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CASE REPORT 1

A RARE CAUSE OF OBSTRUCTIVE JAUNDICE

By Justin DeLange, D.O.

INTRODUCTION:

Obstructive jaundice often has a multifactorial etiology and necessitates a careful work-up that often includes imaging such as MRCP, ERCP, ultrasonography, or CT. Obstructive jaundice most likely heralds biliary stricture or choledocholithiasis.

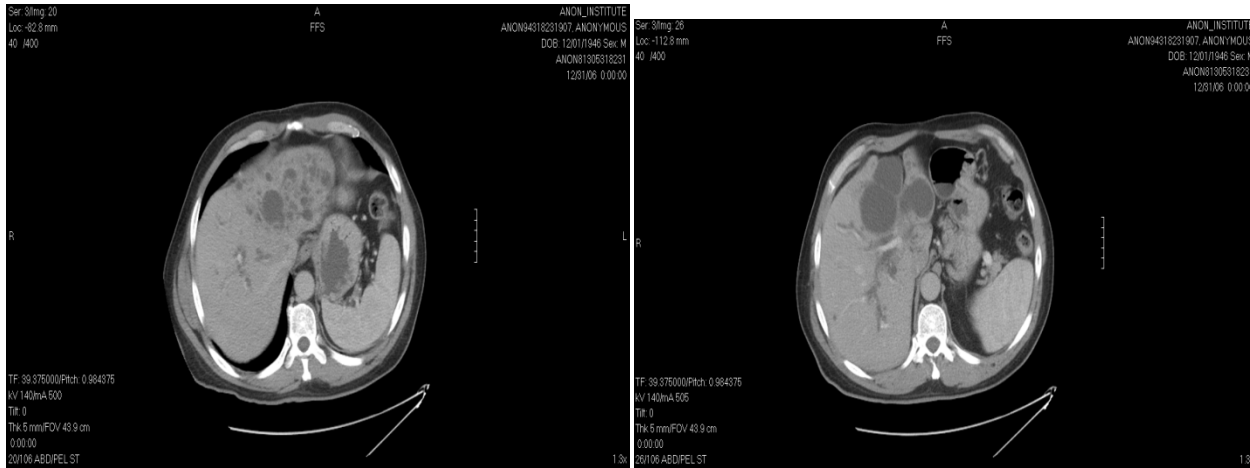
PRESENTATION:

Patient is a 60 year old Hispanic man that presented to the emergency department with a 6-day history of post prandial bilious, non-bloody vomiting. He had progressive dysphagia to solid food but could tolerate liquids. The vomitus was non-bloody but bilious in color. Concurrently, he also reported weakness, jaundice, pruritis, and dark urine which began 6 days ago. The patient also denied any HIV risk factors. He also noted clay-colored stools. He reported a 20 year work history with a waste management company transporting and cleaning portable waste units. On exam, vitals were 178/114, pulse rate of 60, respiratory rate of 16, 96% on room air and afebrile at 97.8° F. Positive exam findings included icterus and had an enlarged liver span up to 14 cm.

ASSESSMENT:

Upon presentation, laboratory data revealed a white count of $8.5 \times 10^3/\mu\text{L}$ with no bands. Furthermore, AST of 53, ALT of 56, total bilirubin of 19, direct bilirubin greater than 15, total protein of 7.6, albumin of 4.5, alkaline phosphatase of 402, and GGT of 97. Additionally amylase was 79, lipase was 91, and synthetic function was preserved with PT 12, PTT 26, and INR 1.1. Hepatitis panel was entirely negative as well. There was no evidence of infection as blood cultures were both negative. Right upper quadrant abdominal ultrasound was obtained and showed a contracted gallbladder with stones, a dilated

common bile duct (6.2 mm), coarse echotexture liver with multiple hypoechoic cysts, multiple small cysts throughout the right kidney, and no evidence of cholecystitis. Subsequently, a CT of the abdomen was obtained which showed extensive cystic disease of the liver with intrahepatic duct dilation and distortion of anatomy consistent with Caroli's Disease. Enlarged cystic kidneys were also seen consistent with polycystic kidney disease. (See Fig. 1, 2, and 3)



Figures 1, 2. Actual CT images from our patient demonstrating intrahepatic ductal dilation and extensive polycystic disease of both kidneys pathognomonic for Caroli's disease

