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Is Hyperuricemia an Independent Risk Factor for Cardiovascular Disease?

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PERMISSION

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Abstract

Different studies have examined the association between hyperuricemia and cardiovascular disease (CVD) and it continues to be a controversial issue. This topic stemmed from a case study of a 46-year-old man who presented to the clinic for evaluation of an acute gout attack in his right great toe. With this initial episode of gout and coexisting elevated serum uric acid level, the risk of developing CVD was questioned. A literature review was conducted to examine if hyperuricemia was an independent risk factor for the development of CVD. Theories on cellular mechanisms of uric acid as being atherogenic in nature were all a common theme found in the reviewed studies. Also, all the studies reviewed did not show consistent findings of hyperuricemia being an independent predictive factor only that there is an association between the two variables. Many studies have concluded that hyperuricemia and CVD are associated as hyperuricemia is found in many people who also have the risk factors for CVD or the diagnosis of CVD itself. Additionally, numerous studies did report that serum uric acid levels should be used as a biomarker for cardiovascular risk as it is inexpensive and modifiable treatment options are available.

Keywords: hyperuricemia, serum uric acid, serum urate, cardiovascular disease

Is Hyperuricemia an Independent Risk Factor for Cardiovascular Disease

Hyperuricemia occurs in the body when the serum uric acid level exceeds 7mg/dl, "at which point it starts to crystalize within the human body" (Kuwabara, 2015, p. 242). There is either a problem related to the overproduction or more commonly, the underexcretion of uric acid. In recent years, there has been ongoing controversy in regards to hyperuricemia as being an independent risk factor for cardiovascular disease (CVD). CVD can be defined as being a, "group of disorders of the heart and blood vessels and they include: coronary heart disease (CHD), cerebrovascular disease, peripheral arterial disease (PAD), rheumatic heart disease, congenital heart disease, and deep vein thrombosis and pulmonary embolism" (World Health Organization [WHO], 2016, para. 2).

The case report discussed throughout the paper includes a 46-year-old man who presented to the clinic for evaluation of what appeared to be a gout attack on his right great toe, also known as podagra. During the interview, the patient did report a past medical history of dyslipidemia, type 2 diabetes mellitus, and hypertension (HTN), all being treated medically. Additionally, his body mass index (BMI) was elevated at 29 mg/k2 putting him in the overweight category. This case report will be discussed throughout the paper and the full report can be seen in the appendix.

Studies have shown that people with HTN, insulin resistance, obesity, and CVD do have a correlating higher baseline serum uric acid level (Sharma, Rathore, Sarkar, & Bidwai, 2016). The purpose of this paper is to define the relationship between hyperuricemia and CVD and if in fact hyperuricemia is an independent risk factor for the development of CVD. Is the patient at a higher risk due to his recent episode of hyperuricemia? Or conversely, is the presence of elevated

serum uric acid levels in combination with the correlating CVD risk factors the contributors to the association between hyperuricemia and CVD?

Case Report

The case report includes a 46-year-old Caucasian man who presented to the clinic for evaluation of his right great toe with complaints of redness, pain, and swelling that had started the same day upon wakening. Subjective information has been obtained. He denied trauma to toe and described the pain as a dull constant throb. Reports the pain as 6/10 in severity. He denied radiating pain and reports no other joints were involved. He had never experienced these symptoms before. Pain was aggravated with ambulation and weight bearing. He had not attempted treatment.

Pertinent past medical history includes type 2 diabetes, dyslipidemia, and HTN. He reported conditions are well-controlled on medications and with diet. Blood sugar readings are normally low 100s. He could not remember his last A1C value but knew it was in the normal range. He also reported having kidney stones on two separate occasions. He initially passed the stones without intervention and underwent a lithotripsy for his second episode. Unaware of the stone type.

Current medications include: Hydrochlorothiazide (HCTZ) 25 mg by mouth (PO) daily; Lisinopril 20 mg PO daily; Metformin 500 mg PO daily; Simvastatin 20 mg PO daily; and Aspirin 81 mg PO daily. He reported taking medications as prescribed. Denied usage of over-the-counter medications.

