chelating agent is recommended.

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Gastric Perforation

(cont. from p.5)

In the stomach, there were multiple foci of perforation with a corresponding focus of tumor metastasis involving the full thickness of the stomach wall. The tumor was prominently pleomorphic, had a solid sheet-like architecture, extended into lymphatics, and had no evidence of necrosis.

antibiotics. In the stomach, there were multiple foci of perforation with a corresponding focus of tumor metastasis involving the full thickness of the stomach wall. The tumor was prominently pleomorphic, had a solid sheet-like architecture, extended into lymphatics, and had no evidence of necrosis.

DISCUSSION

Bevacizumab is a monoclonal immunoglobulin G1 antibody directed against vascular endothelial growth factor (VEGF) that inhibits new blood vessel formation and growth. [1]Bevacizumab was initially approved in 2004 by the US Food and Drug Administration (FDA) for use in metastatic colon cancer. Then FDA approved it for the management of non-small cell lung cancer, renal cell carcinoma, and recurrent glioblastoma, with several other indications pending and under research. [2]

With increased use of Bevacizumab, serious adverse effects are being reported more frequently, including hypertension, proteinuria, hemorrhage, thrombosis, fistula formation, and bowel perforation. [1,3] The reported incidence rate of bowel perforation has ranged from 0.3% to 2.4% in the clinical trials.[2]In patients with pneumoperitoneum (a sign of bowel perforation in radiologic tests), mortality rates have been reported as high as 15% [4].

Several mechanisms of action have been described to explain the development of viscous perforation as a result of Bevacizumab, including the inhibition of VEGF leading to thrombosis of smaller splanchnic or mesenteric vessels, resulting in bowel ischemia and ultimately bowel perforation [5,6] . Constant bowel wall proliferation and healing is dependent on microcirculation, protection with nitrous oxide, prostacyclin, and normal platelet function, all of which depend on VEGF. In addition, tumor structure may provide some stability to the intestinal wall itself, and tumor death creates an area of disruption susceptible to perforation. [5,6,7]

Several risk factors for bowel perforation have been identified in clinical trials and case reports. Some of the most frequently reported established risks for perforation include history of bowel surgery, ulcers, and certain types of cancer.

Symptoms of viscos perforation, if present, are highly dependent on the site of involvement. [8]Although 50% of bowel perforations that occur in patients with intact primary tumor involving the bowel will occur at the tumor site, [8] any part of the bowel can be involved.

