Drug Induced Thrombocytopenia: A Case Report.
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INTRODUCTION
The list of medications associated with Drug induced thrombocytopenia is vast and growing. Heparin and anti-cancer drugs are thought to be most commonly associated drugs with this adverse reaction. This paper presents a rare case of Thrombocytopenia in a 66-year-old male patient treated with antibiotic therapy for allergy/UIR symptoms in a course of 1 month. Stopping antibiotic therapy and treating the patient with corticosteroids, platelet transfusion, monoclonal antibody and IVIG revived the patient and returned the platelet concentration from 0-200,000 in a two-week period of therapy.

CLINICAL PRESENTATION
A 66-year-old Caucasian male admitted to the Emergency Room for a platelet count of 0–1000.
- His past medical history was only significant for hypertension controlled by Lisinopril/HCTZ.
- One month prior to his ER visit he presented to a local urgent care clinic with symptoms suggestive of upper respiratory infection (nasal congestion, sore throat, subjective fever). He was diagnosed with bronchitis and a first round of antibiotics was started (Ceftin 500 mg b.i.d. for 14 days & Rocephin/ Bimatmethosnae IM injections). At the time, blood work indicated his platelet count was 199,000.
- He completed his first round of antibiotics, but his symptoms did not resolve. He presented with worsening symptoms to another physician, and was started on azithromycin for 5 days. During this time he reported noticing symptoms of easy bruising post minimal trauma, lethargy and still worsening URTI symptoms. He returned to the original physician he went to at the urgent care clinic complaining of the same symptoms he presented with a month ago. Again, he was prescribed a different antibiotic, Levaxin daily for 10 days in addition to Rocephin and Bometalebons IM injections. This time he only took 5 days of the antibiotics because he started to notice occasional gum bleeding post brushing leukemic stocch/methemoglobinemia affecting the gingiva and palatine above (Figure 1).
- He returned to the urgent care clinic for the third time to the same physician this time concerned of these recent findings.
- Blood work was repeated and he was found to have a critically low platelet count of 0–1000. Coagulation panel resulted in PT of 12.8 and INR of 0.96.
- Family history was unremarkable with no first degree family members with bleeding tendency. There were no personal records of significant bleeding in his family.
- He was transferred to the ER because of his critcal low platelet count.
- Blood work was repeated and he was found to have a critically low platelet count of 0–1000. Coagulation panel resulted in PT of 12.8 and INR of 0.96.
- He was transfused with 1 unit of platelets and antiplatelet antibody levels returned negative. Second day post transfusion the platelet count dropped to 4 and remained 4-6000 for the next two days.
- A bone marrow biopsy revealed a normocellular bone marrow, adequate megakaryocytes with slight leftward shift in maturation and adequate iron storage pigment. Patient was started on a single dose of Rituximab, which brought the platelets up to 16,000.
- The next day the platelet count dropped slightly to 12,000. The decision was made to start IVIG, which brought the platelet count up to 34,000 the following day.
- The patient was discharged and returned to St. Vincent’s East Family Practice Clinic one week later with a platelet count of 200,000.

INTERVENTION/TREATMENT
- The patient was started on Prednisone and Solu-Medrol upon admission. All other medications were withheld at this time to prevent further exacerbation of his current condition.
- The hematologist reviewed the patient history and laboratory data. Peripheral smear showed evidence of marked thrombocytopenia, no anisocytosis ruling out DIC. His white blood count was normal with a slight left shift. His initial evalulation suggested the diagnosis of ITP, possibly medicine induced.
- He was transfused with 1 unit of platelets and antiplatelet antibody levels were ordered. Post transfusion his platelet count went up to 17,000. Tests for platelet direct antibody IgG and IgM returned negative. Second day post transfusion the platelet count dropped to 4 and remained 4-6000 for the next two days.
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DISCUSSION
- This clinical scenario most likely suggests the patient suffered from cephalosporin allergy resulting in drug-induced thrombocytopenia.
- These patients present with petechiae hemorhages and occasional ecchymoses.
- The type of treatment is to discontinue the sensitizing medication. Typically there is little evidence that corticosteroids are helpful if the thrombocytopenia is drug induced.
- Additionally, intravenous immune globulins and plasma exchange have shown minimal benefit. However, in this case report the combination of corticosteroids, IVIG, rituximab were utilized to successfully return the patients platelet count to a normal range (Table 1).
- Patients should be given ample time to excrete the drug from the body and advised to permanently avoid the medication. One proposed mechanism that has been suggested is classified as "hapten-dependent antibody." It is thought that small protein metabolites of the drugs called "hapten" can act as sensitizing agents allowing antiplatelet antibodies to become activated and bind epitopes that usually reside on glycoprotein IIb/IIIa or IIb/IIIa platelet complexes with higher affinity and as a result induce a drug-specific immune response.1
- Another proposed mechanism is that the drug itself reacts directly with the antibody and induces it to make immune complexes, which specifically target platelet antigens resulting in their destruction. The general consensus is that this reaction continues until either the drug or the hapten is cleared from the body. Typically this only takes a few days to a week. However, if the patient is given multiple doses of the same medicine the body may take longer to return platelets to their normal range as exemplified in this case report. The antigens these sensitized antibodies target are usually specific to the drug and thus antibody tests are often helpful if the thrombocytopenia is drug induced.
- The best option for treatment is to discontinue the sensitizing drug and combination of corticosteroids, IVIG, rituximab are usually specific to the drug and thus antibody tests are often helpful if the thrombocytopenia is drug induced.
- Patients should be given ample time to excrete the drug from the body and advised to permanently avoid the medication. One proposed mechanism that has been suggested is classified as "hapten-dependent antibody." It is thought that small protein metabolites of the drugs called "hapten" can act as sensitizing agents allowing antiplatelet antibodies to become activated and bind epitopes that usually reside on glycoprotein IIb/IIIa or IIb/IIIa platelet complexes with higher affinity and as a result induce a drug-specific immune response.1

Figure 1: Patient presents to the St. Vincents East ER with microangiopathic petechies, purpura and ecchymosis

CONCLUSION
Drug Induced Thrombocytopenia is a serious condition and considered a rare side effect of numerous medicines, namely anti-cancer drugs and antibiotics like Cephalospurins.
- Treatment requires immediate discontinuation of the drug and combination of corticosteroids, IVIG, immunochemotherapy to successfully normalize platelet count.
- Further research in this area is necessary to allow clinicians to target specific antibodies responsible for inducing this degree of thrombocytopenia among different drug classes. This will create individualized therapy and more importantly help physicians to distinguish Drug induced thrombocytopenia from its close counterpart Immune thrombocytopenic purpura.