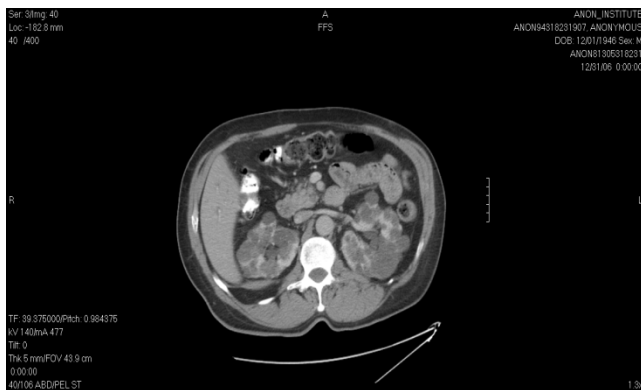


Figure 3. CT Abdomen in our patient showing PCKD.

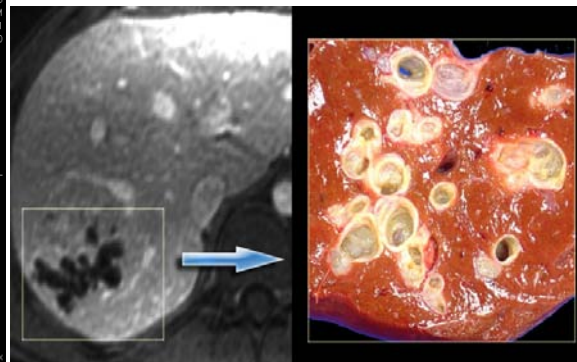


Figure 4. Gross specimen (not our patient) demonstrating dilated bile ducts consistent with Caroli's disease.

MANAGEMENT:

Ursodiol was started to alleviate the intense pruritis this patient was experiencing secondary to bilirubin deposition into the skin. On ERCP, high grade common hepatic duct stricture involving the right main hepatic duct was found with marked common hepatic duct dilatation. Bilateral stents were placed in the right and left sides respectively and bile duct brushings were taken. These features were highly suspicious of cholangiocarcinoma complicating Caroli's Disease.

DISCUSSION:

Caroli's Disease is a disease that manifests itself with multifocal, segmental dilation of large intrahepatic bile duct tracts and varying degrees of renal cystic disease. This disease is often transferred to offspring in an autosomal recessive fashion. Accordingly, Caroli's disease is most often associated with autosomal recessive polycystic kidney disease⁽¹⁾. Dr. J Caroli, a French internist, initially described two variants, one of which includes biliary duct ectasia without fibrosis in addition to the more common presentation of tract dilation with fibrosis⁽¹⁻²⁾. The anomalous architecture of both liver and kidney in this disease localizes to a genetic defect in fibrocystin. Fibrocystin is a protein that helps to regulate cellular proliferation and growth in both organs⁽¹⁾.

Often, the biliary tract dilatations in Caroli's disease may be come ulcerated or hyperplastic and as noted above, are often associated with hepatic fibrosis^(1, 3-4). Thus, the risk of cholangiocarcinoma in this population has been reported from anywhere to 7-15% with some reports that state overall incidence as high as 28%^(1, 3). It is believed that the hyperplastic nature of these dilatations and the build-up of unconjugated secondary bile salts, along with bile stasis, are to blame for this predisposition. Other common associations with Caroli's disease may include biliary sludging, intraductal lithiasis, bacterial cholangitis, abscess formation and portal hypertension^(1, 2).

The major treatments for Caroli's disease are largely based upon alleviation of symptoms that must be tailored to the patient's illness. These treatments include antibiotics to guard against infection and fat-soluble vitamins for nutrition augmentation. Clinicians should also monitor for variceal bleeding and have a high suspicion for cholangiocarcinoma in Caroli's patients with an unexplained clinical deterioration or with presentation of biliary strictures.^(1, 4)

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CASE REPORT 2

AN UNUSUAL CAUSE OF ANGINA

By: Rajeev R. Fernando, MD

Keywords: discrete sub-aortic stenosis (DSS)

INTRODUCTION

Aortic stenosis has conventionally been classified as valvular, subvalvular, and supra-ventricular. Sub-aortic stenosis assumes two forms: the discrete type and the tunnel type. The latter is characterized by a diffuse, long segment fibromuscular narrowing of the left ventricular vestibule, while a crescent-shaped or sometimes circumferential membrane or fibromuscular band below the aortic valve causes the discrete form of subaortic stenosis. The presence of this discrete ridge or membrane usually results in symptoms of obstruction after the first decade of life. Presentation and progression of the disease vary with age and is the object of the discussion.

