Non resolving Cellulitis/Ulcers: Have you checked the medications?
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BACKGROUND:
Cellulitis imparts a major burden in acute admissions, there were about 82,113 hospital admissions with cellulitis in England and Wales in 2008–9, with a mean length of stay of 7.2 days [1]. This case is reported with a view to documenting an uncommon but debilitating side effect of apixaban and highlighting the need to review medication when patient complaints of recurrent ulcers following start of a new medication.

CASE REPORT:
A 63-year-old lady presented with erythematous, swollen right leg with ulcers. It started with a few blisters in the lower part of right leg, involved larger area up to right knee over a period of 18 months, with recent worsening in last 1 month.

Examination revealed: Multiple oozing ulcers with undermined edges covered with sloughs and blisters were noted over right leg. Marked tenderness and localised increase in temperature was present.

Medication review: Patient was on oral anticoagulation for Atrial Fibrillation, initially with warfarin for 5 years, later switched to apixaban 18 months ago.
She developed blisters which coalesced to form large ulcers after 3 weeks of starting apixaban.
Admitted in the hospital 3 times for cellulitis. Every time treated with Injectable Flucloxacillin, but recurred after 2-3 weeks time.

Investigations:

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<td>11.7/ 9.62</td>
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<td>19/4/2017</td>
<td>7/ 4.39</td>
<td>34</td>
<td>Staph Aureus</td>
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</tbody>
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IMAGES: X-ray Right leg - No Osteomyelitis.

MANAGEMENT:
- Apixaban was stopped immediately and switched to warfarin for AF.
- Treated ulcer with IV vancomycin and switched to oral linezolid on discharge (According to the sensitivity chart).
- Inflammatory markers settled.
- Followed up in virtual clinic - ulcers were improving, no new blisters.
- Reported in Yellow card scheme

DISCUSSION:
Skin eruptions (e.g. blisters, cellulitis, ulcers) induced by ever expanding list of medications are very common. Apixaban has become a popular drug used for anticoagulation. But recently, some cases of new onset or aggravating cellulitis are being reported.

Mechanism of Apixaban induced cellulitis is unclear. For a convincing explanation, larger population based data is required. More risk of developing cellulitis in patients who take apixaban have one of the following factors [3]:
- female,
- 60 years or more,
- have been taking the drug for <1 month,
- concomitant prescription of furosemide, and
- history of Stroke.

Between January 2004 and October 2012, A total of 365 patients reported different adverse effects who were taking APIXABAN, of which 19 individuals taking APIXABAN reported Cellulitis to the FDA. [2]

As, now a days, Apixaban is being used frequently for better safety, efficacy and convenience. Disability from recurrent long term non resolving cellulitis must be taken into account while prescribing. Certainly, early detection of adverse effects can minimize hospital admissions and long lasting disability.

LEARNING OBJECTIVES
1. Clinicians should be aware of the ability of apixaban to induce blisters and ulcers that may be misdiagnosed or late diagnosed.
2. Though Cellulitis is assumed to be an easy to treat condition, but recurrence rate is very high, specially in patients with multiple co-morbidities.
3. More population based studies to be planned to document uncommon side effects of newer anticoagulants in BNP.
4. Recurrence of ulcers in an immunocompetent, patient requires review of drug chart as some of the regularly prescribed medications can cause cellulitis (e.g. aspirin, furosemide, bisphosphonates etc).

REFERENCES: