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Adverse Reaction to Prophylactic Amoxicillin: A Case Report

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Abstract - *Antibiotic prophylaxis is required prior to invasive dental procedures for those patients at risk of bacterial endocarditis. The clinician should be aware of the possibility of allergic reaction to the antibiotics and be prepared for the medical management of the symptoms. This paper presents a case of an allergic reaction to prophylactic amoxicillin administered orally to a patient prior to dental treatment.*

KEY WORDS: Bacterial endocarditis, Antibiotic prophylaxis, Penicillin allergy.

INTRODUCTION

It is well known that some dental procedures can produce a bacteraemia which can cause distant infections such as infective endocarditis[1,2]. In order to diminish or, even, eliminate such a problem prophylactic antibiotics can be given[3]. Whenever antibiotics are given, it is important for the clinician to consider their risk, cost and benefit[4]. Antibiotics account for between 15 and 30% of the worlds drug expenditure; the penicillin's comprise the largest class in this group[5]. The most significant adverse reaction associated with the use of is hypersensitivity which can range from a troublesome rash to anaphylaxis[4].

This paper presents a case of an allergic reaction to orally administered amoxicillin. In addition, we provide a literature review on antibiotic prophylaxis and penicillin hypersensitivity with management recommendations being discussed.

CASE REPORT

A 57 year old Caucasian female attended for non-surgical periodontal therapy as part of her long term periodontal maintenance, following a referral in 1976 for the treatment of Chronic Adult Onset Periodontitis. In 1976 the patient was fit and well and had no serious general health problems. In 1988 a referral to a Cardiologist followed a complaint of chest pain and shortness of breath. After investigation, the diagnosis of angina was made and the presence of mitral valve incompetence noted. The patient was advised by the cardiologist of the need for antibiotic prophylaxis for certain dental procedures. From the case notes, it was noted that from 1988 to the date of the visit reported here the patient had received oral amoxicillin prophylaxis on 15 occasions without complication. The last recorded episode of antibiotic prophylaxis being 18 months prior to the visit being discussed in the paper. A recent check of the patient's medical history also revealed that the patient suffered from asthma and had hyperthyroidism. However, it is not clear from the clinical records as to when they were diagnosed.

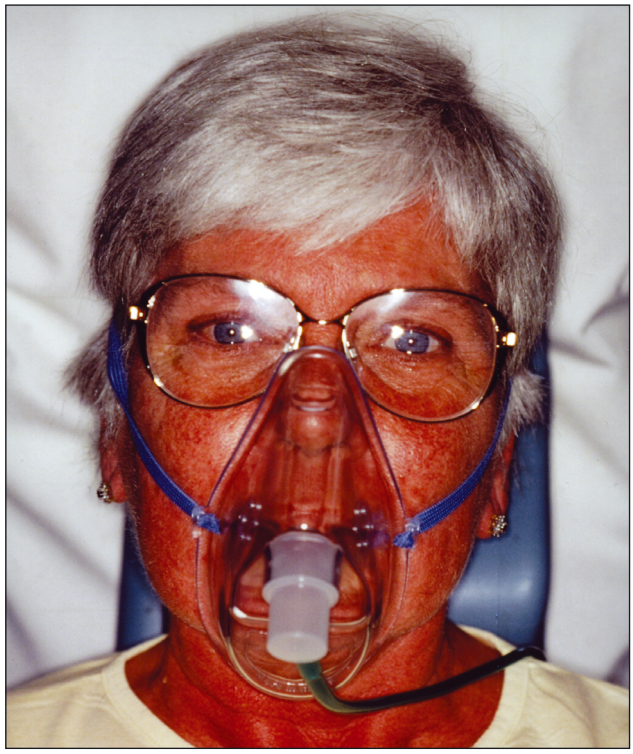

Figure 1. *Oxygen was administered as the first line of management. Note the redness of the face and neck.*

On the day in question, the patient was given 3g amoxicillin orally and asked to wait in the waiting area. Whilst waiting to be seen the patient and her husband noticed that her face, neck and arms had become red. The staff were informed of this development some 30 minutes after the antibiotic had been given at which time the patient's neck was slightly swollen but breathing was normal. Oxygen was immediately administered *(Figure 1)*, the patient canulated and her blood pressure and pulse rate measured: BP 149/60, pulse rate 83. In light of the slow onset of the symptoms, the consultant in charge of

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Figure 2. *Patient's face following administration of antihistamine and prior to discharge. The rash has improved markedly.*

the session decided against administering adrenaline or hydrocortisone but to administer 10 mg piriton intravenously. Within 18 minutes the patient's rash started to improve. A second 10mg dose of piriton was given 32 minutes after the first after which the rash improved markedly. Throughout the observation period the patient's blood pressure and pulse rate were monitored constantly. The canula was removed 1hr 40 min after canulation and the patient deemed well enough to be discharged (*Figure 2*). The patient's doctor was informed by letter of her allergic reaction to amoxicillin. A few months later, the treatment was completed without problem utilising 600 mg oral Clindamycin as antibiotic prophylaxis.

