The Journal of Laryngology and Otology
May 1996, Vol. **110,** pp. 466–467

Drug induced otalgia due to mesalazine and sulphasalazine

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Abstract
A case of left otalgia in a patient suffering from longstanding ulcerative colitis is reported. The patient was treated for an exacerbation of his disease with courses of mesalazine and sulphasalazine during which time he developed otalgia. The otalgia disappeared with cessation of the drugs. It is concluded that in the absence of any other head and neck cause that the otalgia was a complication of the drug therapy.

Key words: Earache; Salicylazosulphapyridine.

Case report

A 46-year-old man with a 25-year history of ulcerative colitis presented with a six-day history of extreme, deep-seated continuous left otalgia. There were no other associated otological symptoms and no symptoms from areas referring pain to the ear. He had, however, started Asacol (mesalazine, 5-amino salicylic acid) 400 mg t.d.s., 16 days previously for a mild exacerbation of his ulcerative colitis, which had previously been kept under control with predfoam enemas and oral prednisolone. Full ENT and neurological examination was normal and a contrasted sagittal CT scan from the level of the pituitary fossa to the hyoid bone was likewise normal. At the same time as the scan was being undertaken he stopped taking the Asacol which resulted in a cessation of his symptoms.

His condition remained stable for a further five months until a further exacerbation of his ulcerative colitis. This was treated with Salazopyrin (sulphasalazine) 1 g t.d.s. A matter of days after starting this, however, he experienced a similar deep seated otalgia, but this time affecting the right ear. This responded to stopping the Salazopyrin.

Since then he has remained in remission on Predfoam enemas and oral prednisolone but is about to undergo panproctocolectomy for the risk of malignant change.

Discussion

Sulphasalazine was developed and evaluated for the treatment of patients with colitis in the 1930s. Promising results led to its widespread use in the treatment of colitic patients although its effectiveness has been limited by the high incidence of side effects. Sulphasalazine is a diazo bond dimer of sulphapyridine and 5-aminosalicylic acid (5-ASA) and it has become apparent that it is the sulphapyridine which is responsible for the majority of the toxicity associated with its use. These side-effects can be categorized into dose-related intolerance effects (headache, nausea, arthralgia, malaise and haemolytic anaemia) and allergic type/idiosyncratic reactions (fever, rash, hepatitis and oligospermia) (Ruderman, 1990). These adverse effects are reported to occur in between 20 to 45 per cent of patients and although the majority are mild, 25 per cent of patients will discontinue treatment within six months of starting (Pullar, 1992). It has also become apparent that it is the 5-ASA that is the active moiety. Efforts have consequently been concentrated on development of this agent alone. The pharmaceutical challenge has been to protect the 5-ASA from rapid small bowel absorption, as it works by a topical action in the large bowel. This has been achieved in Asacol by coating it in Eudragit S, an acrylic resin which requires a pH greater than seven for it to dissolve. The incidence of side effects with mesalazine is considerably less than with sulphasalazine and no dose relationship is apparent. Gastrointestinal effects predominate although it is often difficult to distinguish between drug and disease effects. Rare side effects include pancreatitis, alopecia (Hadjigogos, 1991), lung toxicity (Reinoso *et al.*, 1992), lupus-like syndrome (Pent *et al.*, 1992), nephrotoxicity (Masson and Rhodes, 1992) and lichen planus (Alstead *et al.*, 1991).

Headache is present in around two to three per cent of patients on mesalazine and this appears to be dose-independent (Brimblecombe, 1990). The headaches with sulphasalazine tend to be, by contrast, dose-dependent. To our knowledge there is no previous report of otalgia sufficient to require cessation of therapy. It is interesting that it is the 5-ASA that would appear to be responsible here as only small amounts are absorbed into the systemic circulation although cross reactivity of specific side-effects with sulphasalazine and 5-ASA is well recognized (Fardy *et al.*, 1988). Whether the otalgia was of local or central cause is uncertain although it is more likely that this is a headache variant and consequently central as labyrinthine function was unimpaired. 5-ASA is related to aspirin and has a theoretical risk of specific labyrinthine toxicity but it would be expected to manifest itself with more localizing symptoms. This labyrinthine toxicity would also be expected to be markedly dose-dependent and require large doses to be present if through the same mechanism as aspirin.

We would recommend the practising otologist to be aware of drug reactions as a possible cause of isolated otalgia.

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Accepted for publication: 2 March 1996.

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