Reumatol Clin. 2016;12(2):100–102

Reumatología Clínica

www.reumatologiaclinica.org

Case Report

Joint Involvement Secondary to Epstein–Barr Virus☆

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ARTICLE INFO

Article history:
Received 28 April 2015
Accepted 29 May 2015
Available online 23 February 2016

Keywords:
Epstein–Barr virus
Arthritis

ABSTRACT

We describe a group of patients with Epstein–Barr virus (EBV) infection and joint involvement. Between February 2011 and January 2012, there were six cases in our unit. Two presented with a pattern similar to rheumatoid arthritis, three had polyarthralgia with an inflammatory pattern and only one patient had asymmetrical oligoarthritis of large joints. They were all women aged between 25 and 75 (4 were of childbearing potential). Diagnosis in all the cases was made by exclusion of other possible causes and negative IgM were obtained for the rest of the "Herpesviridae" family viruses. In our series, EBV joint involvement was more common in women of childbearing potential. Clinical presentation was heterogeneous but was predominantly in the form of inflammatory joint pain. When it presents in the form of symmetrical polyarthritis, it can become chronic and require the use of disease-modifying anti-rheumatic drugs.

Afectación articular secundaria a infección por virus de Epstein-Barr

Palabras clave:
Virus de Epstein Barr
Artritis

RESUMEN

Describimos un grupo de pacientes con infección por virus de Epstein-Barr (VEB) y manifestaciones articulares. Entre febrero del 2011 y enero del 2012 se ha recogido un total de 6 casos en nuestra sección. Dos de ellos se presentaron con un patrón similar a la artritis reumatoide, en forma de poliartritis simétrica de pequeñas y grandes articulaciones. Tres presentaron poliartralgias de ritmo inflamatorio y solamente una de las pacientes presentó una oligoartritis asimétrica de grandes articulaciones. Todas fueron mujeres con edades comprendidas entre los 25 y los 75 años (4 de ellas en edad fértil). En todas se realizó el diagnóstico de exclusión de otras posibles etiologías y se obtuvieron IgM negativas para el resto de virus de la familia Herpesviridae. En nuestra serie, la afección articular por VEB fue más frecuente en mujeres en edad fértil, con una presentación clínica heterogénea, predominando la forma de artralgias inflamatorias. La presentación en forma de poliartritis simétrica puede cronificarse y hacer necesario el uso de fármacos antirreumáticos modificadores de la enfermedad.

Introduction

Viruses can act as adjuvants in the development of autoimmunity, non-specifically stimulating the innate immune response (mast cells, dendritic cells, Toll-like receptors and complement receptors).[1] Many viruses have been involved in the pathogenesis of different inflammatory arthropathies.[2–5] Although joint manifestations have been reported in relation to rubella, HTLV-1, parvovirus B19[2] and hepatitis B and C viruses,[1] there are few publications dealing with the joint condition produced by Epstein–Barr

☆ Please cite this article as: Feced Olmos CM, Fernández Matilla M, Robustillo Villarino M, de la Morena Barrio I, Alegre Sancho JJ. Afectación articular secundaria a infección por virus de Epstein-Barr. Reumatol Clin. 2016;12:100–102.

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2173-5743/

Table 1
Presentation and Clinical Signs and Symptoms of the Patients.

	Sex and age (yr)	Season of presentation	Form of presentation	CRP (mg/dL)	EBV IgM/IgG serology at beginning of study	Time to negative IgM test	Time from initiation of the study to clinical resolution	Treatment
Case no. 1	W 25	Winter	PAIJPSLJ	23	IgM+/IgG+	3 months	1 month	NSAID
Case no. 2	W 30	Spring	SPASLJ	32	IgM+/IgG+	Positive after 12 months	Control of symptoms with DMARD 4 months	Required DMARD after failed disease control with NSAID/corticosteroids
Case no. 3	W 32	Winter	AOLJ	45	IgM+/IgG+	11 months	2 months	NSAID/short course of oral corticosteroids
Case no. 4	W 37	Spring	PAIJPSLJ	17.5	IgM+/IgG+	Positive after 12 months	2.5 months	NSAID
Case no. 5	W 54	Spring	SPASLJ	75	IgM+/IgG+	6 months	Control of symptoms with DMARD 3 months	Required DMARD after failed disease control with NSAID/corticosteroids
Case no. 6	W 75	Winter	PAIJPSLJ	51	IgM+/IgG+	Positive after 12 months	1.5 months	NSAID/short course of oral corticosteroids