DISCUSSION

Bacteraemias associated with dental procedures are dependent on the procedure being performed. Traumatic procedures, such as extraction and periodontal therapy, are more likely to produce bacteraemia than less invasive therapy like dental prophylaxis and endodontics[3]. The degree of gingival inflammation correlates positively with the incidence and magnitude of bacteraemia[6,7]. Nevertheless, bacteraemia can occur in patients with clinically healthy gingivae[8].

The need for antibiotic prophylaxis was originally based on the assumption that:

1. specific cardiac defects predispose to infective endocarditis
2. the micro organisms most commonly responsible for causing infective endocarditis are susceptible to antibiotics. Even antibiotics without bactericidal activity were deemed to be useful as they could prevent microbial adherence to damaged endocardium or suppress the growth of attached bacteria.
3. the risk for infective endocarditis is increased following the bacteraemia from invasive dental, gastrointestinal or genitourinary procedures and antibiotics decrease the incidence or severity of the bacteraemia associated with the procedure[9].

The use of antibiotic prophylaxis in restorative dentistry is controversial[10]. However; national guidelines exist to help practitioners rationalize the prescribing of chemoprophylaxis in dentistry. Guidelines from the British Society for Antimicrobial Chemotherapy (BSAC)[11] for antibiotic prophylaxis exist (*Table 1*).

The British Cardiac Society and Medical Practice Committee and Royal College of Physicians Clinical Effectiveness and Evaluation Unit have published new recommendations on the dental aspects of endocarditis. Their document recommends the use of antibiotic prophylaxis for a wider range of dental procedures than previously recommended by other sources. It also redefines "high-risk" patients to a larger group than those recommended previously. It is important to remember that these recommendations are not approved as national guidelines at this point in time and they may not come into practice at all. It is interesting to note that, despite no evidence as causative in the production of infective endocarditis that rubber dam placement, matrix band use, retraction cord and wedge placement are advocated as requiring antibiotic prophylaxis in the high-risk group[12].

A recent publication from by the Cochrane group[13] notes that there is a general lack of substantiary evidence on the effectiveness or ineffectiveness of antibiotic prophylaxis against bacterial endocarditis. The authors concluding that it is a practioner's ethical duty to discuss with their patients the potential benefits and risks of antibiotic prophylaxis before their administration. Although most attention has focused on antibiotic prophylaxis there is evidence that antiseptic mouthwashes used prior to dental treatment may reduce the prevalence and severity of bacteraemia[14,15].

Possible risks associated with antibiotic prophylaxis

One to ten percent of people given penicillin experience an allergic reaction[16,17]. The literature shows that

Table 1. *BSAC guidelines for antibiotic prophylaxis*[4]

Conditions predisposing to infective endocarditis
• History of infective endocarditis
• Ventricular septal defect
• Patent ductus arteriosus
• Coarctation of aorta
• Prosthetic heart valves
• Rheumatic and other acquired valvular disease
• Surgical constructed systemic-pulmonary shunts
• Persistent heart murmur
• Atrial septal defect repaired with a patch
• Hypertrophic cardiomyopathy
• Marfan's syndrome
Special risk patients
• Those with a previous history of infective endocarditis
• Those who require a general anaesthetic and have a prosthetic heart valve or are allergic to penicillin or who had penicillin more than once in the previous month

Table 2. *BSCA recommended antibiotic regimens*[11]

No allergy to penicillin and penicillin not received more than once in the past month	*Patients allergic to penicillin or who have received penicillin more than once in the past month*
Local anaesthesia	
Amoxicillin 3g orally 1 hour before treatment	Clindamycin 600mg orally 1 hour before treatment
General anaesthesia	
Amoxicillin 3g and probenecid 1g orally 4 hour before surgery or amoxicillin 3g orally 4 hour before and 3 g after procedure orally or amoxicillin 1g IV at induction and 500 mg orally 6 hours later	See the regimen for special risk patients
Special risk patients	
IV amoxicillin 1g and IV gentamycin 120mg before surgery or at induction and amoxicillin 500mg orally 6 hours later	IV teicoplanin 400mg and IV gentamycin 120mg before procedure or at induction or clindamycin 300mg given IV over 10 minutes in 50ml before surgery or at the induction and 150mg oral or IV 6 hours later or vancomycin 1g slow IV infusion over at least 60 minutes followed by gentamycin 120mg IV before surgery or at induction
For children under 10 years half and childern under 5 years a quarter of the adult dose of amoxicillin	
For children under 10, 6mg/kg body weight of clindamycin	
For children under 10 years, 20 mg/kg of vancomycin and 2mg/kg gentamycin should be used	
For children under 14 years, 6 mg/kg teicoplanin should be used	

