Do we overtreat patients with presumed neutropenic sepsis?

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Introduction

Many aspects of the management of patients with neutropenic sepsis remain controversial. These include the choice of empiric antibiotic, the duration of antibiotic therapy and the possibility that very low risk cases may be managed safely with oral rather than intravenous therapy.

Methods

This was a retrospective cohort study conducted in Dumfries Royal Infirmary, a district general hospital serving a population of 148,000 in south west Scotland. During 2019, 127 of 253 patients with neutropenia were admitted to our acute medical unit (see flowchart). Fifty one patients with a cancer diagnosis whose neutrophil count was less than 1.0 x 10^9 per litre within 21 days of their last chemotherapy, were treated with antibiotic. We considered three categories of patient: 4 with positive blood cultures (Group 1); 12 with a clinical focus of infection but no clear pathogen (Group 2); and 35 with presumed neutropenic sepsis of unknown origin when neither source nor pathogen was identified (Group 3).

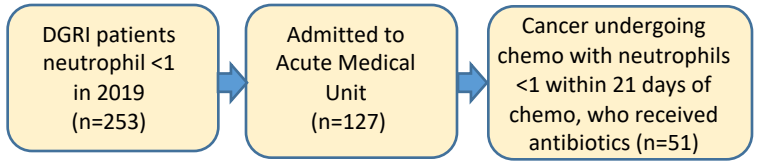


Table 1 Positive blood cultures

Case	Cancer diagnosis	Aerobic culture	Source of infection	Outcome 30 days
78M	Lymphoma	E.coli	Pneumonia	Died
77M	Lymphoma	K.pneumoniae	Pneumonia	Alive
53M	Lymphoma	S.parasanguinis	Pneumonia	Died
71M	Lymphoma	S.epidermidis	PICC line	Alive

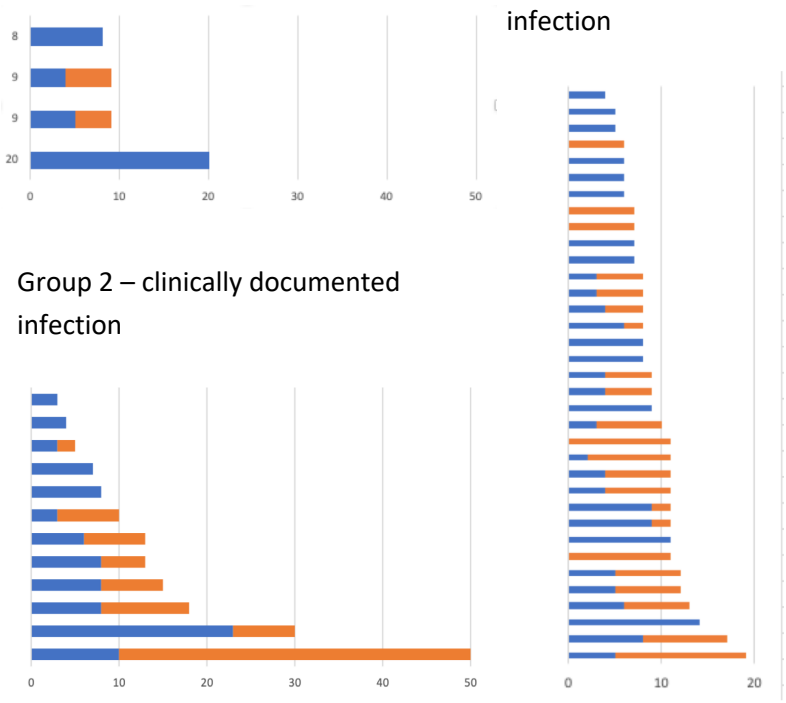
Table 2 Antibiotics, neutrophil recovery and hospital stay

Median duration in days (range)	Group 1 and 2 (with evidence of infection) n = 16	Group 3 (without evidence of infection) n = 35
IV antibiotic	8.0 (3-23)	5.0 (0-14)
IV plus oral antibiotic	11.5 (3-50)	9.0 (4-14)
Time to neutrophil recovery >500	2.5 (0-8)	2.0 (0-7)
Hospital stay	9.5 (3-23)	7.0 (1-17)

Figure 1 Duration of IV and oral antibiotic

Group 1 – blood culture positive

Group 3 – no documented infection



Group 2 – clinically documented infection

Results

The average age of the 51 patients was 66 years (range 35-89 years). There were 24 men and 27 women, 32 solid tumours and 19 haematological malignancies. Clinical details of the 4 patients with positive blood cultures are shown in Table 1.

Group 1 and 2 patients had significantly longer duration of IV antibiotic (p=0.04) and longer hospital stay (p=0.01) than those without evidence of infection. Median duration of IV antibiotic and hospital stay in Group 3 patients were 5.0 and 7.0 days respectively. Group 3 patients received a total of 176 days of intravenous antibiotic including 1.93kg of piperacillin/tazobactam. Figure 1 shows duration of IV (blue) and oral (orange) antibiotic in each of the groups.

Retrospectively, we calculated Multinational Association of Supportive Care in Cancer (MASCC) scores for group 3 patients to determine whether they may have been candidates for outpatient management using oral antibiotics. 23/35 (66%) patients in Group 3 had MASSC risk index greater than 21 suggesting they were at low risk of complications.

Conclusions

Our study adds to a body of evidence that most patients with presumed neutropenic sepsis do not have microbiologically proven infections. It seems likely that many of our neutropenic cancer patients with negative blood cultures and no obvious source of infection could have been managed as effectively and safely with shorter course of antibiotic, with oral rather than IV antibiotic, and as outpatients rather than inpatients.

References

NICE. Neutropenic sepsis: prevention and management in people with cancer Clinical guideline. 19 September 2012 available at www.nice.org.uk/guidance/cg151

Taplitz R. Outpatient Management of Fever and Neutropenia in Adults Treated for Malignancy: American Clinical Practice Guideline Update. *Journal of Clinical Oncology* 2018; 36:1443-1453