Social history obtained. He denied smoking and illicit drug use. Reported drinking 3 to 4 beers per week. Last drink was last night. His family does also own a butcher shop, so he did

admit to eating sausage frequently. He participates in curling once a week, otherwise no formal exercise.

His review of systems was negative except what was noted in the history of present illness (see Appendix to read full case report).

Exam and Treatment

The patient's vital signs were within normal limits for his age except his BMI, which was elevated at 29 mg/k2. Upon physical exam, erythema and inflammation were noted on the metatarsal-phalangeal joint of the right great toe. No wounds or open areas. Otherwise exam was unremarkable.

Diagnostic work-up included lab work. A complete blood count (CBC), basic metabolic profile (BMP), and a serum uric acid level were completed. Findings included an elevated serum uric acid level at 10.9 mg/dl with the other labs unremarkable.

The patient was diagnosed with a gout attack. His symptoms, exam findings, and elevated serum uric acid level were consistent with this diagnosis. If additional testing were needed an arthrocentesis could have been performed to analyze the synovial fluid of the affected joint for definitive diagnosis and to rule out pseudogout.

At that time, he was on the medication HCTZ, which can contribute to gout. Due to his recent episode, he was told to discontinue the medication and continue to monitor his blood pressure. He was initially treated with Indomethacin 50 mg PO for 10 days. His BMP was unremarkable and he denied gastrointestinal reflux disease and peptic ulcer disease. Education included: avoid weight bearing and rest, ice and elevate extremity as needed. Encourage fluid intake to prevent dehydration, 8-10 glasses per day. Dietary restrictions: avoid high purine diet, including alcohol, red meat, sea food, aged cheeses, oatmeal, and sweet breads. Follow-up was

scheduled for one week to recheck blood pressure and reevaluate for any improvement in symptoms. He was instructed to follow-up sooner if symptoms worsen or do not improve. Worsening symptoms include fever or worsening redness, pain, and swelling. Patient agreed to the above treatment plan (see Appendix for full case report).

Pathophysiology

The physiology of how uric acid production and excretion occurs in the body is a key aspect to understanding the basis of the paper. Normal serum uric acid ranges can vary depending on differing facilities and also based on gender. In males, the normal value can range from 3.5 mg/dl-7 mg/dl and in females the range is usually 0.5-1 mg/dl lower. So, hyperuricemia occurs due to an imbalance of overproduction and/or underexcretion of uric acid in the body, with serum values usually above 7 mg/dl. Also, genetics can play a role but this will not be covered in the paper (Gustafsson, 2013).

In humans, uric acid is the end-product of purine metabolism. Overproduction is a result of excess purine intake either from oral intake and/or biosynthesis. Oral intake consists mainly due to dietary consumption. Certain foods such as organ and red meats, high fructose foods, seafood, and alcoholic beverages are higher in purine content. Ingestion and absorption of food occurs in the digestive tract and from there it is metabolized into uric acid. Biosynthesis occurs with, “the major energy source in humans, adenosine triphosphate (ATP) structure, centers on adenine, which is converted to hypoxanthine, xanthine, and eventually uric acid during ATP metabolism, and is subsequently excreted from the cell and into the blood,” thereby increase the uric acid level (Kuwabara, 2015, “Physiological Mechanisms,” para. 4). The patient had reported eating a large quantity of red meat, including sausage, in addition to drinking 3-4 beers per week, all increasing in his risk for hyperuricemia and potentially his gout attack.

In terms of uric acid reabsorption and secretion, the kidney and digestive tract are primarily responsible. The urate transport 1 (URAT 1), located in the proximal renal tubules, is largely responsible for the reabsorption of urate. There are other urate transporters, a few located in the digestive tract, that deal with the reabsorption and secretion pattern of urate. Renal handling of urate includes the processes of glomerular filtration, reabsorption, and two secretory phases (Kuwabara, 2015; Qazi, 2016).

Underexcretion, the most common cause of hyperuricemia, can occur either with alterations in the above processes, drug intake, or the acquisition of certain medical conditions. For example, if the person is in a state of acidosis, as in diabetic ketoacidosis, the acids accumulate and compete with urate during the tubular secretory phase. Additionally, certain medications can influence uric acid levels by affecting the proximal renal tubular absorption and excretion. The patient in the case study was taking HCTZ, a thiazide diuretic, which has potentially been shown enhance reabsorption of uric acid (Kuwabara, 2015; Qazi, 2016).