there are conflicting ideas as to whether the benefits of antibiotic prophylaxis exceed the risks. Pallasch[18] states that the death rate from endocarditis exceeds that of penicillin anaphylaxis. Tzukert *et al.*[19] state that 1.36 people per million of population are likely to die from penicillin anaphylaxis whereas only 0.26 deaths per million of population are due to a dentally induced endocarditis. Additionally, Tzukert *et al.*[19] also state that penicillin prophylaxis for infective endocarditis is justified only for high risk patients and that it should only be given orally. Another potential unwanted effect from regular use of antibiotics is the development of bacterial resistance. The World Health Organisation has recognised antimicrobial resistance as a global problem[20].

Hypersensitivity to penicillins

Retrospective studies suggest that the incidence of penicillin allergy varies with its route of administration: oral (0.3%) intravenous (2.5%) and intramuscular (5%)[21]. The most common reactions to penicillins are urticarial and irritating rashes, but sometimes a serum like sickness reaction with joint pains and fever follows some days or weeks after administration[22]. For patients who are allergic to penicillin, alternative antibiotic prophylaxis regimens are available against bacterial endocarditis (*Table 2*).

Mechanism of penicillin allergy

The major antigenic determinant appears to be penicilloyl group that binds to body proteins to become antigenic. Most people receiving penicillin develop IgG or IgM antibodies but these only occasionally cause adverse reactions. Specific IgE antibodies are responsible for anaphylactic reactions, but fortunately these only form rarely. IgE causes the problems by binding to mast cells and triggering the release of inflammatory mediators which cause smooth muscle relaxation and vasodilation which is responsible for the many symptoms that can be observed when anaphylaxis occurs[22].

Management of anaphylaxis and hypersensitivity reactions

A hypersensitivity reaction can take place within a few minutes of injection but is often delayed after oral administration as it takes time for the drug to be absorbed[22]. Anaphylaxis requires prompt and energetic treatment if laryngeal oedema, bronchospasm and hypotension are encountered. In the cardiovascular system the hypotension is a direct result of vasodilatation, increased vascular permeability, tachycardia and cardiac arrythmias. First line treatment includes: securing the airway, restoration of blood pressure by laying the patient flat with their feet raised and the administration of oxygen and intramuscular adrenaline. 500 micrograms of adrenaline is administered and repeated, if necessary, at 5 minutes intervals according to blood pressure, pulse and respiratory function. As adrenaline increases vascular resistance, reduces vascular permeability, causes brochodilatation and increases cardiac output it is well suited to the treatment of anaphylaxis. It is also relatively easy to administer. An antihistamine (e.g. chlorpheniramine) given by slow IV injection in a dose of 10–20 mg is a useful adjunct to treatment as they block the effects of histamine. Deterioration of symptoms requires further treatment including the administration of IV fluids, assisted respiration and possible tracheotomy. An IV corticosteroid e.g. hydrocortisone in a dose of 100–300 mg, is of secondary value in initial management of anaphylactic shock as the onset of action is delayed for several hours.

Unfortunately, anaphylaxis can be the first manifestation of sensitivity to penicillin; therefore, it is important to remember that a negative history only reduces the risk but does not totally exclude the possibility of anaphylaxis. From a practical and medico legal point of view reliance has to be placed on an accurate medical history and an alternative antimicrobial agent should be administered when patients claim to have an allergy to penicillin[22]. It is important that any history of allergic reaction is divorced from mistaken side effects by patients. The British

National Formulary defining severe hypersensitivity to penicillin as a confirmed history of anaphylaxis, urticaria or rash immediately after drug administration. Diarrhoea is a side effect of broad spectrum penicillin's and not an allergic reaction[23].

CONCLUSIONS

Allergy can develop over a period of time. A history of no allergy is not an excuse for complacency when prescribing any form of medication to patients. The dentist (and his support staff) needs to be acutely aware of that allergic reactions can occur at any time. When they do, they need to be managed. It is hoped that this paper highlights these issues. Importantly, the dentist needs to be well aware of the cost, benefits and risks of providing any medication to patients. It is clear from the current literature that with respect to certain procedures in restorative dentistry that further investigation and clarification on the use of antibiotic prophylaxis is needed.

ADDRESS FOR CORRESPONDENCE

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