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The Association Between Metabolic Syndrome and Gallstone Disease: A Case Report

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METABOLIC SYNDROME AND GALLSTONE DISEASE

PERMISSION

Title

Department   Nursing

Degree      Master of Science

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Date ___03/27/2019________________
Abstract
Metabolic syndrome and gallstone disease are becoming more prevalent and cause significant morbidity and mortality, as well as cost to the healthcare system. They share common risk factors, and recent evidence has shown that metabolic syndrome may be associated with subsequent gallstone disease. In this case report, a 47-year-old female patient, with a history consistent with metabolic syndrome, presented with right upper quadrant abdominal pain, nausea, and vomiting and was subsequently diagnosed with gallstone disease. A literature review was conducted to determine what the association is, if any, between metabolic syndrome and gallstone disease. Many factors in the case report were consistent with evidence found in the literature review that metabolic syndrome is associated with the development of gallstone disease. Practitioners should be aware that patients with metabolic syndrome may be at risk for developing gallstone disease and institute preventive measures. Preventative measures include supporting patients gradual weight loss to ideal body weight, strict glycemic control, regular moderate exercise, and eating a non-hypercaloric healthy diet.
The Association Between Metabolic Syndrome and Gallstone Disease: A Case Report

**Background**

A 47-year-old female patient, with a history consistent with metabolic syndrome, was seen in clinic for right upper quadrant abdominal pain, nausea, and vomiting. A thorough history and physical exam was performed, as well as laboratory studies and imaging. She was subsequently found to have acute cholecystitis. Her obesity and diabetes were known risk factors for both metabolic syndrome and gallstone disease. Lifestyle, dietary factors, and comorbid conditions in her case may have affected the course of her disease and been possible opportunities for prevention if successfully identified and intervened upon.

Cholelithiasis, or gallstones, will develop in up to 20% of adults with >20% of this population developing symptoms or acute complications, such as acute cholecystitis, requiring treatment (Lammert et al., 2016). Metabolic syndrome is common and increasing in prevalence across all sociodemographic groups with more than one third of US adults meeting definition and criteria for the syndrome (Moore, Chaudhary, & Akinyemiju, 2017). Metabolic syndrome is defined as being present when three out of five criteria are met: elevated waist circumference, elevated triglycerides or treatment for it, low HDL or treatment for it, hypertension or treatment of hypertension, and elevated fasting glucose or treatment for it (Moore et al., 2017).

Treatment of gallstone disease, including cholecystectomy, is common and imparts risk of morbidity and mortality on patients as well as significant costs to the healthcare system. With the significant costs, morbidity, and mortality associated with gallstone disease it becomes important to identify risk factors that can be mediated and measures instituted for prevention of gallstones.
This is a case report of a patient with a history consistent with metabolic syndrome and diagnosed with gallstone disease. Many of the risk factors for both metabolic syndrome and gallstone disease are potentially modifiable (Di Ciaula, Wang, & Portincasa, 2019). In this case it was unknown if the patient history of metabolic syndrome contributed to her eventual development of gallstone disease or if the two diseases simply have shared risk factors. It was also unknown if preventive measures or treatment of metabolic syndrome could be a factor in prevention of gallstone disease.

**Case Report**

A 47-year-old, Caucasian female presented to the clinic with concern for severe epigastric and right upper quadrant abdominal pain that began after eating the previous evening. The pain was unremitting and associated with nausea, vomiting, and radiation of the pain from the midline epigastric area, across the right upper abdomen, and into the right shoulder. She had felt warm and feverish but had not taken her temperature. She denied hematemesis, diarrhea, constipation, melena, or hematochezia. Treatment at home with heat was unsuccessful and the pain was made worse with movement and lying flat. There was no history of recent travel, no recent illness, and no changes in weight. She had similar pain after meals in the recent past that went away without treatment but were not as severe in intensity as the current episode. She did not regularly check her blood glucose at home.

Past medical history included diabetes mellitus type 2, hypertension, and obesity. These were being managed with metformin 1000mg/day and lisinopril 20mg/day. She had no prior history of surgery. Family history was remarkable for mother with gallstone disease and father with stroke at 65 years of age. The patient denied ever using tobacco or illicit drugs. She regularly drank 1-2 glasses of wine most nights and had ingested 1-2 glasses more than usual the
prior 2 days. Her lifestyle was sedentary, without regular exercise, and diet included high fat and carbohydrate “comfort foods”.

On physical exam she had tachycardia with a heart rate of 102, mild distress, and grimacing at rest. Her temperature was 99.5, blood pressure 116/70, respirations 20, and a BMI of 30. She did not appear jaundiced with clear eyes and appropriate skin color for ethnicity/race. Lungs were clear to auscultation. Heart sounds regular S1 S2 without murmur, friction rub, or gallops. Abdomen was soft, round, and obese with active bowel sounds. No organomegaly was palpated. There was guarding and diffuse tenderness to palpation in the right upper quadrant with positive Murphy sign. No ascites or fluid wave was appreciated. No edema was present.

Differential diagnosis included acute cholecystitis, biliary pancreatitis, choledocholithiasis, and peptic ulcer disease. Classic indicators for cholelithiasis were present: female, fat, forties, fertile, and fat intolerant.