PRESENTATION

A 42-year-old Middle Eastern woman was admitted to the coronary care unit with a four day history of left-sided, midsternal, 10/10, sharp, stabbing chest pain, which radiated to the left arm and back. Chest pain was exertional and decreased with nitroglycerin. Pain was episodic and was associated with some shortness of breath, diaphoresis and nausea. She endorsed 3 to 4 pillow orthopnea as well as paroxysmal nocturnal dyspnea. Past medical history was significant for type 2 diabetes mellitus and hyperlipidemia. She has a child at the age of 10 years with congenital subaortic membrane who has had several surgeries to correct this problem. On examination, temperature was 97.2 degree Fahrenheit, pulse was 73 beats per minute, respirations were 18/min, blood pressure was 113/69 mm Hg and oxygen saturation was 98% on room air. She had a loud ejection systolic ejection murmur (grade 4/6) at the left sternal border not modifying its intensity with Valsalva maneuver or with squatting and bibasilar crackles.

ASSESSMENT

A complete blood count and basic metabolic panel returned the following values: white cell count $7.9 \times 10^3/\mu\text{L}$ with a normal differential, hemoglobin 12.8 g/dL, and platelet count $194 \times 10^3/\mu\text{L}$, and her electrolytes, renal function and liver function tests were within normal limits. EKG and cardiac enzymes were unremarkable and a left heart catheterization revealed no angiographic disease. Transthoracic echocardiography (TTE) showed normal left ventricle (LV) dimensions with an ejection fraction of 64%. On apical five chamber view, the peak velocity and the peak gradient across the membrane were 3.8 m/s and 57 mmHg respectively. Color-Doppler analysis detected mild aortic regurgitation. Systolic anterior motion (SAM) of mitral leaflets was not present and pulsed-wave (PW) Doppler mapping of left ventricular outflow tract (LVOT) showed only a modest acceleration of blood flow. Because parasternal views did not permit a satisfactory evaluation of aortic valve, transesophageal echocardiography (TEE) was performed which showed a discrete subaortic membrane with stenosis. The peak velocity across the membrane was 4 m/sec and the peak gradient was 64 mmHg. The interatrial septum was intact without shunting by color Doppler and agitated saline contrast. All four pulmonary veins drained into the left atrium. Patient consented to surgery. There was a near circumferential sub-aortic membrane noted during surgery that was partially calcified creating a significant narrowing of the LVOT. It was about 0.5 cm below the annulus. After removing the membrane, a transesophageal echocardiogram showed complete resolution of the left ventricular outflow tract obstruction (LVOTO). The pathology report for the sub-aortic membrane showed fibrotic tissue with myxoid degeneration, consistent with aortic valve.

