INTRODUCTION

The discovery of Mycobacterium tuberculosis by Robert Koch (1843-1910) in 1884 was a breakthrough in the study of tuberculosis, especially for the form of pulmonary tuberculosis, which afflicted humanity from the antiquity [1, 2]. Due to this discovery the scientists could now focus on a treatment which could treat more effectively the patients. However, it took several years until Alexander Fleming (1881-1955) in 1928 discovered penicillin and introduced an accurate treatment for tuberculosis in clinical practice [3]. The Mycobacterium tuberculosis infection was not limited only to the lung, having in mind that pulmonary tuberculosis was very common and a lethal disease, but many other forms of this infection were also detected. Among those forms, a very distinctive one was the ocular tuberculosis where almost all the anatomical structures of the eye could be infected. During the 19th century many studies and great effort were made in order to understand and describe this specific form of infection.

Ocular tuberculosis
The birth of pathological anatomy at the first third of 19th century gave new potentials in the study of all the pathological phenomena in medicine [4]. Although from the 18th century a serious effort was made in order to examine the histological characteristics of various diseases, with the works of Giovanni Battista Morgagni (1682-1771), the introduction of more powerful, for the time being, microscopes and the systematic approaches by various physicians was necessary, in order to have clear conclusions concerning the histological disorders in the pathological phenomena [5]. On the other hand, especially for ocular tuberculosis, the invention of ophthalmoscope in 1851 by Hermann von Helmholtz (1821-1894) played an important role as well for the detection of tuberculosis [6].

Although in the previous centuries the inflammation and the ulcers on the ophthalmic tissues were observed - Antoine Maître-Jan is believed to
describe ocular tuberculosis in 1711 - the scientific study of ocular tuberculosis began at the early 19th century [7]. The first scientific observations considered choroidal tuberculosis were made by Johann Hermann Heinrich Ferdinand von Autenrieth (1772-1835) in 1808 [8]. Noël-Francois-Odon and Guéneau de Mussy (1813-1885) in 1837 were the first ones who pointed the infection in choroidal after autopsy, where the specific granuloma of tuberculosis was observed [9]. Eduard Jäger von Jaxtthal (1818-1884) in 1855 was the first to describe tuberculosis in fundus after ophthalmoscopy [10]. In 1858 Wilhelm Manz (1833-1911) was the first to give a detailed description of the microscopic findings in choroidal tuberculosis [11]. Julius Friedrich Cohnheim (1839-1844) in 1867 was also the first to combine the findings in ophthalmoscopy with the histological image in choroidal tuberculosis [12]. Giuseppe Gradengo’s (1859-1926) observation of iris tuberculosis granuloma in 1869 was the first not only of iris tuberculosis but also of the fact that ocular tuberculosis could be primary and not only secondary as believed before, because the earlier observations were made in patients suffering mainly by pulmonary and meningitis tuberculosis, while his patient had no other tuberculosis infection in his body [13]. Giuseppe Arcoleo (19th century) noted for first time tuberculosis in cornea in 1867, Eugène Bouchut (1818-1891) in retina in 1869, Köster W. (19th century) in conjunctiva in 1873, Antonin Poncet (1849-1913) in vitreous body in 1875, Hubert Sattler (1844-1928) in optic nerve in 1878, and Köhler (19th century) in 1884 in sclera [10,14-17]. In addition, Louis Alexander (19th century) and Hans Adler (19th century) were the first, in 1875, to describe the conjunctiva tuberculosis in the form of lupus vulgaris, which is facial tuberculosis known by that name in those years [18, 19]. A year before Koch’s discovery, in 1883, Julius von Michel (1843-1911) identified the tubercle in the eye [20].

The main interest in the study of ocular tuberculosis during the 19th century was the detection whether ocular tuberculosis was primary or secondary. This distinction played a crucial role at the time, because in case of secondary, the physician should find the primary place of the infection on the body and the patient should be examined thoroughly and treated with great care. Apart from problems in vision, special clinical characteristics were assigned according to each structure of the infected eye [21].

 Conjunctival tuberculosis was considered either primary or secondary. In primary type it was believed that the Mycobacterium tuberculosis had entered conjunctiva through wounds of the conjunctiva or after an operation. Two forms were distinct: the acute and the chronic. The acute form could be misdiagnosed as acute trachoma or Parinaud’s conjunctivitis, as in this form numerous small nodules, which grow and coalesce, appeared. In the chronic form the appearance of an irregular shallow ulcer on the palpebral or ocular conjunctiva is characteristic. Therefore, it can be misinterpreted as chalazion or epithelioma. The chronic form is known as the lupus vulgaris disease [22].

 Corneal tuberculosis was rarely believed to be primary and affecting both eyes. Three clinical images of this infection were described. The interstitial keratitis, the sclerosing keratitis, and the appearance of grayish opacities situated deep in the corneal tissues and lead to superficial ulceration of the cornea [23].

 The tuberculosis of sclera was extremely rare as a primary infection, while more frequent was the extension of the infection by uveal tract, Tenon’s capsule, optic nerve and cornea. Episcleritis or scleritis were the main symptoms [24].

