The AFIP history of ocular leprosy

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Abstract

Purpose: To investigate the Armed Forces Institute of Pathology (AFIP) experience with Ocular Leprosy.

Methods: The AFIP data banks were screened for cases with diagnosis of ocular leprosy. Files and slides stained with Hematoxylin-eosin and acid-fast staining were reviewed by the Division of Ocular Pathology and by the Infectious Diseases Pathology Branch.

Results: Twenty-five cases were found from 1951 to 1985 and there were 15 males and 7 females and in 3 cases the sex was not given. The disease process ran from 4 months to 50 years in this series. Three patients also had systemic mycobacterium tuberculosis infections. The clinical manifestations of leprosy did not correlate with the histopathological findings. Clinically, corneal manifestations were the most common clinical presentation in 15 cases with only one perforation, iridocyclitis following in 9 patients and eyelid abnormalities ranging from ectropion to trichiasis in 7 patients. Two patients at autopsy had lepromatous cells in the ciliary body as the only ocular manifestation.

Conclusions: In summary, this paper represents a series of ocular leprosy cases from the AFIP which shows the severity of ocular involvement, the predilection of anterior segment involvement and a large number of histopathologic indeterminate cases. The current immigrant and refugee crisis warrants revisiting this ancient disease in the differential diagnosis.

Keywords: Mycobacterium tuberculosis, Armed forces institute of pathology, Cornea, Anterior segment, Histopathology, Autopsy

Introduction

Leprosy, which is primarily a skin, upper respiratory tract, peripheral nerve and joint disease remains an important cause of morbidity and mortality worldwide. In terms of diseases, leprosy has plagued humankind since antiquity and it is still prevalent in some communities today. It has tremendous psychosocial ramifications and it often poorly understood by patients. The prevalence of leprosy is estimated to be 1 per 10,000 patients worldwide, but in India the prevalence is 3.8 per 10,000.1 Two hundred ninety four new cases of leprosy were reported in the United States in 2010 and nearly 70% were from California, Florida, Hawaii, Louisiana, Massachusetts, New York and Texas.2 During 1994 to 2011, the incidence of leprosy in the United States was highest among persons born in Oceania; 97% were born in the Federated States of Micronesia or the Marshall Islands, but 56 cases were diagnosed in US born citizens each year during that interval.3 Historically, the United States had two active leprosariums one in Carville, Louisiana in the southeastern part and on the remote island of Molokai, Hawaii in the Pacific Ocean.

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Parikh et al. recently reviewed three hundred eight-six Indian patients with treated multi-bacillary leprosy and found significant ocular morbidity. Specifically, there were high rates of blindness, cataracts, lagophthalmos and corneal anesthesia.

Unlike the skin disease, the diagnosis and treatment of ocular leprosy is challenging in the absence of clinically apparent skin or joint disease. There is often a significant delay in diagnosis. Also, the relative infrequency of the disease in Europe and North America provides an opportunity for misdiagnosis due to presentation to providers who have no experience with the disease. The diagnostic challenge is also complicated by difficulties in obtaining ocular tissue, the rarity of the disease process and the variability in clinical presentation.

The diagnosis of ocular leprosy is typically made when there is evidence of eye involvement with demonstration of acid-fast bacilli (AFB) under microscope using the Fite Faraco staining or Ziehl Neesen staining.

In this retrospective study, we provide the clinical profile and histopathologic features of ocular tissue of patients with the diagnosis of leprosy supported primarily by acid-fast staining in an attempt to provide clinically relevant details for diagnosis and management based on a gold standard of tissue examination. Immunofluorescent technique or PCR amplification were not used.

