Ertapenem induced encephalopathy- look at your drugs!

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Overview

A 63 year old male with PMH of COPD/DM2/seizure and cancer, presented to the hospital for a makoplasty procedure. At POD 10 the patient experienced fever, warmth, and redness at surgical site. At POD 12, the patient was taken to OR for an I&Ds where a deep hematoma/seroma was appreciated. Cultures were taken but there was no active puss from the seroma. Cultures showed ESBL E.coli and the patient was taken off zosyn and placed on ertapenem based on the merino trial. On POD 15 the patient was discharged to rehab but came back on day 27 with AMS and R hip redness. On POD 28 the patient experienced worsening confusion and was promptly transferred to the ICU. Finally, on POD day 31 primary team assumed ertapenem induced encephalopathy and switched the patient to bactrim. On Day 32 the patient was entirely back to baseline mentation.

Carbapenems and potential AEs

- Carbapenems are antimicrobial medications used to treat infections and are not known to frequently cause encephalopathy. Data on Carbapenems causing encephalopathy is fairly limited; however, a literature review found that Ertapenem has a 1% risk of causing seizures in patients as it is the better known neurological adverse effect ^4. When these neurological adverse effects are reported from Carbapenem use, they're mostly in conjunction with end stage renal disease or acute renal failure leading to decreased clearance of the medication causing pathological neurological symptoms as a result.
- Our patient experienced ertapenem induced encephalopathy in the absence of any form of renal disease or renal failure. This encephalopathic display was highlighted by altered mental status in the form of heightened confusion and aggression, decreased cognitive functioning, and personality changes which abated one day after discontinuation of Ertapenem.

Lab values on admission

Parameters	Readings NL ranges
WBC	5.34 3.6-11.1 K/mm3
Hb	9.3 12.9-16.1 g/dL
Platelets	237 165-353 k/mm3
Na	134 135-145 mmol/L
K	3.5 3.5-5.1 mmol/L
BUN	9 7-26 mg/dL
Cr	0.99 0.5-1.3 mg/dL
Calcium	8.8 8.4-10.2 mg/dL

Albumin	2.8 3.5-5 g/dL
Total Bilirubin	1.8 0.2-1.2 mg/dL
ALP	63 40-150 U/L
ALT	24 0-55 U/L
AST	45 5-34 U/L
TSH	4.603 0.35-4.94 IU/mL
Free T4	0.87 0.70-1.48 ng/dL

Discussion

- Our patient demonstrates a rare occurrence of Ertapenem induced encephalopathy without concomitant renal failure.
- There were no other medication changes that took place during this time and clinical evidence is suggestive of Ertapenem as the culprit for the ensuing pathological encephalopathy.
- The symptoms that coincided with our patient's encephalopathic episode post administration of Ertapenem, were identical to previous case reports involving ertapenem induced encephalopathy accompanied by renal failure.

Figure 1: Blood culture susceptibility 6/17/22

Antibiotic	Mic interp Mic dilutn
Amikacin	S <=16
Ampicillin	R >16
Aztreonam	R >16
Cefepime	R >16
Ceftazidime	R 16
Ceftriaxone	R >32
Gentamicin	R >8
Levofloxacin	R >4
Meropenem	S <=1
Pip/Tazo	R <=4
Tobramycin	R >8
TMP/SMX	S <2/38

- As seen in Figure 2, our patient's creatinine levels remained steady throughout this pathological course, as did blood urea nitrogen and other electrolytes indicating that there was no acute or chronic renal dysfunction taking place at the time of encephalopathic symptoms. During the 5 days the patient suffered from these symptoms, the patient was administered a pain medication regimen which included daily Norco 5mg-325mg and morphine 2mg/1mL which notably provided no observable waxing or waning changes in the patient's mental status.

Figure 2: Kidney function before, during, and after treatment

Date	BUN	Creatinine Na K
6/21/22*	8	0.79 135 3.1
6/22/22	<5	0.66 138 3.5
7/4/22**	11	1.15 133 4.3
7/5/22	8	1.18 134 4.2
7/6/22	6	0.93 135 4.0
7/7/22	6	0.84 135 4.0
7/8/22	8	1.08 140 4.4
7/9/22***	14	1.02 142 4.3

*- start of Ertapenem therapy
**- date of admission for encephalopathy
***- day 1 after of ertapenem discontinuation

- Providing absolute evidence of medication induced adverse effects like encephalopathy can be extremely difficult. There are various tools in the literature that can be used to bridge the gap of understanding in these types of clinical dilemmas. While we are unaware of a definitive method to prove absolute causation, they can be used as a marker that may imply the possibility of correlation.
- Thus, we chose to employ the Naranjo score, as seen in table 5, to indicate the probability that Ertapenem administration in our patient was the culprit to the ensuing encephalopathy. The Naranjo score in our patient was 5 which scores a "probable" adverse drug reaction.
- There are risk factors for developing Ertapenem induced encephalopathy which have been thinly outlined in the literature; the most important being renal dysfunction ^6. While our patient lacked renal dysfunction, one identifiable risk factor for ertapenem induced encephalopathy in our patient was his history of seizures ^5. This may have been a key factor in our patient susceptibility to experiencing encephalopathy.

Conclusion

- Our patient's case illustrates the ability of one to succumb to neurotoxic adverse effects from Ertapenem administration in the absence of concomitant renal failure.
- These distinctions are immensely important as risk factors can be identified in the future and patients can be spared quality of life issues, costly lab, and imaging workups as well as time consuming reconciliation activities.
- Simple discontinuation of Ertapenem abated all our patients' encephalopathic symptoms, and he quickly returned to baseline cognitive functions.

Key Points

1. Ertapenem induced encephalopathy without concomitant renal failure is rare but CAN happen
2. It is important to monitor a patients mentation before and after surgical procedures.
3. Having information on a patient's baseline status clinically can help the patient in the long run
4. When in doubt, look at your drugs!

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