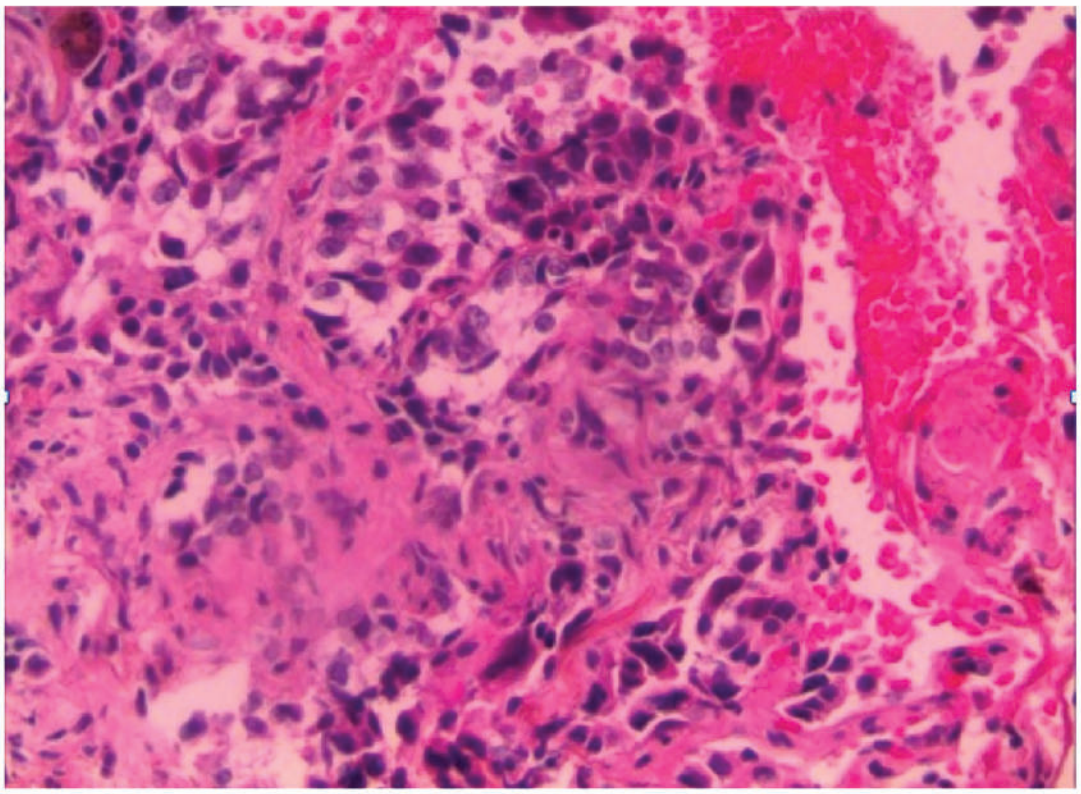

Figure 3: Transbronchial biopsy demonstrated poorly differentiated non-small cell carcinoma (six month back)

Pelvic pain may occur with rectosigmoid colon perforation, while nausea, vomiting, and obstipation may occur with bowel obstruction. [9] Gastrointestinal complaints should be given careful consideration, as bowel perforations may be hard to diagnose.

In the Dutch Colorectal Cancer Group phase III study [8] most cases (89%) of perforation occurred within 15 weeks after the start of Bevacizumab treatment and anywhere prior to the fifth cycle of chemotherapy. This period is when a physician must have the highest level of suspicion for perforation and lowest threshold for ordering diagnostic imaging. A radiograph of the kidneys, ureters, and bladder may show free peritoneal air, but CT should be considered the diagnostic study of choice because it may reveal pneumoperitoneum, small bowel loops caused by obstruction, or even pneumatosis intestinalis. [10,11]

The initial approach to bowel perforation in patients receiving Bevacizumab is surveillance and prevention. When steroids and NSAIDs are used together, use of either a proton pump inhibitor or a prostaglandin agonist should be considered to prevent peptic ulcer disease.

When surgery are planned, Current recommendations for elective surgery include a 60-day wait period after Bevacizumab administration and a 30- to 60-day wait period to restart Bevacizumab therapy after surgery. If at all possible, the wait period for elective surgery should be at least 3 half-lives of the drug (or until 87.5% of the drug is eliminated). In most patients, this period would be about 60 hours (with a 20-hour half-life), but in some patients it could be up to 150 days. [2]

Once bowel perforation does occur in patients receiving Bevacizumab, the perforation is managed conservatively or surgically. The decision regarding treatment can be complicated because patients typically have a terminal illness and are taking a drug that causes poor wound healing and dysfunctional platelets. The mortality rate for patients with Bevacizumab-induced bowel perforation has been reported as high as 50%. [7,12] For this reason, patients with multiple risk factors (e.g., recent surgery, radiologic evidence of incompletely healed bowel, presence of a pretreated tumor with multiple chemotherapy regimens) may be considered for alternative regimens if the goal is palliation.

If a patient is treated with surgery, Bevacizumab therapy should not be restarted after recovery because of increased risk of recurrent perforation. [13]

CONCLUSION

Viscous perforation is a potentially fatal adverse effect of Bevacizumab therapy. Gastrointestinal complaints in those patients should be given careful consideration, as perforations may be hard to diagnose. Most cases of perforation occurred within 15 weeks after the start of Bevacizumab treatment and prior to the fifth cycle of chemotherapy. During this period physicians must have the highest level of suspicion for perforation and the lowest threshold for ordering diagnostic imaging.

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Lipomatous Hypertrophy

(cont. from p.6)

increase in frequency of surgical resection of these lesions, the majority of which may not be compromising the hemodynamics of the individual. The few situations that may warrant intervention are presence of atrial arrhythmias, heart block or vena caval obstruction to mention a few. Antiarrhythmic agents may suffice in cases with atrial arrhythmias [3] but surgical resection and septal reconstruction is the management of choice in cases with heart blocks or severe obstruction [4].