Finally, a combination of underexcretion and overproduction can ensue with the main causative factor being alcohol intake. This mechanism, “results in accelerated hepatic break down of ATP and the generation of organic acids, that compete with urate for tubular secretion” (Qazi, 2016, “Pathophysiology,” para. 8). Another increasingly popular combined cause includes the intake of fructose-sweetened soft drinks. The patient in the case study did admit to drinking 3-4 beers per week and in combination with his reported dietary intake and HCTZ medication, this could have all contributed to the development of hyperuricemia and gout attack.

Hyperuricemia can lead to non-crystal deposition disorders and urate crystal deposition disorders. The later condition includes gout, chronic kidney disease, and nephrolithiasis (Becker, 2017). The patient did present with an acute gout attack, with the serum uric acid level 10.9

mg/dl. His nonmodifiable risk factors for developing gout included his age and male gender. He denied a family history of gout. Modifiable risk factors included his overweight BMI, dietary and alcohol intake, his medical history of HTN and type 2 diabetes mellitus, and the use of a thiazide diuretic (Becker, 2017).

Literature Review

The information provided below will relate to the case study presented above. The goal of this paper is to look at the relationship of hyperuricemia and CVD. Is hyperuricemia an independent risk factor in developing CVD? Is the patient in the case study at a higher risk for developing CVD? A complete literature review will be conducted and will examine the causes of hyperuricemia and its relationship with CVD based on the latest evidence.

Theories Postulated on the Relationship Between CVD and Hyperuricemia

When taking a closer look at this relationship, there are a few cellular mechanisms that have been addressed by research possibly linking the two conditions together**.** Most all studies summarized in the literature review below have made references to these mechanisms. The areas to be discussed include, “effects of oxidative stress during uric acid production, disorder via urate transporter, and hyperuricemia-induced vascular disorders (facilitation of arteriosclerosis by monosodium urate crystals)” (Kawabara, 2015, pp. 249-250).

The first angiopathic mechanism is directly related to the production of uric acid. As discussed above, the production of uric acid occurs in numerous way relating to underexcretion and overproduction. From human consumption of food and alcohol to different conditions occurring in the body, such as anaerobic metabolism, all require the utilization of ATP and xanthine oxidase. This consequently produces uric acid as an end-product. A reactive oxygen species is formed during the conversion of hypoxanthine to uric acid via xanthine. This

mechanism is presumably what leads to arteriosclerosis in two ways. The first being, “the chronic xanthine oxidase activity causes vascular remodeling…” and secondly, “the reactive oxygen generated during the course of uric acid production binds to NO [nitric oxide], a vasodilator substance, and suppresses the function of NO…” which leads to vasoconstriction (Kuabara, 2015, p. 249).

The second mechanism is related to the urate transporters. The transporters are located in the endothelial and smooth muscle cells throughout the body. Once the transporters are activated, the uric acid enters the cell for reabsorption and the growth factors and the inflammatory and vasoconstrictive mediators (i.e. endothelin-a & angiotensin II) are released. Cellular proliferation and arteriosclerosis are thought to be the result of this process (Kanbay et al., 2017; Kawabara, 2015).

Finally, the last mechanism is due to the accumulation of monosodium urate crystals. With an elevated serum uric acid level, uric acid does not dissolve and will form crystals in the blood vessels. Blood coagulation is affected and inflammatory mediators are released. Arteriosclerosis is facilitated by “the release of superoxides, LDL (low density lipoprotein) oxidation, and disorders of the endothelial cells and blood platelets” (Kuwabara, 2015, p. 250).

Synthesis of Current Research

In total, 11 articles related to the association between hyperuricemia and CVD will be critically analyzed in this literature review. A search using the University of North Dakota’s Harley French Library of the Health and Science was completed using the CINAHL and PubMed databases to find evidence on the topic. All searches were narrowed down to publications within the last eight years.