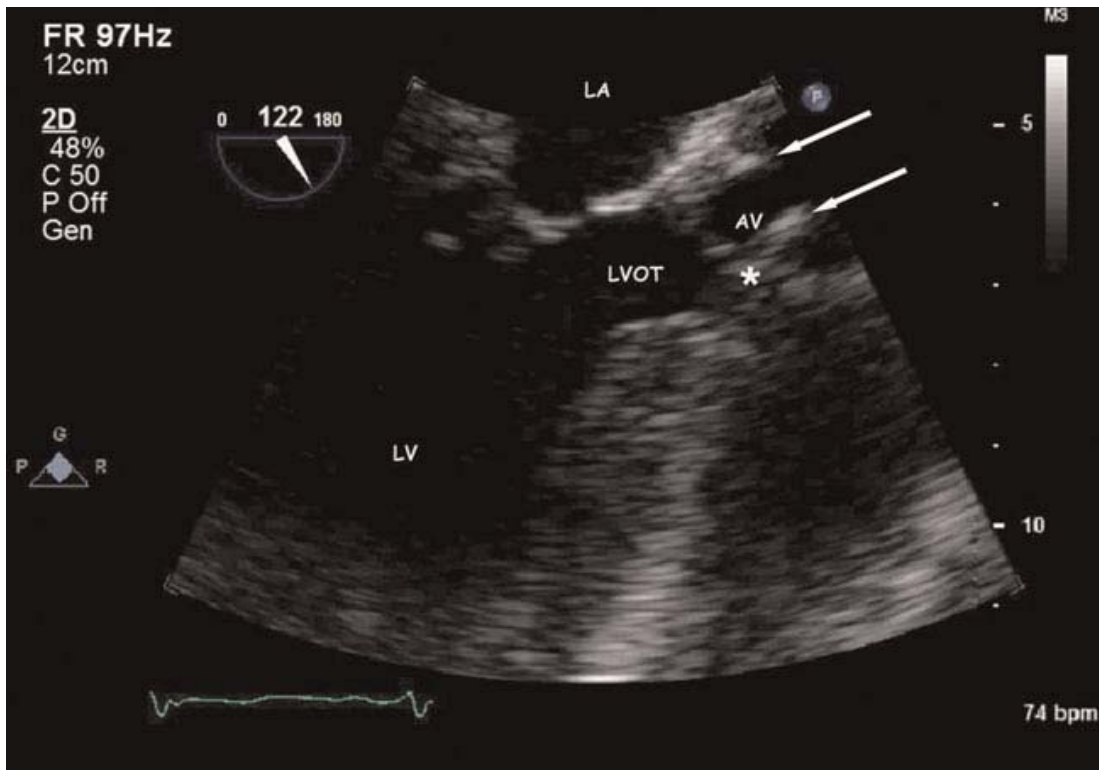


Figure 1 Transoesophageal echocardiography. Mild restrictive movement of aortic valve leaflets (arrows). The membranous ridge (*) is located in the LVOT proximal to the aortic valve (AV). LV, left ventricle; LA, left atrium.

DISCUSSION

Discrete subaortic stenosis (DSS) accounts for 6.5% of all adult congenital heart disease and is associated with another CHD in 44% of patients. The two most common cardiac malformations associated with DSS were ventricular septal defect and aortic coarctation, but DSS was also associated with atrioventricular septal defect, patent ductus arteriosus, bicuspid aortic valve or double-outlet right ventricle. In most cases, DSS appeared as a secondary lesion years after the surgical repair of the associated cardiac malformation. The presence of DSS after surgical correction of aortic coarctation, ventricular septal defect, congenital valvular aortic stenosis, double outlet right ventricle and other CHDs has been described. Khoshnevis et al.¹ reported three patients with rheumatic heart disease who developed severe stenosis by a sub-aortic membrane many years after the prosthetic replacement of the mitral valve.

