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Original article

Severe infectious mononucleosis in immunocompetent adults

Mononucléose infectieuse grave de l'immunocompétent

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Abstract

Objectives. – To determine the risk factors for severe infectious mononucleosis (IM) occurrence in immunocompetent adults.

Methods. – We performed a multicenter, retrospective case series including immunocompetent adults presenting with confirmed IM between 2001 and 2011. Severe presentations were compared with uncomplicated presentations using Stata® 9 software. The significance level was set at 5%.

Results. – In univariate analysis, age over 30 years ($n = 13$ or 41.9% vs. $n = 5$ or 12.8%; $P = 0.006$), prior use of non-steroidal anti-inflammatory drugs (NSAIDs) ($n = 7$ or 87.5% vs. $n = 1$ or 12.5%; $P = 0.009$), and smoking ($n = 13$ or 68.4% vs. $n = 6$ or 31.6%; $P = 0.013$) were associated with severe IM onset. In multivariate analysis, only age over 30 years (OR = 3.55; $P = 0.05$) and prior use of NSAIDs (OR = 15; $P = 0.05$) remained associated with severe IM onset, without reaching significance level ($P = 0.05$).

Conclusion. – Our study confirmed that age over 30 years is a risk factor for severe IM onset. Prior use of NSAIDs also seems to be correlated with severe presentations. This new data needs to be confirmed in a prospective study.

Keywords: Infectious mononucleosis; Epstein-Barr virus; Primary infection; Severe presentation; Risk factors

Résumé

Objectif. – L'objectif de notre étude était de déterminer les facteurs de risque de survenue de mononucléose infectieuse (MNI) grave chez l'immunocompétent.

Matériels et méthodes. – Étude rétrospective cas-témoins multicentrique incluant les adultes immunocompétents ayant présenté une MNI prouvée par sérologie entre 2001 et 2011. Les formes graves ont été comparées aux formes simples à l'aide du logiciel Stata® version 9. Le seuil de significativité a été fixé à 5 %.

Résultats. – En analyse univariée, l'âge supérieur à 30 ans ($n = 13$, soit 41,9 % vs. $n = 5$, soit 12,8 % ; $p = 0{,}006$), la prise d'anti-inflammatoires non stéroïdiens (AINS) ($n = 7$, soit 87,5 % vs. $n = 1$, soit 12,5 % ; $p = 0{,}009$) et le tabagisme ($n = 13$, soit 68,4 % vs. $n = 6$, soit 31,6 % ; $p = 0{,}013$) étaient des facteurs associés à la survenue d'une MNI grave. En analyse multivariée, seuls l'âge supérieur à 30 ans (OR = 3,55 ; $p = 0{,}05$) et la prise initiale d'AINS (OR = 15 ; $p = 0{,}05$) restaient associés à la survenue d'une MNI grave, avec des résultats à la limite de la significativité.

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Conclusion. – Cette étude souligne, à l'instar des données de la littérature, que l'âge supérieur à 30 ans est un facteur de risque de survenue de MNI grave. La prise initiale d'AINS semble être également associée aux formes graves, donnée inédite méritant d'être confirmée par une étude prospective.

Mots clés : Mononucléose infectieuse ; Virus d'Epstein-Barr ; Primo-infection ; Gravité ; Facteur de risque

1. Introduction

Epstein–Barr virus (EBV) primary infection is a common disease. It is often asymptomatic or paucisymptomatic when contracted during childhood. Infectious mononucleosis (IM) is the clinical manifestation of this infection; it is most commonly observed in adolescents and young adults (15 to 24 years) [1].

Considering the high incidence of IM (1/50,000 per year in the general population and 1/1,000 per year in young adults [2]), the infection is frequently observed in primary care settings.

Commonly thought to be benign, IM may lead to rare complications (hematological, splenic, hepatic, neurological, cardiac, ENT, renal, and pulmonary) that can be life-threatening.

Identifying risk factors for complications at IM diagnosis is important to adjust the clinical and biological surveillance strategy. These factors have scarcely been studied in the literature; former studies only focused on age. We aimed to determine the risk factors for severe IM in immunocompetent individuals.

2. Patients and methods

We performed a retrospective, multicenter case-control study in three military hospitals of Paris (Bégin, Percy, and Val-de-Grâce) from January 2001 to December 2011. We compared epidemiological, clinical, and biological data of patients presenting with severe IM with that of patients presenting with uncomplicated IM.

2.1. Inclusion criteria

We included all immunocompetent adults (minimum age: 15 years and 3 months) with a diagnosis of IM confirmed by EBV serology (negative for anti-EBNA IgG antibodies and positive for anti-VCA IgM antibodies) who consulted at the three participating hospitals.

2.2. Exclusion criteria

We excluded all immunocompromised patients (positive serology for HIV, long-term immunosuppressant treatment, cancer or treated hemopathy, diabetes), patients presenting with another concomitant viral infection, patients whose chart did not include EBV serology, or patients with a positive EBV serology indicative of a previous infection (positive for anti-EBNA IgG, negative for anti-VCA IgM).

2.3. Defining severe presentations

Severe IMs were defined by the occurrence of death, ENT locoregional complications (upper airway obstruction due to hyperplasia of oropharyngeal lymphoid tissues such as tonsils, adenoids, phlegmon), splenic complications (splenic hematoma, splenic rupture), pulmonary complications (interstitial lung disease), cardiac complications (myocarditis, pericarditis), hepatic complications (ALT > 10 × ULN, symptomatic hepatitis (icterus, nausea), hematological complications (macrophage activation syndrome defined by the combination of ferritin levels > 10,000 ng/mL, bicytopenia, cholestasis/cytolysis, increased lactate dehydrogenase levels, increased triglyceride levels, and reduced fibrinogen levels, hemolytic anemia < 8 g/dL, thrombocytopenia < 50,000/mm^3 and/or hemorrhagic manifestations, neutropenia < 500/mm^3), neurological complications (encephalitis, meningitis, acute polyradiculoneuritis, facial nerve palsy), digestive complications (colitis), and/or ophthalmologic complications (uveitis).

2.4. Chart selection (Fig. 1)

Medical charts of patients were selected using two types of resources:

- extraction from the French diagnosis related groups program database (French acronym PMSI) (code B27.0) of participating hospitals;
- extraction from data of the biomedical laboratory – serologies indicative of an EBV primary infection were selected.

A total of 149 charts were selected from the PMSI: 51 were included, 59 could not be used, and 39 were excluded (incomplete charts, $n = 18$; absence of serology, $n = 9$; negative serology, $n = 7$; serology indicative of a reactivation, $n = 2$; cytomegalovirus [CMV] infection, $n = 19$; Parvovirus infection, $n = 1$; measles, $n = 2$; dengue, $n = 2$; idiopathic myocarditis, $n = 1$; immunodeficiency factors, $n = 2$).

A total of 147 serologies performed in the participating laboratories were indicative of an EBV primary infection: 19 were included, 100 could not be used, 28 had already been included using the first method of selection.

2.5. Data collection

Data was retrospectively collected based on the analysis of the charts of included patients.

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