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Clozapine-induced liver injury

benign increase in liver enzymes, it also lists associated commonly with a transient and symptoms and signs.

ation, when considering nonspecific clinical larly in the 4-5 weeks following clozapine initi-

toxicity with associated pleural effusion.

describe a case of clozapine-induced hepato-
case studies report a wide variation in comor-
such presentations. In this case study we

to undergo these investigations.

cluded by the patient withholding her consent

and autoantibodies [(antinuclear antibodies

serology. Levels of serum immunoglobulins
ty tests were negative, as were CMV and EBV

copper and caeruloplasmin levels were within

ment.

ineffective and contributing to LFT derange-
tinued seven days after onset of symptoms

ithromycin, and subsequently piperacillin/

diagnosed as a lower respiratory chest infec-

small left basal effusion. Although initially

which chest X-ray indicated the presence of a

transaminase (AST) 338 U/L (n.r. 4-32),

(ALT) 707 U/L before

values of bilirubin 86 umol/L, ALP 406 U/L, AST

sisting lethargy. Liver enzymes reached peak

Clinical History

no history of drug aller-

No significant medical disorders were present

initial prescription. Liver enzymes reduced

569 U/L, GGT 173 U/L, and ALT 707 U/L before

Thirty days following clozapine prescription,

two days of clozapine cessation.

cough and left basal crepitations. Blood inves-

Positive and negative symptoms.

over this period, with improvement in both

mild sedation

over a three week period with mild sedation

and blood tests, including liver function tests

Abdominal ultrasound was normal, while

Drug Therapy

Two distinct mechanisms for such reactions

Other cases of drug-induced liver injury

References

9 describe a
city in onset of symptoms (4-5 weeks following clozapine initiation), clozapine dose (300-500 mg daily) and duration before normalization of laboratory results (4-6 weeks), although the LFT figures reported in Ms. A’s case surpass those described in existing literature. It should be noted that in many of these cases, clinical symptoms were non-specific, as in Ms. A’s case, or absent altogether.

The authors fully acknowledge that the patient’s pleural effusion may have occurred due to other etiologies, an assertion that may have been supported by investigations declined by Ms. A. We do, however, believe that the close correlation of clinical symptoms with laboratory tests and the rapid resolution of effusion in the absence of antibiotic therapy support an association with hepatotoxicity. It is also noted that clozapine-induced pleural effusion is not unprecedented in the literature.

Whilst both the unsuccessful and successful re-challenges with clozapine therapy following adverse reactions are documented in existing reports, re-challenge was considered inappropriate in Ms. A’s case, given the extent of LFT derangement and clinical symptoms.

This case supports existing literature in advocating a high index of suspicion, particularly in the 4-5 weeks following clozapine initiation, when considering clinical symptoms and signs commonly associated with other pathologies. Whilst the documented prevalence of transient LFT elevation should urge caution in the premature cessation of clozapine therapy, clinicians should maintain a low threshold for monitoring such parameters following the emergence of innocuous symptoms and signs.

References