 Tuberculosis of iris (Figure 1) was considered as a children’s or young boy’s disease, because it was very rarely diagnosed in people older than twenty years. This could be primary or secondary. It had two forms. The first one miliary tubercles of the iris had the form of small gray elevations which had a thickened hyperemic base. The second one appeared as conglomerate tubercle, where a large mass of tubercular tissue developed from one or from numerous foci. Both forms could be misdiagnosed as syphilitic iritis [25].

 Chorioidal tuberculosis was considered a disease either of the choroidal stroma or the choroid. It was believed to be secondary. In this condition the miliary tubercles were detected at the posterior part of the fundus and were not visible until they occasionally disturbed the retinal pigment layer [26].

 Tuberculosis of the retina was believed also to be secondary (Figure 2). The detachments of the retina or the choroid were among the characteristic...
symptoms of these two types of tuberculosis. Retinal tuberculosis occurs most often as a vasculitis or a peri-vasculitis of the retinal vessels which appear as white infiltrates surrounding and attacking the vessels [23]. Tuberculosis of optic nerve was believed to be present only after a trauma or surgery. Optic neuritis was the primary symptom, while tubercle tumors could arise in every portion of the optic nerve [27].

Ocular tuberculosis diagnostic tests
The clinical image of ocular tuberculosis and the lesions found during ophthalmoscopy were the main means for diagnosis of ocular tuberculosis before Koch’s discovery. The earlier diagnosis of tuberculosis in another organ helped many physicians to reach this diagnosis. After the discovery of Mycobacterium tuberculosis, four tests were introduced in clinical practice in order to diagnose ocular tuberculosis, when the patient did not have another obvious form of tuberculosis and the symptoms in the eye showed mycobacterial infection, namely: the Calmette’s ophthalmo-tuberculin reaction, the von Pirquet’s reaction, the Moro test and the Koch subcutaneous tuberculin test. Calmette’s ophthalmo-tuberculin reaction was the only test applied directly to the eye, because a drop of 1% tuberculin in aqua solution was instilled in the eye and the physician waited for its irritation during the next 24 hours. Von Pirquet’s reaction and Moro test had to do with the application of tuberculin on the skin either on the inner surface of the arm, or on the chest (or the abdomen). All these methods were not considered secure and had low value for the diagnosis. The more preferable one was the Koch’s subcutaneous tuberculin test where 0.1 mg of tuberculin was injected subcutaneously [28].

Treatment of ocular tuberculosis
After Koch’s discovery of tuberculin, apart from being a mean to diagnose the disease, tuberculin was also used as the main treatment in ocular tuberculosis, firstly used by this physician in 1890. Two forms were used: the old and the new tuberculin. The old tuberculin consisted of broth culture of the tubercle bacillus of the human type boiled and concentrated, from which the bacilli had been removed by filtering. New tuberculin was a suspension of pulverized tubercle bacilli in water with an addition of an equal volume of glycerin. New tuberculin was also produced by bovine bacilli. Tuberculin was mostly injected. At that time it was believed that tuberculin could be used for the immunization of the population,
therefore it was used also as a vaccine, but with
great controversy, and finally this idea was aban-
donned. Before Koch’s discovery, a popular treat-
ment for ocular tuberculosis was the use of mer-
cury as collyrium [28].
The discovery of X-Rays by Wilhelm Conrad
Röntgen (1845-1923) in 1895 was a breakthrough
not only in radiology but for the entire medicine,
because these rays were used for the treatment of
many diseases, including ocular tuberculosis. The
main treatment by X-rays was 10 sessions with
duration of 10 minutes. This treatment was main-
ly tried against lupus vulgaris, but it was also
used for conjunctival and iris tuberculosis [29].
A different treatment but with good results was
applied against intraocular tuberculosis. This
treatment, introduced by Köster, intended to
cure intraocular tuberculosis by injecting ster-
ile air into the anterior chamber, a portion of the
aqueous humor. It was considered as effective in
the superficial forms of keratitis, scleritis, ker-
to-conjunctivitis of phlyctenular origin, central
and marginal ulcer of the cornea, with or without
hypopyon. During this treatment the needle tip of
a sterile hypodermic syringe filled with air drawn
through an alcohol flame was entered beneath the
conjunctiva leaving the sterile air [28].
Surgery had also a major role in the treatment
of ocular tuberculosis, when the pharmaceutical
and others treatments had failed. Enucleation of
the eye was necessary in cases of retinal, corioidal
tuberculosis or in cases of optic nerve tuberculosis.
In cases of iris tuberculosis, iridectomy was
a solution. Cautery was used in external lesions
mainly on the lids and in lupus vulgaris [30].

■ CONCLUSION

The history of ocular tuberculosis during the 19th
and the early 20th century can be divided in four
periods: before and after the introduction of the
study of pathological anatomy and before and af-
after Koch’s discovery of Mycobacterium tuberculosis.
The study of pathological anatomy gave the op-
portunity to understand the histological lesions
provoked in this disease and specific pathologi-
cal characteristics were attributed to the disease.
Therefore, the histological image could distinct
the disease from other ocular pathologies, which
could provoke confusion when only the clini-
cal characteristics were examined. On the other
hand, Koch’s discovery gave the opportunity for
specific pharmacological treatment with tubercul-
in to have the primordial role that time. Ocular
tuberculosis was a serious pathological condition
attracting the interest of physicians, and as a re-
result almost all the text books of ophthalmology
include special chapters for this disease.

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