Qin et al. (2014) conducted a population-based cross-sectional study to determine the significance of elevated serum uric acid levels and if it is associated with CVD. The population included in this study were 8,510 Chinese individuals 40 years of age and older, excluding people with CHD or history of a stroke. A biochemical profile was completed on the participants looking for metabolic syndrome. A diagnosis of stroke and/or CHD were the CVD outcomes measured. After the CVD risk factors not included as outcomes and the components of metabolic syndrome were adjusted for, the results indicated an association between elevated serum uric acid level and CVD (Qin et al., 2014). This article was relevant to the topic because it directly addressed an association of elevated serum uric acid and CVD independent from the other CVD risk factors and components of metabolic syndrome. The patient in the case study did have components of metabolic syndrome and risk factors for CVD and still independent of this, he was at a higher risk for CVD due to his elevated uric acid level. However, he was not of Chinese ethnicity, which could sway results.

Nossent, Raymond, Divitini, and Knuiman (2016) conducted a prospective analysis with a 15-year follow-up time, using the data from the Brusselton Health Study and outcomes obtained from state-wide hospital discharge and mortality registries. A baseline plus specific time-averaged serum uric acid levels were obtained from the study population with the researcher's end-goal to determine if "increased baseline and timed average uric acid levels alone or together with a history of gout were risk factors for cardiovascular events and mortality…" (Nossent, Raymond, Divitini, & Knuiman, 2016, "Background," para. 2). Interestingly, the results did not show that the serum level was an independent predictive factor in the development of CVD but that in individuals with preexisting CVD and gout there was an increased risk of cardiovascular death related to hyperuricemia (Nossent et al., 2016). This article

was relevant to the topic. The patient did have gout in combination with risk factors for the development of CVD but did not have an actual diagnosis of CVD. If he would develop CVD with subsequent episodes of gout the results found in this article placed him at an increased risk of cardiovascular death.

Zhoa, Huang, Song, and Song (2013) conducted a meta-analysis of prospective studies with a long follow-up period examining if baseline serum uric acid levels are an independent risk factor for cardiovascular or all-cause mortality events in the general population. The findings of the current meta-analysis did support the theory that elevated serum uric acid levels do correlate with higher risks of cardiovascular and all-cause mortality. A gender specific association was found in males; they were found to have an increased risk for all-cause mortality at higher rates than women with elevated serum uric acid levels (Zhoa, Huang, Song, & Song, 2013). Although, our patient did not have a baseline serum uric acid level, his was elevated at 10.9 mg/dl which, according to this study, places him at higher risk for cardiovascular and all-cause mortality, especially due to his male gender.

Zalawadiya et al. (2015) conducted a cohort study using the National Health and Nutrition Examination Survey (NHANES) III. They wanted to examine the association between serum uric acid and CVD mortality taking into consideration ethnicity and a population free of CVD and diabetes. The population included 11,009 adults with a mean follow-up time of 14.5 years. The participants were subject to questionnaires, physical examination and laboratory testing. The results of the study concluded that serum uric acid level is not an independent predictor for CVD/CHD mortality regardless of ethnicity and gender (Zalawadiya et al., 2015). The patient discussed in the case study did have a diagnosis of type 2 diabetes mellitus, so this article's findings would not pertain to him.

Capuano et al. (2017) conducted a 10-year prospective cohort study to "examine the potential link between uric acid levels and classic risk factors and, in particular, to verify the role of hyperuricemia in the development of major cardiovascular events" (p. 159). The population studied totaled 1,175 randomly chosen men and women between the ages of 25-74 years located in Southern Italy. The findings reported that out of 1,175, 135 people reported at least one major cardiovascular event (MACE) and to note these individuals all had higher serum uric acid levels compared to the individuals that did not experience MACE. They concluded that hyperuricemia is associated with higher cardiovascular risk and should be considered an independent risk factor (Capuano et al., 2017). This study was very relevant to our patient despite the location of study. It did address MACE but not the actual development of CVD but still pertains to the patient's over health. This study also recommends including hyperuricemia in cardiovascular prevention strategies.