Patients and methods

This retrospective study was approved by the Armed Forces Institute of Pathology (AFIP) Institutional Review Board in Washington, DC in January 2007 and continuing review granted in July 2012. This institution is now closed. A portion of this current presentation was presented previously to the First Assembly of the International Ocular Inflammation Societies and was hosted by the India Uveitis Society in 2011 in Goa, India. In this project, the AFIP data banks were screened for cases with diagnosis of ocular leprosy using key words of leprosy and mycobacterium. All files and slides stained with Hematoxylin-eosin and acid-fast staining were reviewed by the Division of Ocular Pathology and by the Infectious Diseases Pathology Branch. Clinical analysis included the age, sex and medical history of each patient, year of diagnosis, clinical description and the duration of treatment prior to biopsy. When AFB were identified in tissue, their location, ocular or extra-ocular sites was recorded. The cases with necrotizing granulomatous inflammation of the ocular or ocular adnexal tissue which were negative for AFB were excluded. Emphasis was placed on skin, nerve and systemic involvement.

Results

Twenty-five cases were found from 1951 to 1985. There were 15 males and 7 females and in 3 the sex was unknown. In three cases, the slides could not be used due to age and damage and their information was provided solely by report. Ziehl-Neesen or Fite-Faraco acid-fast staining of the ocular tissues was used and PCR and immunofluorescence were not used. The average age was 47 years. The majority of cases came from USA (8), Columbia (3), Nigeria (3), Brazil (3), Congo (2), Panama (2), India (2) and Philippines (1). Please see Chart 1. The disease process ran from 4 months to 50 years in this series. Three patients also had systemic Mycobacterium tuberculosis infections. As has been reported previously, the clinical manifestations of leprosy did not correlate with the histopathological findings. There was a tremendous variety in histology presentations mostly likely due to the duration of the disease process.

Clinically, corneal manifestations were the most common presentation in 15 cases with only one perforation. Iridocyclitis occurred in 9 patients and eyelid abnormalities ranging from ectropion to trichiasis in 7 patients. The histopathologic corneal manifestations included corneal leproma (5), fibrovascular lesion (2), chronic corneal ulceration with perforation (2), staphyloma (2), perilimbal mass (3) and corneal opacity. The external eye manifestations included eyelid nodule (4), brow papule (1), anesthetic brow lesion (1) and ectropion (1). Two patients at autopsy had lepromatous cells in the ciliary body as the only ocular manifestation. In two patients with eyelid abnormalities, biopsy failed to reveal organisms.

Secondary glaucoma occurred in two patients, white iris nodules in one patient and a serous retinal detachment in another patient. Four patients were totally blind.

Alternate diagnoses were proposed in the initial consultation and these included squamous cell carcinoma, fibrous histiocytoma, neurofibromatosis and concomitant onchocerciasis in two patients. In two patients from India with longstanding leprosy, both with corneal leproma, AFB organisms were not seen. There were no cases of atypical mycobacteria in the review.

Histopathologically, the external ocular and adnexal manifestations included 4 indeterminate cases, 2 lepromatous cases and 1 tuberculosis case. Two long-standing cases of patients with leprosy had no AFB organisms seen on eyelid biopsy. The majority of the corneal manifestations of ocular leprosy were of the histiocytic variant appearing like a fibrous histiocytic tumor. This is best seen in Fig. 1. There was histopathologic evidence of ciliary body involvement in 8 of 25 cases with the majority presenting as granulomatous inflammation. Fig. 2A-D shows a variety of manifestations in our AFIP series.
Discussion

World prevalence rates of leprosy are 1 to 2 cases per 10,000 and the recent worldwide immigration and refugee crises warrant increased vigilance with simple monofilament skin testing. There is an association with armadillos which is the only known host of the mycobacterium and this organism is difficult to culture. Because the ocular manifestations of systemic leprosy are so devastating, we believe it is important to revisit this ancient disease.

This study was completed by analyzing the data banks and the repository at the AFIP in Washington, DC during a period of robust ocular pathology work at that institution. Although this study, similar to our work at the AFIP with ocular tuberculosis suffers foremost primarily from selection bias as a tertiary ocular pathology referral center and is dependent on the history provided by the referring physicians, it does offer ample opportunities for histopathological correlations and also provides a historical background as one of the final ocular pathology studies from that august institution. To be specific, one of the major deficiencies of this fellowship work, is that it was difficult to decipher from the referral consults based on the Ridley-Jopling classification, what clinical form, either lepromatous, tuberculoid or indeterminate the patients suffered from at consultation. Another issue was the aging of the material after fifty or sixty years of storage.

