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Corticosteroids and peritonsillar abscess formation in infectious mononucleosis

Brendan C. Hanna, Ronan McMullan, Samuel J. Hall

Abstract
Peritonsillar abscess formation is an uncommon complication of infectious mononucleosis (IM). Early case reports implicated corticosteroids in the development of such abscesses, however, subsequent studies suggested that these drugs do not promote the formation of abscesses at several sites outside the central nervous system. It has recently been demonstrated that zwitterionic polysaccharides, in bacterial capsules, form complexes with $CD4^+$ T lymphocytes leading to abscess formation. A patient is presented who developed peritonsillar abscess a few days after initiation of corticosteroid therapy for IM; the medical literature was reviewed in respect of this subject. It appears that the occurrence of these abscesses in IM is not strongly linked to corticosteroid treatment. The authors, therefore, recommend that steroids should not be withheld from patients with severe IM on the basis that they may precipitate the development of peritonsillar abscess.

Key words: Infectious mononucleosis; Peritonsillar abscess; Adrenal cortex hormones

Introduction

The clinical manifestation of infectious mononucleosis (IM) represents the host immune response to Epstein-Barr virus (EBV) infection.[1] It would therefore seem rational that pharmacological agents known to suppress these effects, such as corticosteroids, should produce clinical improvement; the effectiveness of such treatment has been proven in controlled clinical trials.[2,3,4,5] Three double-blinded and one matched-control trial have shown significant reductions in the duration of fever, pharyngitis, and abnormal haematological findings among young adults with IM following corticosteroid therapy. No significant increase in either adverse effects observed or the occurrence of bacterial superinfection was noted. Indeed, corticosteroids were frequently deployed in the treatment of infectious mononucleosis in the 1960s. However, in 1979 Handler and Warren[6] reported an association between steroid treatment and peritonsillar abscess formation, on the grounds that three of the four published cases of peritonsillar abscesses in IM had occurred in patients who had received corticosteroids. They recommended that only those patients with infectious mononucleosis who had tonsillar enlargement sufficient to produce dysphagia or potential airway obstruction should receive corticosteroids. This resulted in a shift away from their prescription in almost all patients with IM, which has persisted for several decades. The authors believe that the evidence for Handler and Warren's recommendation should be reviewed in light of evolving clinical and scientific knowledge.

Case report

A 17-year-old girl presented to hospital with a four-day history of sore throat, fever and painful swallowing. Previously she had had a right-sided peritonsillar abscess and recurrent tonsillitis. A Monospot™ test was positive and the peripheral blood lymphocyte count was elevated; she was treated with oral cefuroxime and intravenous fluids. She became progressively more unwell during the following six days with worsening sore throat, continued fever, cervical and axillary lymphadenopathy, elevated liver enzymes and enlarged tonsils. Intravenous dexamethasone 4 mg daily was commenced. Following four days of steroid therapy, although she felt better, there was a right-sided peritonsillar abscess. Purulent material was aspirated and *Bacteroides fragilis* and *Prevotella melaninogenica* were cultured. Dexamethasone was discontinued and intravenous metronidazole commenced. She was discharged on oral antibiotics and was well at subsequent review.

Discussion

No randomized-controlled trials that test the hypothesis that corticosteroids influence abscess formation in IM have been published. The trials, which examined the impact of steroids on IM, were not adequately powered to address their possible role in the development of abscesses. An adequately powered study would require enrolment from such a vast population base (approximately five million to demonstrate a 10-fold increase in risk) it is economically impractical. Therefore, the physician is forced to interpret inadequate data when attempting to determine whether this is an important adverse effect of steroid therapy.

Including this case, 32 cases of peritonsillar abscess complicating IM are documented, in the English language medical literature.[7–11] Corticosteroids had been administered to six patients and in these instances an abscess occurred between days 10 and 20 of the illness. The duration of steroid administration prior to abscess forma-

From the Departments of ENT, Craigavon Area Hospital, 68 Lurgan Road, Craigavon, and Infectious Disease and Microbiology*, Royal Victoria Hospital, Grosvenor Road, Belfast, N. Ireland.
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tion was recorded in four reports and ranged from two to seven days. In the remaining 26 cases not given steroids, peritonsillar abscess occurred between days two and 24 of the illness.

- **The treatment of patients with infectious mononucleosis with steroids has been shown to hasten clinical recovery. However there are previous reports that have suggested that such treatment may also promote peritonsillar abscess formation**
- **There are no proper controlled trials on this subject**
- **This is a case report of a girl who developed an abscess following steroid therapy**
- **The authors review all the literature on this subject and conclude that there is actually no evidence to conclude that steroids should be withheld in such cases**

Of those who received corticosteroid treatment, it was not commenced until at least day six of the illness. To conclude that the subsequent development of peritonsillar abscess is a complication of the corticosteroid treatment implies that abscess formation after day six would have been less likely if corticosteroids had not been administered. Figure 1 displays the number of patients developing a peritonsillar abscess in the second, third and fourth weeks of IM. Although the numbers are small, the timing of peritonsillar abscess formation six days after the onset of IM is of a similar pattern in both those treated and those not treated with corticosteroids. Seventy-five per cent of the group treated with corticosteroids developed a peritonsillar abscess in the second week and 25 per cent in the third week. Of those not given corticosteroids, 66 per cent developed a peritonsillar abscess in the second week and 26 per cent in the third week.

