ANNALES
UNIVERSITATIS MARIAE CURIE-SKŁODOWSKA
LUBLIN – POLONIA
VOL. LIX, N 1, 35 SECTIO D 2004

Department of Infectious Diseases, Skubiszewski Medical University of Lublin

HANNA FOTA-MARKOWSKA, ROMANA ROLLA-SZCZEPAŃSKA, ALINA CHUDNICKA, MAŁGORZATA GRABSKA-MODRZEWSKA, ANNA DOMINIK

Candidosis of the pharyngeal mucosa in patients with infectious mononucleosis

Infectious mononucleosis (IM) is a primary, symptomatic infection with Epstein-Barr virus (EBV), characterised by a generalised, self-limiting lymphoproliferative reaction.

In taxonomy EBV is classified into the large family of *Herpesviridae*, the subfamily of *Gammaherpesviridae* and the genus of *Lyphocryptovirus* (1, 15). There were two types of the virus discovered in the eighties of the past century: EBV1 (type 1) and EBV2 (type B). The type A is widespread in the whole world, especially in the Western Europe and North America. The type B, however, is spread mainly in the Central Africa and New Guinea, where it has also been proved to play a role in the development of the Burkitt's lymphoma (12, 13). Other neoplasms, which are etiologically linked with EBV infection, include the Hodgkin's disease, nasopharyngeal carcinoma, non-Hodgkin lymphomas and some sarcomas (4).

Seroepidemiologic examinations showed the presence of EBV infection markers in about 80–90% of the population, with only 3–10% of adults over 40 years old being uninfected (5, 10). In Poland, IM is the prevalent form of a primary virus infection and effects mostly young people. It must be stressed that the disease is characterised by a variety of clinical symptoms, which, in the acute phase of the infection, can make a correct early diagnosis very difficult.

The frequently observed pharyngitis and tonsillitis of a different degree of seriousness – from a simple inflammation to an important angina accompanied by vast pseudomembranes similar to those seen in diphtheria – can imitate a bacterial infection. According to the Infectious Disease Society of America, EBV belongs to the most frequent nonbacterial pathogens that cause a phlegmonous tonsillitis (2, 16). Such a clinical picture could suggest using an empirical antibiotic therapy, which is a case in common practice.

The aim of our study was to assess the frequency rate of *Candida* yeast-like fungi in isolations from nasal and pharyngeal mucosa in patients diagnosed with IM who had undergone an antibiotic therapy.

MATERIAL AND METHODS

The study was performed in 51 patients, aged 17–33, treated in the Outpatient Department of Infectious Diseases of Medical University of Lublin in the years 2000–2003.

The diagnosis of IM was made on the basis of clinical symptoms, haematological, biochemical and serologic examinations results. The diagnosis was confirmed by a positive latex reaction with

heterophile antibodies (ELISA, Organon, Technika) or by an anti-VCA IgM level greater than 20 AU/ml (ELISA, Organon, Technika). The material consisted of nasal and pharyngeal swabs, inoculated into Sabouraud and Chromagar *Candida*-Becton-Dickinson mediums. The identification of *Candida* species was done according to the routine microbiological diagnostics.

RESULTS

The analysis of the results showed that *Candida albicans* was the unique species isolated only from pharyngeal swabs (Table 1).

Table 1. Frequency of isolation of *Candida* yeast-like fungi

Species	Frequency of isolation			
	pharynx		nose	
	number of patients n = 51	percentage	number of patients n = 51	percentage
Candida albicans	14	27.4	-	-

DISCUSSION

There has been a noticeable rise in the number of mycotic infections both in hospitals and in outpatients clinics recently. It seems interesting that among over 200 species of *Candida* yeast-like fungi, only some of them are pathogenic. These are, e.g. *C. albicans, C. tropicalis, C. parapsilosis, C. crusei, C. lusitaniae, C. quilliermondi* and *C. glabata* (2, 6, 11).