As with our work with ocular tuberculosis in which we showed that the disease process often masqueraded as retinoblastoma in two patients, squamous cell carcinoma in one and juvenile xanthogranuloma in another, ocular leprosy in our series masqueraded as neurofibromatosis, squamous cell carcinoma, fibrous histiocytoma and onchocerciasis. We also learned in our series, that squamous cell carcinoma was overlooked in one patient with ocular leprosy. We also learned that systemic involvement of the liver and kidney presented in a minority of these patients as compared to our series with ocular tuberculosis in which it was much more prevalent. Secondary glaucoma and corneal scleral perfora-

Fig. 1. Histopathological photos showing a nodular fibro-histiocytic tumour with spindle shaped cells arranged in intertwining pattern (Original magnification x4.5 in A and x15 in B Hematoxylin and eosin).
tions were present but not as common as ocular tuberculosis in our series.

It is generally agreed that there is involvement of the eye in a majority of systemically infected leprosy patients and that there is a high incidence of blindness.

As the initial AFIP intake forms did not include visual acuities and intraocular pressures and optic nerve examination findings we are unable to assess the incidence in this histopathological report. Classically, it has been thought that ocular leprosy typically involved the anterior segments of the ocular surface and anterior chamber, but work by Prendergast involving a histopathologic study showed choroidal inflammatory lesions in 15 of 28 eyes of which nine had AFB present. In our series, only three cases had posterior involvement. One presented with a serous retinal detachment, another with a chronic retinal detachment and another with choroidal and ciliary body involvement.

Recent work from taxonomic analysis of leprous skin lesions similar to previous work in patients with psoriasis from Brazil revealed considerable differences in the distribution of Proteobacteria, Bacteroidetes, Firmicutes, and Actinobacteria, with the first two phyla enriched and the other markedly diminished in the leprous lesions, when compared with healthy skin. Propionibacterium, Corynebacterium and Staphylococcus, resident and abundant in healthy skin, were underrepresented in skin from leprous lesions with the Burkholderia, Pseudomonas and Bacillus genera being over-represented which suggest that other resident subspecies may play a role in the tissue damage in the eye also.

The 2015 data from the United States National Hansen’s Disease Program was released in early 2016, which recorded 178 new cases of leprosy in 2015 with a majority of cases occurring in Florida, California, Louisiana, New York and Hawaii with the largest group identifying as Asian or Pacific Islanders. This shows an overall slight increase over the past decade in the US. In 2008, M. lepromatosis, another organism, was discovered in Mexico, mostly commonly involving internal organs and causing diffuse lepromatous leprosy and this form is endemic in Central and South America.

In summary, we present a series of ocular lesions in patients with leprosy cases from the AFIP which shows the severity of ocular involvement, the predilection of anterior segment involvement, and a large number of histopathologic indeterminate cases. We believe that the current immigrant and refugee crises and changing migration patterns warrants revisiting this ancient disease. In the future, leprosy should be considered in the differential diagnosis and further work-up should attempt to use qPCR analysis of M. leprae and M. lepromatosis and look at the prevalence of CD4+ cells in the granulomas. As Drs. Margaret and Paul Brand and coworkers have commented from their work in Nepal with both orthopaedic and ophthalmic patients, the “loss of peripheral sensation or limb dysfunction produce an obvious reduction of the quality of the patient’s life, yet is seems surprising and encouraging to see how well the individual copes, even with extreme disabilities...To the individual with insensitive extremities, blindness is disastrous and few have the resources to live with it.”

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Fig. 2. (A) Blue Arrow shows perilimbal infiltrate (Original magnification ×15 Fite Furaco). (B) Blue Arrow shows dense ciliary body infiltrate and anterior chamber infiltrate (Original magnification ×15 Fite Furaco). (C) Histopathological photo showing clusters of pinkish infiltrate within the confines of the peripheral cornea and limbus seen in (A) (Original magnification ×45 Ziehl-Neelson). (D) Histopathological higher power photo showing the infiltrate in a ciliary body specimen (Original magnification ×72 Fite Furaco). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)
Declaration of Competing Interest

Author declares that there is no conflicts of interest.

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