AST, ALT, alkaline phophatase and bilirubin were mildly elevated. WBC’s also very mildly elevated. Blood glucose was 213. Amylase, calcium, and other serum chemistries were normal. Abdominal ultrasound showed cholecystitis.

General surgery was consulted. Pain and nausea control would have been implemented. Patient was counseled to schedule an appointment after surgery for counseling and management of her lifestyle including diet, exercise, blood glucose control, and alcohol intake to prevent further complications of her existing medical problems.

**Literature Review**

The patient in the case report had a history of type 2 diabetes mellitus, hypertension, and obesity. Her obesity, although unmeasured, had the appearance and characteristics of abdominal
obesity. This history meets the established definition and criteria for metabolic syndrome (Moore et al., 2017). Her presentation was classic for acute cholecystitis. What was interesting in this case was the presence of metabolic syndrome and if it contributed to her development of symptomatic gallstone disease. If metabolic syndrome was a contributing factor to gallstone disease then metabolic syndrome components and treatment may be a target for future prevention efforts to decrease the cost, morbidity, and mortality associated with gallstone disease.

A review of the literature was conducted utilizing PubMed, CINAHL, and Cochrane Database of Systematic Reviews. Relevant search terms utilized were gallstone disease, cholelithiasis, and metabolic syndrome. Search results were limited to within the past 5 years. After full text review eleven studies and articles were found to match search criteria and suitability to the case report. The overall quality of evidence, on the association between metabolic syndrome and gallstone disease, was low as most studies and articles were cross sectional, retrospective, expert opinion, or expert review. Two studies had higher levels of evidence. One was a large prospective cohort study. The other study was a cohort study that compared the cohort findings with a systematic review and meta-analyses.

Five recent studies found an association between metabolic syndrome and gallstone disease (F. Ahmed, Baloch, Memon, & Ali, 2017; M. Ahmed et al., 2018; Lin et al., 2014; Shabanzadeh, Sørensen, & Jørgensen, 2016; Zhu et al., 2016). Expert opinions and reviews noted an increased risk of gallstones in patients with metabolic syndrome or metabolic syndrome as a risk factor for gallstone disease (Di Ciaula et al., 2019; Garruti, Wang, Di Ciaula, & Portincasa, 2018; Portincasa et al., 2016; Feakins, 2016). However, the recent studies differed somewhat on which determinants of metabolic syndrome were present in association with
gallstone disease. There were no studies found in the literature that were designed to determine if metabolic syndrome was causative of gallstone disease. Further research would be necessary to determine if there is causality.

All five studies analyzed the metabolic syndrome criteria in relation to gallstone disease. The combined body of evidence showed that all the metabolic syndrome criteria are associated with gallstone disease to some extent. However, the individual study findings were heterogenous on which components of metabolic syndrome were associated with gallstone disease. The differences between individual studies make it less clear whether metabolic syndrome may be a cause of gallstone disease or if they merely share some of the same risk factors.

**Risk Factors**

Patients can have multiple shared risk factors for both metabolic syndrome and gallstone disease. Obesity, diabetes, sedentary lifestyle, and poor diet with overnutrition are all factors in the development of both metabolic syndrome and gallstone formation. Metabolic syndrome is characterized by increased insulin resistance and hyperinsulinemia (Feakins, 2016). Insulin resistance, along with type 2 diabetes, is an independent risk factors for the development of gallstones and gallstone disease as it promotes the hypersecretion of biliary cholesterol (Lammert et al., 2016). The pathological connection makes sense as metabolic syndrome would lead to increased insulin resistance which would lead to increased risk for the development of gallstone disease.

Sedentary lifestyle and poor diet, even without the presence of metabolic syndrome, puts patients at risk for gallstone formation and subsequent gallstone disease. Overnutrition and
A sedentary lifestyle lead to increased synthesis of hepatic cholesterol (Lammert et al., 2016), which is a factor in the formation of gallstones.

Lin et al. (2014), in a large cross-sectional cohort, found abdominal obesity, elevated blood sugar, hyperglycemia, low HDL, and high triglycerides to all be associated with a higher probability of gallstone disease. Abdominal obesity was found to be the most significant of these risk factors (Lin et al., 2014). Shabanzadeh et al. (2018) noted that increasing BMI and obesity are associated with increasing residual volumes in the gallbladder and impaired contractility which favor bile stasis and gallstone formation. These are consistent with metabolic syndrome criteria and show a clearer correlation between metabolic syndrome and gallstone disease.

Low HDL levels were found to be a factor in the association between metabolic syndrome and gallstone disease (Lin et al., 2014; Shabanzadeh et al., 2016). Increased HDL levels are associated with rising bile acid synthesis, which would decrease the cholesterol saturation index, and protect from gallstone formation (Shabanzadeh et al., 2016) and low HDL levels the opposite. Knowing patients HDL levels helps determine if these levels are a factor in metabolic syndrome and subsequent gallstone disease.