The effect of corticosteroids, as part of therapy for different diseases, on the formation of abscesses at various sites outside the central nervous system has been examined by several investigators.[12–14] Hansen *et al.*[12] presented a cohort of patients with small cell carcinoma of the lung who were treated with combination chemotherapy, 79 of whom also received high dose steroids (more than 40 mg of prednisolone per day). Five (6.3 per cent) of the steroid treatment group developed lung abscesses as did eight (4.3 per cent) of the remaining 184. This difference was not significant.

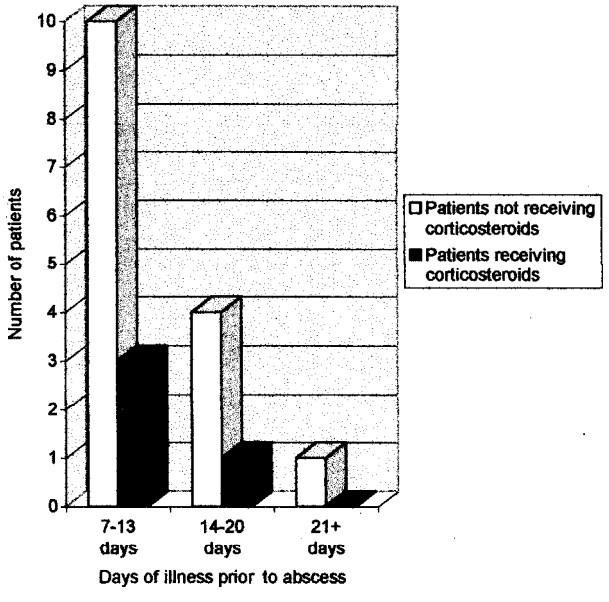

FIG. 1

The timing of peritonsillar abscess formation in patients with infectious mononucleosis after the first six days of illness.

Felder *et al.*[13] studied the safety of corticosteroid therapy in patients with Crohn's disease and a palpable abdominal mass. Twenty-four patients were treated with high dose steroids. In 15 the mass resolved completely and in another nine it decreased by at least 50 per cent. In 13 patients the mass was later proven to have contained an abscess. They concluded that using high dose corticosteroids to treat severe Crohn's disease with an abdominal mass is safe and effective even if an abscess is present.

Joiner *et al.*[14] studied the effect of corticosteroids on subcutaneous abscess formation in mice innoculated with either *Staphylococcus aureus* or sterile caecal contents. They found that prolonged high dose steroid administration did not interfere with the process of containment and encapsulation of subcutaneous abscesses and, in fact, reduced mean abscess volume.

An explanation of why corticosteroids should not promote abscess formation is offered by Tzianabos and Kasper.[15] The capsule of bacteria such as *Bacteroides fragilis* contains polysaccharides with zwitterionic (both positively and negatively charged) substituent groups. These have been demonstrated to activate $CD4^+$ T lymphocytes which in turn produces a cascade of events leading to polymorphonuclear cell recruitment and abscess formation. Human studies of the effect of inhaled corticosteroids on peripheral blood T lymphocytes have demonstrated downregulation of $CD4^+$ and $CD8^+$ T cells.[16] Therefore, if activation of T cells by zwitterionic polysaccharides in the bacterial wall capsule is the process which triggers abscess formation, the downregulation of $CD4^+$ T cells by corticosteroids would be expected to have an inhibitory effect.

The Infectious Diseases Society of American (IDSA) have published recommendations regarding steroid use in IM. They suggest that steroids should not be routinely used in the treatment of all patients with IM, but should be prescribed when there is risk of impending airway obstruction. These recommendations acknowledge that steroids may also benefit other patients with IM. This may include those with persistent, severe, disease or exhaustion due to generalized EBV infection. The IDSA working group suggest that such patients could be identified by the presence of unusually high fevers, weight loss, arthritis or a prolonged illness.[17]

As in this case, abscess formation continues to be reported as a complication of IM, however, it is unusual for corticosteroids to have been administered in such cases. In fact, IM is complicated by peritonsillar abscess in one per cent of patients admitted to hospital.[8] There is a widely held belief that corticosteroids may predispose to abscess formation,[9,11,18] but there is no reliable evidence to support this. Indeed, it is reasonable to postulate that steroids may reduce the likelihood of abscess development. Therefore, the authors recommended that corticosteroids are not withheld from patients requiring hospitalization with a severe or prolonged IM syndrome solely on the grounds of possible abscess formation.

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Address for correspondence:
Mr Brendan C. Hanna,
3 Ashdale Gardens,
Ardglass,
Co Down,
N. Ireland.

Fax: 028 3833 1947
E-mail: Barney@doctors.org.uk

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