As our data suggest, *C. albicans* was the only pathogen isolated from patients in the acute phase of IM. It must be stressed that candidosis was observed in every fourth patient (27.4%).

It is also remarkable that such a percentage correlates with a rate of phlegmonous pharyngeal lesions estimated at 19% in cases of EBV infection and can indicate that the antibiotic therapy is the direct cause of the candidosis.

It is known that *C. albicans* constitutes a normal physiologic flora of mucous membranes of the nasopharynx, digestive tract and vagina. An imbalance of this flora plays the clue role in the pathogenesis of candidosis by initiating an adhesion of mycotic cells to host cells and releasing proteolytic enzymes. All that leads to the colonisation, forming aggregates, causing a damage of epithelium cells and allowing an invasion of *C. albicans* into the tissue (8).

From this point of view, we cannot exclude the fact that the pharyngeal candidosis showed by our research in the course of IM can be caused by an activation of an endogenic infection. A further diagnostics and assessing the serum level of *Candida* mannan antigen should be indicated in order to analyse the range of this process.

Most mycotic infections are secondary, opportunistic and in cases of low immunity they can lead to a generalised infection and a development of a systemic mycosis (fungaemia). Over 60% of these systemic infections are caused by *C. albicans* (6).

In the acute, symptomatic EBV infection immunological reactions, which are responsible for a course and effects of the infection, lead to the weakening of the body immunity mechanisms. An example of this is neutropenia, which usually appears in the first 4 weeks of the infection and can be observed at different stages. Clinical observations show that in about 10% of patients the neutrophil count falls down to 500–1000/μl but more often, especially in young children, it falls down to less than

500/μl (14). There have also been some cases of granulocytopenia, or even agranulocytosis in literature, seen in the course of EBV infection with a serious bacterial co-infection (9).

Our observations show that in the acute phase of EBV infection a different bacterial flora, potentially pathogenic, can be isolated from pharyngeal swabs (7).

From the clinical point of view, the symptoms of pharyngitis last longer or recur in cases with bacterial co-infections, which proves the necessity of antibiotic therapy as a supportive treatment. An early diagnosis of IM, based on such symptoms as fever, lymphadenopathy, pharingitis, splenomegalia and lymphocytic leukocytosis or the presence of atypical lymphocytes in blood cell count, can limit the use of ineffective antibiotic treatment.

Our results suggest the necessity of introducing an efficient, antimycotic prophylactic treatment in this group of patients since candidosis of mucous membranes in the course of IM is a serious complication and lengthens the period of recovery.

CONCLUSIONS

1. Isolation of *C. albicans* in every fourth patient in acute, symptomatic phase of infectious mononucleosis shows an existing imbalance of the physiologic oral flora, which may be caused by the antibiotic therapy.

2. Candidosis of pharyngeal mucous membranes in the course of infectious mononucleosis can be a result of an endogenic infection. In order to analyse the range of this process, a further diagnostics and assessing the serum level of the mannan *Candida* antigen should be indicated.

3. Microbiological nasal and pharyngeal swabs can be useful in the differential diagnosis of infectious mononucleosis and reduce the antibiotic treatment, ineffective in virus infections.