AOLJ, asymmetric oligoarthritis of large joints; CRP, C-reactive protein; DMARD, disease-modifying antirheumatic drugs (methotrexate or leflunomide was used); EBV, Epstein–Barr virus; Ig, immunoglobulin; NSAID, nonsteroidal anti-inflammatory drugs; PAIJPSLJ, polyarthralgia with inflammatory joint pain in small and large joints; SPASLJ, symmetric polyarthritis of small and large joints; W, woman.

virus (EBV). We present a series of patients with inflammatory joint changes secondary to that virus.

Clinical Observation

Between February 2011 and January 2012, 6 patients with joints affected by EBV were treated in our section. The characteristics are shown in Table 1. The clinical onset had taken place within the preceding 3 months, without prodromes or extra-articular manifestations. In the 3 patients with arthritis, the synovial fluid had inflammatory features, without microcrystals, and the cultures were negative. Liver and renal function, electrolytes, creatine phosphokinase (CPK), and urine and blood tests were normal. All the patients tested negative for rheumatoid factor (RF), anti-citrullinated protein antibodies, antinuclear antibodies, anti-extractable nuclear antigen antibodies, human leukocyte antigen B27 and 2-step Mantoux test. Serological tests for hepatitis B and C viruses, parvovirus B19, human immunodeficiency virus, herpes simplex virus types 1 and 2, cytomegalovirus, EBV and varicella zoster virus, showed no evidence of current infection. The radiographic study of thorax, hands, feet and knees was normal.

Discussion

Epstein–Barr virus belongs to the herpes virus family. Nearly 98% of the population aged 40 years or over has been infected by this virus at some time in their lives.[1,6,7] It causes infectious mononucleosis and is associated with B-cell, T-cell and Hodgkin's lymphomas and nasopharyngeal carcinomas. The publications that deal with the effects of the virus on joints focus only on arthralgia and monoarthritis of the knee in relation to infectious mononucleosis.[8]

In acute infection, plasma concentrations of EBV anti-viral capsid antigen (VCA) IgM increase rapidly, decreasing a few months later. Anti-VCA IgG antibodies persist for life, with stable titers.[1] The results have been interpreted in an appropriate clinical context, as positivity for anti-VCA IgM can be found in infections by other viruses of the same family. It is necessary to rule out other autoimmune and/or infectious diseases, since it can become positive in cases of strong immune response. In our patients, we defined the case as secondary to EBV infection in the presence of inflammatory joint involvement with positivity for VCA IgM, after excluding other diseases and infection by a virus of the same family. There is certain controversy concerning the time necessary for a test for IgM to become negative.

The serological determination of viruses like EBV, which are capable of producing clinically relevant joint involvement, may be key in the diagnosis of undifferentiated arthritides (term used when a patient does not meet the criteria for any particular rheumatic disease),[9] as it enables the identification of the etiology or factor that triggered the condition. In situ hybridization of RNA and DNA makes it possible to detect the presence of cytomegalovirus, parvovirus B19, EBV and other viruses of the herpes family in the synovial fluid of patients with different forms of arthritis.[9] This supports a possible major role of these viruses in inflammatory arthropathies.[3] Moreover, there are publications that argue in favor of the possible role of EBV as a triggering factor in rheumatoid arthritis[10] or juvenile idiopathic arthritis.

Conclusion

We report the first series of patients with inflammatory joint manifestations associated with acute EBV infection, excluding other diagnostic alternatives. Our patients were women, several of childbearing age. Disease presentation appeared to be seasonal (winter and spring). The patients with symmetrical polyarthritis required treatment with disease-modifying antirheumatic drugs; thus, that form of presentation seems to indicate a poor prognosis, with a trend toward chronicity. Larger series will be necessary to properly characterize this joint involvement.

Ethical Disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

Conflicts of Interest

The authors declare they have no conflicts of interest.

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