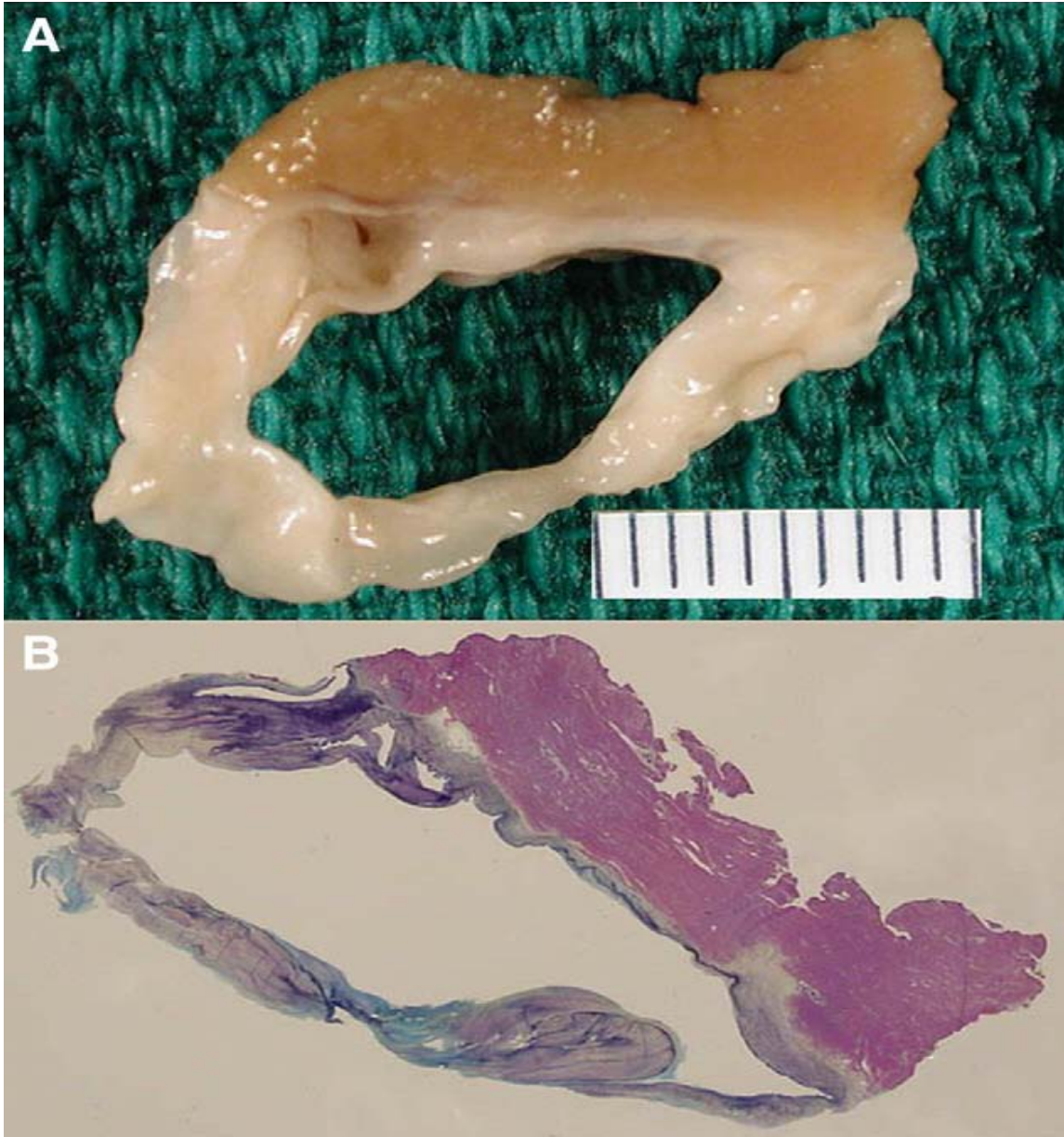


Figure 2 (A) Case 12: excision of an intact pearly white subaortic ring with a sleeve of myocardium. (B) The entire ring has been embedded in its entirety and sectioned (Movat pentachrome).

Irrespective of the presence or absence of the associated anomalies, patients with DSA have an altered geometry of the LVOT in the form of a steeper aorto-septal angle, wider mitral-aortic separation and a narrower LVOT. This induces elevation of the septal shear stress, and a four-stage etiology has been put forth by Cape et al.², whereby altered morphology leads to alteration of shear stress, which in turn triggers a genetic predisposition to induce cellular proliferation at that site. The genetic predisposition may also explain the familial occurrence of some cases of stenoses. It is likely that the earlier in life the septal shear stress is increased, the more intense the response and the more rapid the progression of the LVOTO. This explains the progressive nature of DSS in children, whereas in adults it occurs slowly over decades.

Aortic regurgitation occurs in 81% of adults⁴ with DSS, but is hemodynamically significant (moderate to severe) in only 20% of the patients. It develops due to trauma to the aortic valve from the turbulent jet during left ventricular systole or tethering of the cusps to the fibrous membrane or development of infective endocarditis. Aortic regurgitation (AR) is directly related to the severity of stenosis. However, significant progression of AR during adult life was not found; there was no significant relationship between AR and age and there was no significant increase in AR over time. Progressive left ventricular hypertrophy may produce dynamic obstruction, sometimes due to asymmetrical hypertrophy, simulating hypertrophic cardiomyopathy. In view of these complications and progression, an early intervention and aggressive resection⁴ (membranectomy, myectomy, aortic valve repair or replacement) have been recommended. Despite this, recurrence and progression of aortic regurgitation have been reported after the therapeutic intervention. Therefore, surgical decisions in adult patients diagnosed with DSS should be based not only on the anatomic finding of subvalvular stenosis, but also on the clinical evaluation, left ventricular hypertrophy, systolic function and severity of LVOTO and aortic insufficiency.

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Case Report

An Infective Cancer—A Rare Disease with a Rarer Transformation

Matthew T Burrus, MS III, Yessica Ramos, MD, Maryam Zenali, MD

Introduction:

Recurrent respiratory papillomatosis (RRP) is a rare congenital syndrome caused by peripartum transmission of HPV (most commonly HPV 6 and 11) from an infected mother, and papillomas may develop in any segment of the respiratory tract. Transformation into squamous cell carcinoma (SCC) is a rarely reported consequence of RRP as most cases remain benign. This is a patient with RRP who presented with coexisting malignant transformation and bony metastasis.

