Progress in Retinal and Eye Research 39 (2014) 77–106

Contents lists available at ScienceDirect

Progress in Retinal and Eye Research

journal homepage: www.elsevier.com/locate/prer

Ocular toxoplasmosis past, present and new aspects of an old disease

M. Maenz [a,1], D. Schlüter [b,1], O. Liesenfeld [c,1], G. Schares [d,1], U. Gross [e,1], U. Pleyer [a,*,1]

[a] Eye Clinic – Charité Universitaetsmedizin-Berlin, Augustenburger Platz 1, 13353 Berlin, Germany
[b] Institute of Medical Microbiology, Otto-von-Guericke-University Magdeburg, Germany
[c] Institute for Microbiology and Hygiene, Charité Universitaetsmedizin-Berlin, Germany
[d] Institute of Epidemiology – Friedrich-Loeffler-Institute – Greifswald-Insel Riems, Germany
[e] Institute for Medical Microbiology and German Consulting Laboratory for Toxoplasmosis, University Medical Center Goettingen, Germany

ARTICLE INFO

Article history:
Available online 9 January 2014

Keywords:
Ocular toxoplasmosis
Uveitis
Toxoplasma gondii
Retinochoroiditis

ABSTRACT

Ocular toxoplasmosis (OT) is considered the most frequent form of infectious posterior uveitis and is caused by the protozoan parasite *Toxoplasma gondii*. The resulting vision loss frequently incapacitates patients and places a considerable socio-economic burden on societies in particular in developing countries. Although, toxoplasmic retinochoroiditis is a world-wide phenomenon stark regional differences with regard to prevalence and presumably route of infection exist. This review will discuss our current clinical understanding of OT including typical and atypical manifestations, patient characteristics which influence the course of disease and treatment options. Even though, congenital and acquired OT are not regarded as separate entities, certain differences exist, which will be assessed and evaluated in detail. A strong focus is laid on the disease causing parasite *T. gondii*, since solving the mystery of OT aetiology and the development of improved therapies will not be possibly with clinical science alone, but rather requires a precise understanding of parasitological and immunological pathomechanisms. Additionally, the biology and genetics of *T. gondii* form the foundation for novel and sophisticated diagnostic methods. Scientific advances in the recent years have shed some light on the different role of *T. gondii* strains with regard to OT manifestation and severity of disease. Genetic and environmental factors influencing OT will be presented and commonalities between OT and toxoplasmic encephalitis will be briefly discussed. Furthermore, the laboratory tools to study OT are crucial in our understanding of OT. *In vivo* and *in vitro* experimental approaches will be summarised and evaluated extensively. Finally, a brief outlook is given in which direction OT research should be headed in the future.

Contents

* Corresponding author. Tel.: +49 30 450 554202; fax: +49 30 450 554900.
E-mail address: uwe.pleyer@charite.de (U. Pleyer).

[1] Percentage of work contributed by each author in the production of the manuscript is as follows: Maenz: 30%; Schlüter: 15%; Liesenfeld: 10%; Schares: 7.5%; Gross: 7.5%; Pleyer: 30%.

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http://dx.doi.org/10.1016/j.preteyeres.2013.12.005

1. Introduction

1.1. Historical background

To this day ocular toxoplasmosis (OT) remains a challenging ocular disease with many open questions with regard to disease manifestation, pathophysiology and its management. Our current understanding of OT evolved over the course of more than a century through careful clinical observation, epidemiological and parasitological studies.

Retinochoroidal scars – a clinical hallmark of OT – were probably already depicted in the mid 19th century (Fig. 1). Toxoplasmic retinochoroiditis as part of the disease manifestation of congenital toxoplasmosis in a newborn was first described by the Czech ophthalmologist *Janku* in 1923, and was considered an established medical fact almost two decades later (Janku, 1923; Wolf et al., 1939). After discovery of the parasite by *Nicolle* in 1907 (Nicolle, 1907; Nicolle and Manceaux, 2009), OT was recognised as an ocular pathology in adults by *Wilder* as late as 1952 (Wilder, 1952b, a). The seminal work of *Hogan* sparked and defined research on OT for the better part of the next two decades (Hogan, 1950, 1956, 1958a, b; Hogan et al., 1957, 1964, 1958). Most notably, already at this time the first treatment regimes were introduced in the shape of the antimalarial drug pyrimethamine in combination with sulphonamides and corticosteroids, which are still the most frequently prescribed agents until today (Perkins et al., 1956; Ryan et al., 1954) [see Section 2.5]. Whereas in the past – and with very limited success – clinical researchers attempted to subcategorise OT based on clinical parameters such as localisation of lesions, severity of inflammation, age of first manifestation, mode of infection and type of complications, OT today is understood as a disease with a broad spectrum of manifestations. Regardless of whether toxoplasmic retinochoroiditis occurs in immunocompromised and immunocompetent patients respectively, or whether OT is acquired congenitally or postnatally, no clear distinction between disease entities can be observed. The dogma that OT is an exclusive congenital disease eroded in the 1980s and today it is well recognised that postnatally acquired infection and subsequent ocular inflammation is the most frequent form of OT (Gilbert and Stanford, 2000). Based on advances in the recent decades, we know that OT is the most frequent form of infectious posterior uveitis representing up to 85% of all cases (Talabani et al., 2010). Where data are available pronounced geographical differences in disease prevalence can be observed. Particularly high prevalences are reported for