REFERENCES

1. Agut H.: Human herpesviruses: Foreword. Rev. Prat., 49, 2195, 1999.
2. Alexander B. D.: Diagnosis of fungal infection: new technologies for the mycology laboratory,Transpl. Infect. Dis. 4, suppl. 3, 32, 2002.
3. Bismo A. L., et. al.: Infection Diseases Society of America. Diagnosis and managment of group A streptococcal pharingitis: a practice guideline. Clin. Infect. Dis., 48, 741, 1997.
4. Butel J. S.: Viral carcinogenesis. Revelation of molecular mechanisms and etiology of human diseases. Carcinogenesis, 21, 405, 2000.
5. Bruu A. L. et al.: Evaluation of 12 commercial tests for detection of Epstein-Barr virus-specific and heterophile antibodies. Clin. Diagn. Lab. Immunol., 7, 451, 2000.
6. Dzierżanowska D., Jeljaszewicz J.: Zakażenia szpitalne. α-Medica Press, Bielsko-Biała 1999.
7. Fota-Markowska H., Rolla-Szczepańska R., Chudnicka A. M., Modrzewska R.: Charakterystyka drobnoustrojów izolowanych błon śluzowych jamy nosowo-gardłowej u chorych z mononukleoza zakaźną. Wiad. Lek., 3, 150, 2002.
8. Haynes K.: Virulence in *Candida* species. Trends Microbiol., 9, 591, 2001.
9. Neel E. U.: Infectious mononucleosis : Death due to agranulocytosis and pneumonia. JAMA, 236, 1493, 1976.

10. Polz M., Rajtar B.: Występowanie markerów zakażenia wirusem Epsteina-Barr w wybranych populacjach. Doniesienie wstępne. Mat. Naukowe XIII Zjazdu PTE i LCh. Z, Poznań 494, 1994.
11. Pulimood S. et al.: Polymicrobial candidemia, Diagn. Microbiol. Infect. Dis., 44, 4, 353, 2002.
12. Sculley T. B. et al.: Coinfection with A-and B- type Epstein-Barr virus in human immunodeficiency virus-positive subjects. J. Infect. Dis., 162, 643, 1990.
13. Sixbey J. W. et al.: Detection of a second widespread strain of Epstein-Barr virus. Lancet, 2, 761, 1989.
14. Mahoney D. H., Fernbach D. J. The hematologic response. In: Infectious Mononucleosis, D. Schlossberg, 80-88, Springer-Verlag, New York 1989.
15. Whitley R. J.: Editorial: Our evolving knowledge of herpesviruses. Herpes, 7, 59, 2000.
16. Yoda K. et al.: Oropharyngotonsillitis associated with nonprimary Epstein-Barr Virus infection. Arch. Otolaryngol. Head–Neck Surg., 126, 185, 2000.

SUMMARY

The aim of our study was to assess the frequency rate of *Candida* yeast-like fungi in isolations from nasal and pharyngeal mucosa in patients diagnosed with IM who had undergone an antibiotic therapy. The study was performed in 51 patients aged 17–33. The diagnosis of IM was made on the basis of clinical symptoms, haematological, biochemical and serologic examination results. The material constituted of nasal and pharyngeal swabs. The identification of *Candida* species was done according to the routine microbiological diagnostics. Our results show that among the *Candida* genus, *C. albicans* was the only pathogenic species isolated from patients with IM. It was observed only in pharyngeal swabs in 27.4% of the patients.

Kandydoza błon śluzowych gardła u chorych w przebiegu mononukleozy zakaźnej

Celem pracy była ocena częstości izolacji drożdżaków z rodzaju *Candida* z błon śluzowych nosa i gardła u pacjentów z rozpoznaniem mononukleozy zakaźnej (MZ), po wcześniejszej antybiotykoterapii ambulatoryjnej, leczonych w Poradni i Klinice Chorób Zakaźnych AM w Lublinie w latach 2000 – 2003. Badania przeprowadzono w grupie 51 chorych w wieku 17–33 lat. Rozpoznanie MZ ustalono na podstawie objawów klinicznych, parametrów hematologicznych, biochemicznych i serologicznych. Materiał do badań stanowiły wymazy z błony śluzowej nosa i gardła. Identyfikację gatunków z rodzaju *Candida* wykonywano zgodnie z rutynowo stosowaną diagnostyką mikrobiologiczną. Analiza uzyskanych wyników badań wykazała, że jedynym izolowanym gatunkiem drożdżaków z rodzaju *Candida* był *C. albicans*, stwierdzany wyłącznie w wymazach z błon śluzowych gardła u 27,4% chorych.