Histologically, the lesion is characterized by a non-encapsulated mass of adipocytes interspersed with atypical and hypertrophied myocytes. It may appear encapsulated because of the constraint of the surrounding structures including the fossa ovalis, atrial wall, interatrial sulcus, pericardium of the transverse sinus or posterior atrioventricular groove [5]. Modern imaging techniques such as echocardiography, multislice CT, and MRI are the imaging modalities that may be used to diagnose this lesion. [6] The defining characteristic feature is the specific septal location of the atrial thickening that tends to be greater than 2 cm and typically spares the fossa ovalis, hence taking on a classical dumbbell or hourglass shape which was evidently noted in the images of our patient. Furthermore, the tissue is isodense to the surrounding subcutaneous fatty tissue. As the structural features of this lesion are so distinct from any other intracardiac mass it is now widely accepted that the diagnosis can be made confidently without the need for tissue biopsy. [7]

Our case clearly shows that the diagnosis can be easily and effectively made with the help of noninvasive techniques like TEE or CT and even MRI, if required. Although a clear diagnosis can also be based on MRI, this test remains an expensive technique localized to specialist centers. But the presence of newly diagnosed atrial fibrillation along with hemodynamic compromise in this patient would warrant surgical resection. Our patient's poor respiratory status made any surgical intervention too risky to be carried out.

CONCLUSION

Lipomatous hypertrophy of the interatrial septum (LHIS) is not a true tumor. It is an exaggerated growth of normal fat existing within the septum which rarely requires surgical intervention. Initially thought to be a rare finding, it is being increasingly diagnosed with the use of imaging modalities like CT scan and TTE. Histological confirmation is not essential to make a diagnosis of LHIS.

Characteristic findings of non-enhancing homogenous lipomatous density confined to the upper 2/3rds of the interatrial septum,

Composite Carcinoid Adenocarcinoma of Colon

(cont. from p.7)

combination of exocrine and neuroendocrine components 5]. In 1987, Lewin classified these neoplasms into three subtypes; collision tumors, combined tumors, and amphicrine tumors [6]. In 2000, WHO classification, mixed exocrine endocrine tumors were defined as tumors with each component to be at least 30% [7,8].

Different hypotheses are suggested to explain the existence of a neoplasm with both mucinous and endocrine elements such as transformation of primary mucinous malignant cells into endocrine cells [9], hybridization of neoplastic mucinous and endocrine cells to form hybrid tumors [10], gene mutations [11] and finally, endodermal stem cells of crypt base to be the origin of neoplastic cells [12].

Composite carcinoid adenocarcinoma may have several other names in the literature such as mucin-producing carcinoid, composite carcinoid tumor mixed adenocarcinoid and composite glandular neuroendocrine mixed tumor. These neoplasms are reported in the esophagus, stomach, ampulla of vater, ilium and large bowel. The majority of these tumors are reported in the appendiceal area. This area is also the most common site of GI tract carcinoid tumors. La Rosa et al [7] reviewed 60 cases that have been reported in the literature. Most of the reported cases were men with the average age of 65 [7]. All four cases that were reported by Knight et al presented with advanced intestinal obstruction [4]. They reported tumors in the ascending colon and the rectosigmoid region of the large bowel [4].

Pulitzer et al reported four cases of composite adenoma-carcinoid tumors in the large intestine, which are believed to have favorable neutral history. Large intestinal microcarcinoids are rare, and the majorities are reported in patients with chronic colitis, especially ulcerative colitis [13].