Advancing age has been shown to be an independent risk factor for both gallstone disease and metabolic syndrome (Lammert et al., 2016; Moore et al., 2017). The prevalence of both metabolic syndrome and gallstone disease increases with age (Lin et al., 2014). Aging leads to longer exposure to the chronic factors that underlie metabolic syndrome and gallstones, namely insulin resistance from diabetes and obesity. However, not all evidence showed age to be a factor in the association between metabolic syndrome and gallstone disease (Zhu et al., 2016). This may be a case of age being a separate independent risk factors for each process and not necessarily being correlated with metabolic syndrome leading to gallstone disease.
The role of the hypertensive component of patients metabolic syndrome in gallstone formation is less clear in the literature. Both Lin et al. (2014) and Zhu et al. (2016) found higher blood pressure to be positively associated with the development of gallstone disease, the exact mechanism of why this is so is unclear. Shabanzadeh et al. (2016), in their cohort study with meta-analysis and systematic review, did not find blood pressure to have a significant association with gallstone formation.

**Metabolic Syndrome and Asymptomatic Gallstones**

Patients may have gallstones for many years without being symptomatic, as most patients who do have gallstones remain asymptomatic throughout their life (Portincasa, 2016). Routine screening for asymptomatic gallstones is not recommended. Even if asymptomatic cholelithiasis is found incidentally on abdominal imaging it is managed expectantly (Di Ciaula et al., 2019). This brings up the question of metabolic syndrome being a possible trigger for those who have asymptomatic gallstones to become symptomatic and have acute complications, such as acute cholecystitis. M. Ahmed et al. (2018) found an association between metabolic syndrome and complicated gallstone disease compared to uncomplicated disease, however the sample size was too small and not powerful enough to have statistical significance.

If patients have asymptomatic gallstones, and evidence in the literature suggests metabolic syndrome may increase risk for developing symptomatic gallstone disease, it does not currently affect management until patients become symptomatic. There is no evidence, based on benefits and harms, to support cholecystectomy in an asymptomatic patient (Lammert et al., 2016). Garruti et al. (2018) even argue that cholecystectomy may cause metabolic disturbances and aggravate metabolic syndrome itself. There is no direct cost savings in prophylactically treating asymptomatic patients with cholecystectomy who may be at risk of developing
symptomatic disease, as the treatment is the same. Medical dissolution therapy and extracorporeal shockwave therapy also lack evidence of benefit in asymptomatic gallstone patients, as the rates of cure are low and recurrence high (Lammert et al., 2016).

Discussion

The benefit of the knowledge that metabolic syndrome is associated with gallstone disease, is in prevention, diligent monitoring, and patient education. Metabolic syndrome already carries serious potential consequences, such as increased risk of cancers and cardiovascular disease (Moore et al., 2017). Gallstone disease is yet another reason to prevent or mitigate the risk factors involved in metabolic syndrome. A patient may have several episodes of right upper quadrant abdominal pain after eating before presenting to clinic for the abdominal pain. If metabolic syndrome is recognized at an earlier point, and the patient educated on the association with gallstone disease, they can be taught signs and symptoms of gallstone disease to be aware of. They may present earlier with the first episode of symptoms.

Even more useful would be using this knowledge to help prevent or mitigate risk factors for progression to gallstone disease. As was discussed earlier obesity, sedentary lifestyle, a poor diet, and poorly monitored and controlled diabetes are all contributing factors to metabolic syndrome and gallstone disease. These factors are prime targets for preventive measures and education. Patient’s may be more motivated to diet, exercise, maintain healthy weight, or exercise tighter blood glucose control if they know there are serious consequences that may develop, including the necessity of a major surgery like cholecystectomy. These are the preventive measures that should be taken to avoid subsequent gallstone formation (Lammert et al., 2016).
The current evidence of the association between metabolic syndrome and gallstone formation is increasing, but low level and limited at this time, and needs further study. There have not been random controlled trials to determine causation, nor has there been large-scale well-designed studies elucidating the exact mechanism of their correlation. Even so, the knowledge that metabolic syndrome and gallstone formation share many risk factors and pathogenic mechanisms is useful. Metabolic syndrome is an easily assessable measure (M. Ahmed et al., 2018), which makes it easy for practitioners to recognize it as a potential risk factor for gallstone disease. When a patient is seen in practice with metabolic syndrome practitioners can be alert to the fact they have concurrent risk factors for the development of gallstone disease. This may allow them to implement preventive measures.

The events of this case report are common, and are steadily becoming more so, as the prevalence of both metabolic syndrome and gallstone disease continue to increase (Feakins, 2016). More practitioners need to be aware of the potential association between metabolic syndrome and gallstone disease.

**Learning Points**

- Limited low-level evidence in the literature points to an association between metabolic syndrome and development of gallstone disease.
- Metabolic syndrome and gallstone disease share many of the same risk factors including obesity, diabetes (insulin resistance), increasing age, sedentary lifestyle, and poor diet.
- Patients with metabolic syndrome are prime targets for preventive measures to be instituted to avoid associated gallstone disease and costly cholecystectomy.
Preventive measures to be instituted include gradual weight loss to ideal body weight, strict glycemic control, regular moderate exercise, and eating a non-hypercaloric healthy diet.
References