Presentation:

A 24 year old Hispanic man with a past medical history of congenital laryngeal papillomatosis (diagnosed at age 5) status post numerous surgeries for microdebridement and recurrent pneumonia presented with increasing shortness of breath, hoarseness, fever, productive cough, left chest point

tenderness, and weight loss. Patient normally received microdebridement surgeries every six months but had not had one in almost 1 year. Over this time period, pt had experienced worsening dyspnea and hoarseness. On physical exam, he was thin, tachypneic and tachycardic with severe reproducible back pain and left-sided chest pain. On pulmonary auscultation, decreased breath sounds were noted diffusely over the left lung. Patient was markedly hoarse. He was exquisitely tender over left chest in mid-clavicular line at approximately the 5th rib, and movement and deep inspiration greatly aggravated the pain.

Assessment:

Pertinent positive labs at admission included a Ca^{2+} of 12.8, mixed respiratory and metabolic alkalosis, ABG showed a pH of 7.48, pCO_2 35.8, HCO_3^- 26.3, hemoglobin 11.1, MCV of 78, Iron 18, TIBC 173, platelets 899, WBC count of 28.9 with 71% neutrophils. A chest X-ray was performed and showed worsening of a previously identified left lung cavitory lesions with near complete opacification of the left hemithorax and increased left-sided volume loss. A chest CT with contrast (Image 1A, 1B) showed multiple cavitory nodular opacities and satellite nodules in the right mid and lower lobes with near complete opacification of the left lung parenchyma. In addition, there was destruction of the left lateral T4 and T5 vertebral bodies and the left-sided transverse processes and adjacent ribs. At this point, a tracheal wash showed squamous cells with nuclear atypia, and then IR performed a CT-guided biopsy of both the lung (Image 2A, 2B) and the spine (Image 3) which both demonstrated squamous cell carcinoma metastases. Pain was managed and patient was discharged to follow-up with oncology.

Diagnostic Images:

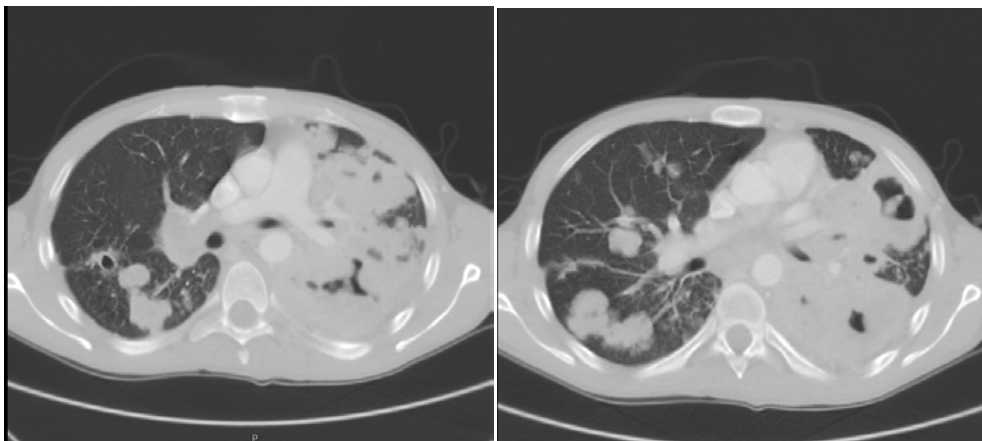


Image 1A, 1B. Chest CT - multiple cavitory nodular opacities with near complete opacification of the left

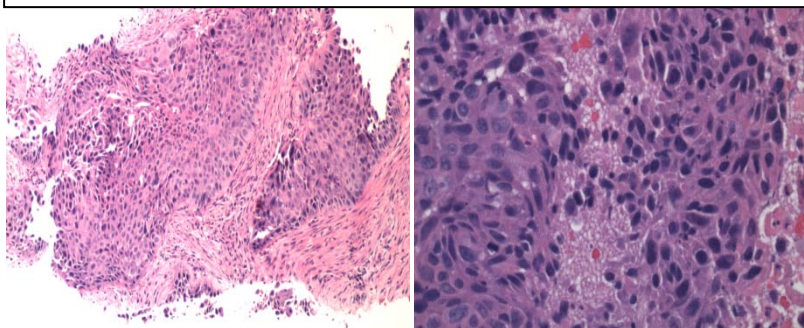


Image 2A, 2B. Lung biopsies show moderately differentiated

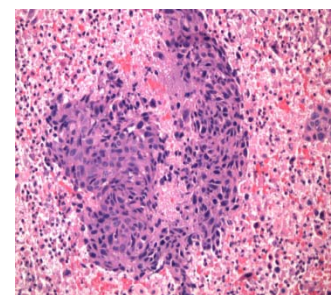


Image 3. Bone biopsy shows metastatic SCC

Discussion:

