Dosing azathioprine in thiopurine S-methyltransferase deficient inflammatory bowel disease patients

With great interest we read the article by Kaskas et al (Gut 2005;52:140–2) about safe treatment of thiopurine S-methyltransferase (TPMT) deficient Crohn’s disease patients with azathioprine (AZA). In this paper it is illustrated that TPMT-deficient patients can be successfully treated with very low doses of AZA (∼10% of standard initial dose).

Unfortunately, this is not the case for all homozygous mutant TPMT allele carriers. This is demonstrated by the case report of homozygous mutant TPMT allele carriers. This rare group of patients does not preclude thiopurine treatment and hence offers a further therapeutic option for this group of patients. This should be done with great caution, however; that is, with very frequent blood tests and 6-TGN monitoring, as in some cases even a 5% starting dose can be dangerous.

Second, although TPMT genotype and phenotype normally show very high correlations, there are exceptional cases. In our case, 6-TGN levels were a far better predictor of TPMT deficiency than was TPMT activity.

Third, despite the TPMT *5A/*5A genotype, it lasted 2 months before leucopenia developed on a standard AZA dose in our patient. This is very unusual as most patients with homozygous TPMT mutant alleles develop myelotoxicity 1–2 weeks after starting standard thiopurine treatment. A longer period of very frequent monitoring is advisable when thiopurine treatment is started in homozygous TPMT mutant carriers. This rare group of patients should be treated with the greatest caution.

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REFERENCES


CORRECTIONS

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There are several mistakes in this article. (1) In the section “Major patterns of chronic hepatitis”, under the heading “HBeAg positive chronic hepatitis B”, the sentence “Spontaneous seroconversion rates remain relatively low in this group at approximately 20% at one year” should read “at 5–15%”.

(2) In table 1, reference 48 should be reference 50 and reference 83 should be reference 111. (5) In table 2, reference 50 should be 52 and reference 83 should be reference 111. (4) Also in table 2, the entecavir 0.5 mg resistance rate in HBeAg negative patients is 0–1%, not 8%.

Persiani R, Biondi A, Larocca L, et al. Intussusception in a 51-year-old male. (Gut 2008;57:242). In this article the third author’s name was published incorrectly as Luigi L: it should be Larocca L.