05 - Agranulocytosis

Agranulocytosis

© SPMM Course Consists of the tetrad of extreme hyperthermia, severe muscular rigidity and confusion, and autonomic fluctuations (BP and pulse rate). Patients may be akinetic and mute. Increased WBC count, creatinine phosphokinase, liver enzymes, plasma myoglobin, and myoglobinuria are noted. Subacute onset in 24 to 72 hours, and if untreated lasts 10 to 14 days. More common in young men, after agitation and when using high potency drugs especially in rapid tranquillisation situations. Dopaminergic drugs on withdrawal can produce NMS. The mechanism may be related to dopamine blockade or hypothalamic sympathetic dysregulation. The mortality rate is around 20-30% if untreated and higher if depot is used. Symptomatic management of vital signs instability, fluid replacement and prevention of renal failure secondary to myoglobinuria and prevention of aspiration pneumonia are main treatment methods after immediate stopping of offending psychotropic. Dantrolene, Bromocriptine or amantadine can be used. Low potency or atypical must be used following recovery for an antipsychotic prescription. Agranulocytosis Occurs in around 1 per 100 patients on clozapine. This is 15 to 30 times higher than the risk associated with phenothiazines and olanzapine. The maximum risk is between 4 and 18 weeks, and after a year the risk is same as with phenothiazines. Weekly monitoring of the white cell count is required for 26 weeks in most countries, with the frequency decreasing to biweekly or monthly thereafter. In the UK, yellow, green and red signals are used in WBC monitoring. When a result is red, clozapine must be stopped and never tried again. If yellow, then monitoring frequency must be increased until a green signal is obtained again. Benign neutropenia is common especially in south Asian and Afro-Caribbean race. Lithium can increase WBC count albeit transiently. Some anecdotal evidence supports using lithium in patients with benign ethnic neutropenia in preparation for clozapine use. But lithium and clozapine together can increase the risk of seizures and confusion. Clozapine, when combined with carbamazepine, phenytoin, propylthiouracil, sulfonamides, and captopril, can increase the risk of agranulocytosis further. Paroxetine may precipitate clozapine-associated neutropenia. Many side effects of clozapine such as salivation, sedation, and weight gain, fatigue and lowering of seizure threshold are dose related. But agranulocytosis and myocarditis can occur at any dose.

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