Presumed anaphylaxis to Hydrochlorothiazide in a 67 year old female with known sulphonamide allergy.

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Abstract

Sulfonamide (sulfa) allergies are the second most common cause of adverse drug reactions following the beta-lactams.[1] Sulfa drugs can be divided into two classes; antimicrobial and non-antimicrobial. These two classes differ structurally and although there is some documentation of cross-reactivity there is little evidence to suggest that this should change prescribing practices.

Our female patient was 67 years old when she experienced an anaphylactic like reaction leading to cardiac arrest following taking one dose of hydrochlorothiazide 25 mg which had been prescribed the day before. The patient had a known sulfa allergy, however she had taken hydrochlorothiazide previously without any similar reaction.

Case History

Identifying data: 67 year old female, married 40 years with two children, works as a receptionist.

Past medical history: hypertension, atrial fibrillation, gastro-esophageal reflux disease, hypothyroidism, recurrent diverticulitis and vertigo.

Surgical history: Bowel resection for recurrent diverticulitis, tubal ligation, tonsillectomy

Medications:

- Pantoprazole 40 mg x BID
- Synthroid 25 mg OD
- Eliquis 5 mg BID
- Losartan 25 mg OD
- Labetalol 100 mg BID

Our patient had previously been prescribed hydrochlorothiazide in 2000 and 2005. To our knowledge the patient had taken this medication with no adverse reaction resulting. In 2007 the patient presented to Pinawa hospital with nausea and dizziness after taking expired hydrochlorothiazide. It is unclear however if this was an adverse reaction to the hydrochlorothiazide as she is known to have a long standing history of nausea and vertigo.

Allergies

- Penicillin (rash)
- Amoxicillin (vomiting, diarrhea)
- Erythromycin (upset stomach)
- Tetracycline (nausea, vomiting)
- Sulphonamide antibiotics (unknown)

Presenting Condition

On August 13, 2016 the patient's husband found her unresponsive on the floor at 0800 and called 911. She had taken her first dose of hydrochlorothiazide ten minutes earlier, which had been prescribed the day prior. She became symptomatic immediately after taking the hydrochlorothiazide and upon EMS arrival at 0813 she was reported as being diaphoretic, short of breath and speaking in two word sentences as well as experiencing the sensation of chest tightness. Paramedics reported findings of diffuse wheezing at initial assessment. Our patient arrived at Pinawa hospital via EMS at 0838 with a diffuse wheeze and no crackles. Patient was given 0.3 mg epinephrine by EMS upon arrival and had vitals of HR 110, RR 36, BP 160/63.

Upon arrival at Pinawa hospital the patient was cool, diaphoretic, lip cyanosis, and non-palpable peripheral pulses, her lungs had decreased air entry and she had a respiratory rate of 38.

At 920 her HR dropped to 50 bpm and she became unresponsive and CPR was initiated and intubation performed. The patient developed a ventricular tachyarrhythmia at 0920 and received one shock which was followed by asystole. Pupils became unresponsive and CPR proceeded until 944 when the patient was pronounced dead.

Vitals

Time	BP	Pulse	RR	Temp	Sp02
813	160/90	90	38		75 on RA
815		88	32		80 on 15L
830	150/P		32	36.8	88
840	154/112	114	38	33.9	89
850	156/80	112	34	34	89
900	161/139	106	30	33.9	89
910	110/74	103	30	33.9	74
920	190/101 (Vtach)	50			
930	157/93				
937	89/42				

Meds

Time	Drug
814	Ventolin 2.5 mg neb
817	Epi 0.3 mg IM
819	Ventolin 2.5 mg neb
831	Epi 0.3 mg IM
920	Epi 1 mg IV

925	Epi 1 mg IV
926	Amiodarone 300 mg IV
930	Epi 1 mg IV
933	150 mg amiodarone IV
935	Epi 1 mg IV
940	Epi 1 mg IV

Autopsy report

Relevant findings include

1. Dilated cardiomegaly (known from previous echo)
2. Mild pulmonary congestion
3. Toxicology was non-contributory
4. Significantly elevated blood tryptase levels. (38 ug/L – normal <10ug/L)

Cause of death was determined to be a cardiac arrhythmia likely secondary to an anaphylactic reaction to hydrochlorothiazide.

Literature review

A review of the literature was undertaken to better understand the pathophysiology of hydrochlorothiazide allergies and to identify any similar case studies and reports of cross reactivity between sulpha antibiotics and sulpha non-antibiotics.

Common adverse reactions to hydrochlorothiazide include; electrolyte abnormalities, hypotension, dermatologic reactions and GI upset. Although not frequently reported there are case reports of severe adverse reactions following hydrochlorothizade therapy including anaphylaxis, myocarditis, pneumonitis, systemic lupus erythematosus and toxic epidermal necrolysis.[1]

The evidence is unclear as to what is the exact pathophysiology underlying these adverse reaction. It has been suggested that the pathogenesis of hypersensitivity reactions to sulfa antibiotics is caused by an N4 amine linked benzene ring which is not present in non-antibiotic sulpha drugs.[2]

No literature was found regarding cross reactivity of different non-antibiotic sulpha drugs including for example hydrochlorothiazide and furosemide which is of clinical significance when deciding if it is safe to prescribe a sulfa diuretic to a patient with a known allergy to a different sulpha diuretic.

It appears that individuals that have had adverse reactions to sulpha antibiotics are at an increased risk of reacting to a non-antibiotic sulpha drugs however most of these reactions are

not severe. This observation may be confounded by the fact that those with known sulfa allergies that are tested for cross reactivity may be at increased risk of multiple drug allergy syndrome rather than a true cross reactivity to the sulpha group.[3]

Evidence is lacking as to whether hydrochlorothiazide causes a true anaphylactic reaction. There are documented cases of hypersensitivity reactions to hydrochlorothiazde including angioedema. The current diagnostic criteria of anaphylaxis includes one of the following[1]

1. Acute onset (minutes to hours) including either respiratory compromise and/or hypotension
2. Two of the following; skin-mucosal involvement, respiratory compromise, hypotension, GI symtpoms
3. Hypotension of <90mmHg systolic or greater than 30% decrease from baseline following exposure to a known allergen

Additional tests that can support a diagnosis of anaphylaxis include plasma tryptase and histamine however these are not diagnostic and cannot rule out anaphylaxis.[4]

Discussion

Although the exact pathophysiology is unknown, clinical presentation and autopsy suggest that the patient suffered an anaphylactic like reaction from taking hydrochlorothiazide which precipitated a ventricular tachyarrhythmia leading to asystole. It is unclear to which extent her preexisting cardiomyopathy and conduction defect may have contributed to this adverse outcome.

Diagnosis of anaphylaxis is supported by clinical presentation and significantly elevated serum tryptase levels at autopsy. It is unclear why this adverse reaction did not present earlier in her life during her previous courses of hydrochlorothiazide.

Conclusion

Allergies to sulpha containing medications are common and a patient with a known severe sulpha allergy should not be prescribed sulpha if other options are available. We are unable to predict however, which of these patients will also react adversely to other sulfa medications including medications of a different class. There is not adequate evidence to suggest avoiding sulfa non-antibiotics in patients with a known sulfa allergy however somethings should be taken into consideration when deciding whether or not to prescribe. This includes the severity of previous reaction, the presence of an adequate alternative medication of a different class, and the likely outcome if the patient does not receive the medication.

References

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