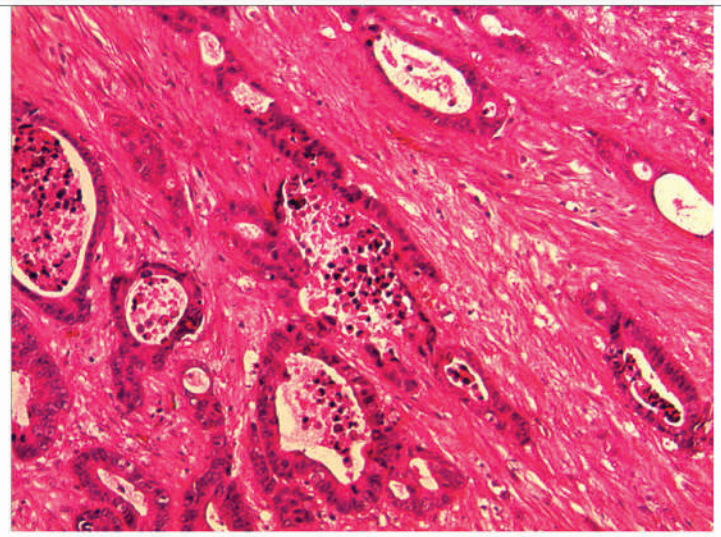

Figure 2: The synaptophysin stain proves the neuroendocrine component. This image shows the more typical adenocarcinoma with the "dirty" necrosis – dead cells occupying the lumen of the glands.

CONCLUSION

Mixed composite carcinoid adenocarcinoma of GI tract is very rare particularly in the mid-descending colon near the splenic flexure. To the best of our knowledge only one case is reported with the same tumor pathology in the same location. Our patient also presented with signs and symptoms of large bowel obstruction at age 41, a young age for this histopathologic tumor presentation.

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the classic dumbbell-shaped appearance of the lesion and the clear sparing of the fossa ovalis are adequate to make the diagnosis if LHIS. Further confirmation can be provided by CT or MRI [8].

In cases such as ours, where the patient has concomitant atrial arrhythmias or hemodynamic instability due to restricted right atrial filling owing to the sheer size of the lesion, surgical resection would be an appropriate approach if the patient's functional status permits the procedure.

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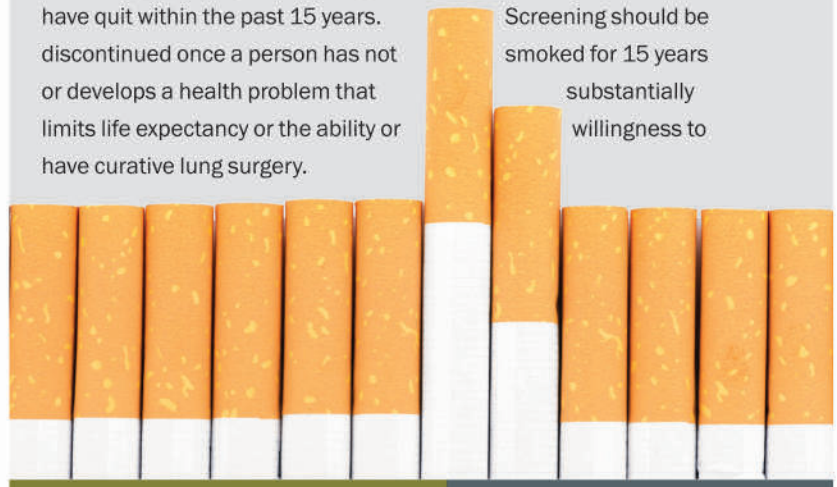
HEALTH FACTS

SCREENING FOR SMOKERS

The USPSTF recommends annual lung cancer screening with low-dose computed tomography for adults aged 55 to 80 years who have a 30-pack per year smoking history and currently smoke or have quit within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.



DID YOU KNOW?

Influenza vaccination reduced cardiovascular events in adults and in the subgroup of patients with a recent acute coronary syndrome, according to a new report by the Centers for Disease Control.

HURRAY FOR A DELAY!

DELAYED

The U.S. House of Representatives delayed a 24% Medicare pay cut for physicians and delayed the ICD-10 implementation for one year. Hurray!

Medication usage in the U.S.

The elderly receive more than 50% of all prescription medications and purchase 40% of over-the-counter medications in the U.S. More than 90% of non-institutionalized patients are on at least one prescription medication. Nearly $15 billion is spent each year on herbal products.

Risk increases with number of medications

Adverse Drug Events increase in relation to the number of medications an individual takes. Risk is 15% with two medications; 58% with five meds; and 82% with more than seven meds.

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