Sharma, Rathore, Sarkar, and Bidwai (2016) conducted a cross-sectional study to evaluate the relationship between serum uric acid levels and other CVD risk factors. The study group included 100 healthy individuals in the control group and the other group consisted of 100 individuals between the ages of 25-80 years with a known history of CVD. Different parameters were measured, a few being BMI, serum uric acid, and a lipid profile. The findings of the study support that hyperuricemia is found more in the CVD group and there is a significant link between serum uric acid levels and the CVD risk factors. They consider hyperuricemia a "red flag" for the development of CVD however, not an independent predictor. One limitation to the study is it was a cross-sectional design. A prospective study could have been more beneficial and gave more information as to the development of CVD (Sharma et al., 2016). This study does relate to our case study. Hyperuricemia was not found to be an independent risk factor but was

shown to be increased in individuals with CVD and risk factors of CVD. Our patient has hyperuricemia and he reported a history of HTN, dyslipidemia, type 2 diabetes mellitus and being overweight, all increasing his risk for the development of CVD.

Krishnan and Sokolove (2011) conducted a literature review to explore the relationship between serum uric acid levels and the risk of cardiovascular outcomes. They wanted to determine if the link was causal or direct. They looked at previous studies that have linked hyperuricemia to other conditions such as HTN, cardiomyopathy, and angina. Other research they reviewed found a possible correlation between C-reactive protein (CRP) and serum uric acid levels as markers for CVD. After reviewing the literature, they concluded that the link between CVD and hyperuricemia may be causal but that serum uric acid concentrations can be used in the same way as CRP, as a cardiovascular risk marker (Krishnan & Sokolove, 2011). This article is relevant to the main topic because it determined the relationship as causal. The man in the case study presented does have elevated serum uric acid concentration, which could be an indicator of cardiac risk however, a baseline serum uric acid level should be drawn once the gout attack has resolved.

Chen, Chuang, Chen, Yeh, and Pan (2009) conducted a prospective cohort study looking at the temporal link between serum uric acid level, cardiovascular mortality, and hyperuricemia in the general population. They reported that research has already shown an increased risk of CVD in high-risk groups including people with HTN, gout, diabetes, etc.. The Taiwanese participants were 35 years of age and older and were split into four groups based on their serum uric acid level. Based on certain criteria, they were also categorized as high-risk or low-risk subgroups. Their study “demonstrated a dose-response effect of increasing serum uric acid levels on mortality, particularly cardiovascular mortality” (Chen, Chuang, Chen, Yeh, & Pan, 2009, p.

231). Additionally, they found that in the general population, hyperuricemia can be considered an independent predictor for all-cause, ischemic stroke, and total CVD mortality. However, they did reference the Framingham Study in their discussion and how people are two times more likely to have coronary heart disease, an entity of CVD, with a diagnosis of gout (Chen et al., 2009). This is a relevant study but not entirely to the case study. The patient did have an elevated uric acid level due to his acute gout attack. In order for this study to pertain to the patient, he would need a baseline lab draw and with his comorbidities he would fall in the high-risk subgroup, which already increases his risk for CVD.

Kivity et al. (2013) conducted a retrospective study aiming to determine if there is an association between serum uric acid and cardiovascular disease in a healthy population, specifically looking at gender differences. The study included 9,139 Caucasian patients of Jewish descent (2,559 women & 6,580 men) with exclusion criteria of patients less than 34 years of age and people with diabetes and CVD. Mean follow-up time was 4.8 years and outcomes measured were a diagnosis of a cardiovascular event including CHD, acute coronary syndrome, acute myocardial infarction, and ischemic stroke. During that follow-up time, 801 CVD events occurred. The authors reported a noteworthy association between serum uric acid level with CVD to a greater degree in women when compared to men. However, the sample of women were smaller which may have skewed results. They admit there is an association between the two variables but not that hyperuricemia is an independent risk factor for CVD. This study is relevant to the overall topic but the inclusion criteria may alter the results (Kivity et al., 2013). The patient in the case study would not be a candidate for the study due to his diagnosis of diabetes.

Wang et al. (2015) conducted a prospective cohort study including 5,115 healthy individuals, aged 18-30 years, looking at the association between serum urate and incident CVD.

