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Fusobacterium necrophorum as the cause of recurrent sore throat: comparison of isolates from persistent sore throat syndrome and Lemierre's disease☆

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Abstract *Objective*. *Fusobacterium necrophorum* is a well established cause of Lemierre's disease (LD); a syndrome characterised by severe sore throat, septicaemia, multiple abscesses and jugular vein thrombosis. There is no published data concerning the role of *F. necrophorum* in recurrent sore throats. As the result of an index case of persistent sore throat attributable to this organism being diagnosed in our laboratory, a subsequent case controlled study (not yet published) isolated *F. necrophorum* from 21% ($P=0.0001$) of cases of persistent, recurrent and chronic sore throats. The object of this study was to compare isolates of *F. necrophorum* from cases of systemic disease with isolates from cases of persistent sore throat syndrome (PSTS) to ascertain whether strains of similar type were responsible for both throat and systemic disease or whether different strains were involved in these presentations.

Methods. Throat swabs were cultured on GN anaerobe medium (Oxoid) and incubated at 37 °C for 5 days. Seventeen PSTS isolates were identified phenotypically. These were compared to 17 strains isolated from blood cultures which were referred to the Anaerobe Reference Unit, (ARU) cardiff, using enterogenic repetitive intergenic consensus-polymerase chain reaction (ERIC-PCR). The control strains *Fusobacterium necrophorum* ssp. *necrophorum* (JCM 3718^T) and *Fusobacterium necrophorum* ssp. *funduliforme* (JCM 3724^T) from the Japanese Collection of Microrganisms (JCM) were tested in parallel with the clinical isolates.

Results. At least 12 separate types were identified. Four of 17 PSTS isolates and seven of 17 blood culture isolates grouped together with the *F. necrophorum* ssp. *funduliforme* control strain. There were also similarities between other proposed

☆ This work was undertaken as part of an MSc degree by one of us (AB) at Birkbeck College, London.

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strains and clinical types but no comparison with the *F. necrophorum* ssp. *necrophorum* control.

Conclusion. These results show that clinical disease caused by *F. necrophorum* has a wider spectrum than first anticipated. Similar strains are able to cause either chronic local or acute systemic disease suggesting that genetic factors such as those relating to major histocompatibility complex (MHC) class may be influencing the outcome of the disease in each patient. Further work is required to produce a more accurate typing scheme and to ascertain the mechanisms of disease caused by this organism.

An age correlation between the high risk groups for onset of infectious mononucleosis (IM), peritonsillar abscess (PTA), LD and PSTS has been noted in adolescents and young adults. Further work is required to investigate whether IM is associated with the onset of PTA caused by *F. necrophorum* which may lead to either PSTS or LD.

Introduction

In London, in 1936, the French microbiologist Lemierre described a condition affecting young adults which began with post-anginal sepsis and progressed to metastatic septic emboli frequently resulting in the death of the patient.[1] With the advent of antibiotic therapy Lemierre's disease has become a rare and 'forgotten disease'.[2–4] The causative organism of Lemierre's disease is an obligate anaerobic, non-motile, pleomorphic Gram-negative rod now recognised as *Fusobacterium necrophorum*.[5]

In 2001, in an index case in the Microbiology Department at University College Hospital, London (UCH), a 41 year old female presented with the acute phase of a persistent sore throat which she had experienced since suffering infectious mononucleosis (IM) at 17 years of age. Despite being treated previously for β-haemolytic streptococcus group A she had continued to suffer from a chronic sore throat which occasionally manifested as a high fever, general malaise, lymphadenitis, tonsillar lesions and dysphagia associated with a classic 'hot potato' voice. On this occasion we isolated a β-haemolytic streptococcus group A together with a heavy growth of *F. necrophorum* from a throat swab. Owing to penicillin allergy the patient was treated with a 7 day course of clarithromycin and a 10 day course of metronidazole. Within 48 h of commencing treatment she reported a dramatic improvement in general health. Her persistent tonsillar swelling, experienced since diagnosis of IM, had resolved, her hearing had improved, and she reported an improvement in her ability to swallow. After completing her treatment she noticed the absence of the low grade lymphadenitis which had characterised her persistent sore throat in the preceding years.

There is no published data concerning the role of *F. necrophorum* in sore throats and as a result of this, we decided to carryout a case control study to investigate the incidence of persistent sore throat syndrome (PSTS) caused by this organism. In this as yet unpublished study carried out by the authors of this paper we isolated *F. necrophorum* from 21% ($P=0.0001$) of cases of recurrent, persistent or chronic sore throat suggesting that *F. necrophorum* can be a pathogen in persistent sore throats in humans without progressing to life threatening systemic disease.

The purpose of this study was to determine whether the same or different types of the organism were responsible for PSTS and LD by using enterogenic repetitive intergenic consensus-poymerase chain reaction (ERIC-PCR) to compare our PSTS isolates with isolates from patients suffering from systemic disease.

Methods

Specimens

Culture isolates were obtained from throat swabs taken from patients suffering from recurrent, persistent or chronic sore throat. Throat swabs were received in the laboratory in Amies's transport medium and cultured the same day.

Media

Primary isolation of *F. necrophorum* from clinical samples was carried out on G-N anaerobe medium (Oxoid) incubated anaerobically for up to 5 days at 37 °C. Subsequent sub-cultures were carried out on blood agar (Oxoid) incubated anaerobically overnight to provide fresh cultures. All isolates were