In the US, RRP incidence is reported as of 4.3/100,000 children and 1.8/100,000 adults with the glottic larynx being the most common location of papillomas. The trachea is involved in only 5% of cases, and less than 1% of cases involve the lungs. Although malignant transformation is a rare occurrence usually seen in older patients with longstanding papillomatosis, therapeutic irradiation, or a history of smoking, squamous cell carcinoma can arise in RRP in the absence of such risk factors. Pulmonary spread represents the majority of cases with spontaneous malignant transformation^(1,4,7), and age at diagnosis and the presence of HPV are the main factors for severity of the disease.⁽⁵⁾ Three clinical patterns of RRP disease exist: juvenile-onset disease, adult-onset disease, and juvenile-onset disease with persistence into adulthood. Juvenile-onset disease tends to be more aggressive and requires more frequent surgical intervention. The current mainstay therapy for children with RRP is surgical debridement, although various adjuvant medical therapies appear to slow disease progression in some patients. Many patients require frequent endoscopic debridement to maintain airway patency and adequate voice quality. Recurrent respiratory papillomatosis can be fatal as a result of chronic pulmonary spread of disease, malignant degeneration of the papillomatous lesions, or acute airway obstruction.⁽³⁾

Tracheal spread has been reported in as many as 26% of children with RRP, but involvement of the distal bronchopulmonary tree occurs in less than 5% of children.⁽⁵⁾ It may manifest as recurrent pneumonia, bronchiectasis, solid or cystic pulmonary masses, atelectasis, cystic pulmonary degeneration, and postobstructive infections requiring frequent hospitalization for antibiotic therapy.

Prognosis in the cases of malignant transformation is poor. In order to catch the disease early, biopsies performed at the time of routine endoscopic debridement are recommended to assess histological changes in the papillomata that may suggest malignant or premalignant changes. In addition, HPV typing is important due to its association with the incidence of malignant degeneration as HPV-11 has been shown to integrate into host DNA and cause a p53 genetic mutation⁽⁴⁾. However, it does not appear that p53 is a molecular marker for monitoring the transformation process.⁽⁸⁾ Unfortunately, it is uncommon to see a histologic progression through dysplasia over time. Thus, these cancers may be very difficult to diagnose histologically and clinically early in the course of the transformation of the disease.⁽⁸⁾