Many measurements were considered in addition to serum urate. A baseline serum uric acid was drawn at year zero than again at years 10, 15, and 20. The results from this study included a 27-year follow-time. They concluded that with time and advancing age, the mean serum uric acid concentrations do increase and could be an early biomarker for CVD in middle-aged adults. They reported a positive correlation between the two variables, especially atherosclerosis, when looking at young to middle-aged adults. However, the coronary artery risk development in young adults (CARDIA) study is ongoing and will continue to study this population group as it ages (Wang et al., 2015). This study is relevant to the overall topic. The man in the case study was 46-years-old, so he would not have fit in this study but it can be used for the overall population as far as prevention. If serum uric acid levels are used as a biomarker for CVD at an earlier age, we could detect those at risk and possibly prevent the development of CVD in later years, thereby improving quality of life.

The last article summarized is a literature review conducted by Gomezjuardo (2016) looking at studies published with in the last six years examining if hyperuricemia is an independent risk factor for the development of CVD. A few of the most commonly diagnosed CVD's include CHD, heart failure, atrial fibrillation, and HTN. They looked at the association between hyperuricemia and these four pathologies. After reviewing the literature, the author found that hyperuricemia is an independent risk factor for the development of HTN and heart failure but not CHD or atrial fibrillation. Overall, he reported that there is insufficient evidence to support that hyperuricemia is an independent risk factor for the development of CVD, despite the findings in regards to HTN and heart failure. Limitations of the study included the short duration of time and it was a non-systematic review (Gomezjuardo, 2016). This article is relevant

to the topic because it did not find hyperuricemia as being an independent risk factor which places our man in the case study presented at a lower risk for developing CVD.

Learning Points

All populations, exclusion/inclusion criteria, and measurable outcomes are different with in each study, which can affect the end results. Some studies looked at the development of CVD, some looked at MACE and others looked at morbidity and mortality. However, all studies did find an association between hyperuricemia and CVD, but not all findings reported hyperuricemia as being an independent risk factor for the development of CVD. After conducting this literature review a few points were consistently seen throughout the different studies and are as follows:

- Uric acid is linked with many CVD risk factors, such as HTN and diabetes leading to the association between the two.
- Hyperuricemia is found more often in people with the risk factors for CVD or CVD itself.
- All studies reference the cellular actions of uric acid as being angiopathic and this possibly being a correlation for the development of CVD. One example being, prolonged hyperuricemia or gout increases the risk for CVD due to endothelial dysfunction and the development of atherosclerosis.
- More studies are needed to confirm that hyperuricemia is in fact an independent risk factor for the development of CVD but many studies have indicated its role as being clinically significant as it can be used as biomarker of cardiovascular risk.

The evidence discovered from this literature review directly affects the patient discussed in the case study. He did have an elevated serum uric acid level, was experiencing an acute gout attack, and had a medical history of HTN and insulin resistance, all increasing his risk for developing CVD. Most studies would agree that he is not at an increased risk of CVD

exclusively from his elevated serum uric acid level. But with all his risk factors, he should be monitored for the development of CVD and treated appropriately.

Summary and Concluding Discussion

In conclusion, many theories have been postulated on the cellular actions of uric acid and its angiopathic mechanisms possibly related to CVD. From this literature, we can take away that hyperuricemia is found more in people with the CVD risk factors or the disease itself and they should be closely monitored for disease onset or disease progression. Some studies have even suggested using serum uric acid levels as a biomarker for cardiovascular risk. It would be an inexpensive test and based on the results, the serum levels can be effectively treated by medications and lifestyle management. One ongoing study that was discussed above was the CARDIA study. It is projected to be completed in 2018. Hopefully, this study can help clarify the determinants of CVD and its risk factors, including hyperuricemia. More research is still needed on the topic of hyperuricemia being an independent risk factor for CVD development.

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Appendix

Subjective:

CC: pain and swelling to right great toe

HPI: 46-year-old man who presents to the clinic today for evaluation of pain, redness, and swelling to his right great toe, which started this morning. Denies trauma to toe. He describes the pain as a dull constant throb. Reports the pain as 6/10 in severity. He denies radiating pain and reports no other joints are involved. He has never experienced this complaint before. Pain is aggravated with ambulation and weight bearing. He has not attempted treatment.

He does have a past medical history of type 2 diabetes and hypertension. He reports both are well controlled on medications and with diet. Blood sugar readings are normally low 100s. He could not remember his last A1C. He also reported having kidney stones x 2. He passed the stone the first time and second episode he needed a lithotripsy. Unaware of the stone type.

Allergies: NKDA

Medications: HCTZ 25mg PO daily; Lisinopril 20mg daily; Metformin 500 mg PO daily; Simvastatin 20mg QHS; Asa 81mg PO daily

Past medical and surgical history: HTN, Type 2 Diabetes, dyslipidemia, nephrolithiasis with lithotripsy (2 years ago)

Pertinent family history:

- Mother: Type 2 Diabetes, HTN
- Father: nephrolithiasis, HTN

Social history: Denies smoking and illicit drug use. Reports drinking 3-4 beers per week. His family does also own a butcher shop so he does report eating a lot of sausage. Exercise: does curling once a week. Otherwise no formal exercise.

ROS:

- **General:** denies fever, chills, and unintended weight loss/gain. Denies recent illness
- **Skin:** See HPI. Denies rashes and lesions
- **HEENT:** denies headaches, dizziness, or syncope
- **Chest:** denies any chest pain/pressure, heart palpitations or peripheral edema.
- **Lungs:** denies cough, wheeze, shortness of breath
- **GI:** denies nausea, vomiting, diarrhea, constipation, and heartburn
- **Musc:** denies any joint stiffness, pain, or inflammation other than right great toe. See HPI
- **Neuro:** denies paresthesia

Objective:

VS: BP-126/78; P-72; T- 37.4C; BMI- 29 kg/m2

Physical exam:

- **General:** 46-year-old male sitting upright on exam table in no acute distress. Patient makes good eye contact. Patient good historian with history reported per patient. Alert and Oriented X 3
- **Skin:** Erythema and inflammation noted to the metatarsal-phalangeal joint of the right great toe. No wounds or open areas.
- **Neck:** Supple, no lymphadenopathy, no thyromegaly
- **CV:** regular rate and rhythm. Normal heart sounds, S1, S2. No murmur
- **Respiratory:** regular rate and depth. Clear to auscultation. No wheezes or crackles
- **Abdomen:** No CVA tenderness
- **Musculoskeletal/extremities:** Normal ROM to right great toe. Dorsalis pedis 2+ equal bilaterally. Capillary refill <2 sec. Full sensation in lower extremities

Labs:

CBC
WBC 9.0
RBC 4.8
Plt 163
Hgb 14.5
Hct 45
MCV 88
MCHC 34
MCH 32

Uric Acid
10.9

BMP
BUN 23
Na 140
K 3.9
Cl 105
C02 27
Glucose 139
Cr 1.15
Calcium 8.8
GFR >60

Differentials:

- Cellulitis
- Rheumatoid Arthritis
- Pseudogout
- Gout
- Osteoarthritis

Assessment:

- **Gout**
    - Sedimentation rate could be done to rule out RA. Also, could do arthrocentesis for synovial fluid if labs were unremarkable.

Plan:

- Discussed the labs with the patient and the treatment plan. He is currently on HCTZ which can contribute to gout. Will discontinue now and continue to monitor his blood pressure. We will treat him initially with Indomethacin 50 mg PO x 10 days. His BMP was unremarkable and he denied a past history of gastrointestinal reflux disease and peptic ulcer disease.
- Education includes pathophysiology and etiology of the condition. Avoid weight bearing. Rest, ice and elevate extremity as needed. Encourage fluid intake to prevent dehydration, 8-10 glasses/day. Dietary restrictions: avoid high purine diet, including alcohol, red meat, sea food, aged cheeses, oatmeal, and sweet breads.
- Lastly, informed him if he does have recurrent gout attacks we may need to place him on a urate lowering therapy to prevent long term complications.
- Follow-up scheduled for 1 week to recheck blood pressure and if any improvement in symptoms. If symptoms worsen or do not improve he should follow-up sooner. Worsening symptoms included fever or worsening redness, pain, and swelling. Patient agrees with treatment plan and voices understanding.