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Images in Clinical Medicine

Calcified Uterine Fibroid Fibroma

By: M. Alejandra Flores, MD and George Manoukian, MD

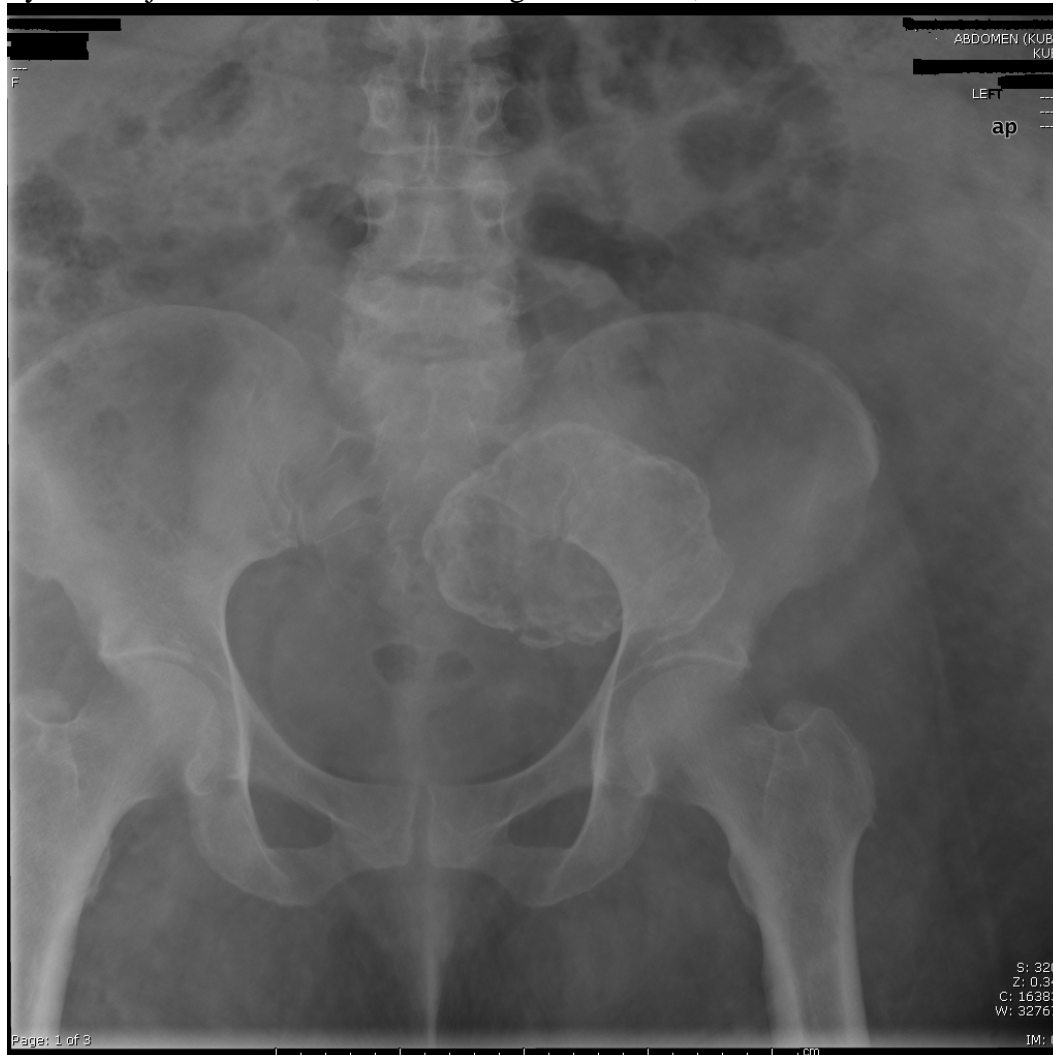


Fig 1. Abdominal X-ray showing a calcified lesion at the left lower quadrant of the abdomen.

A 51 y/o woman with past medical history of diabetes, hypertension, congestive heart failure, menorrhagia and microcytic anemia was admitted to the hospital for heart failure exacerbation. On review of systems, the patient complained of constipation, for which a KUB was done. Pelvic radiography showed a 9 X 12-cm calcified mass overlying the left pelvis. The differential for the mass included an eccentric fibroid, a chronic iliac aneurysm, or less likely, an ovarian/adenexal mass. CT of the abdomen/pelvis was done to further characterize the mass. This showed confirmed the presence of a peripherally calcified mass in the left adenexa and a lobular appearing uterus most likely consistent with

a single calcified uterine fibroid and multiple noncalcified fibroids. This was compatible with her clinical picture of menometrorrhagia, microcytic anemia, and iron studies consistent with iron deficiency anemia.

Abdominal calcifications are quite common, and it is important to be familiar with the different etiologies. Most of them have certain characteristics that will help identify the underlying pathology. Calcifications in the right upper quadrant are usually gallstones or kidney stones. If the calcifications are multiple, are very close together, and lie outside the normal expected area of the kidney, they are most likely gallstones. Gallstones are visible in only 10-20% of cases. Ultrasound is vastly superior but plain abdominal x-ray is often the initial investigation for abdominal pain in a patient. The gallbladder may become calcified after repeated episodes of cholecystitis. This is called a porcelain gallbladder and 11% will become malignant.

The pancreas lies at the level of T9-T12 vertebrae. Calcification occurs in chronic pancreatitis and may show entire outline of the gland.

Between the levels of T12 and L2, nephrocalcinosis may be seen. Calcification of the renal parenchyma indicates pathology including hyperparathyroidism, renal tubular acidosis, and medullary sponge kidney.

Renal calculi tend to obstruct at certain sites, especially the pelvi-ureteric junction, brim of the pelvis, and vesico-ureteric junctions. These are much more commonly identified on abdominal x-ray, though detection depends on the composition of the stone and degree of radio-opacity.

Abdominal aortic aneurysms are usually below the 2nd lumbar vertebra. Calcification may make them obvious and can give a rough indication of the internal diameter. Abdominal ultrasound is required for accurate assessment, and to determine the need for surgery or follow up.

As described in this case, uterine fibroids can become calcified.

In the pelvic region bladder calculi may occasionally be seen. Bladder stones are usually quite large and often multiple. Calcification of a bladder tumor may also occur. Schistosomiasis may produce calcification of the bladder wall.

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