

Onchocerciasis among Ethiopian Immigrants in Israel

Claes D. Enk MD PhD¹, Irene Anteby MD², Nitza Abramson MD MPH⁴, Radgonde Amer MD², Yair Amit MD PhD⁶, Tamar Bergshtein-Kronhaus⁴, Evelyne Cohen C.Orth², Zalman Greenberg PhD⁵, Flory Jonas BSc¹, Shlomo Maayan MD³, Esther Marva PhD⁵, Uri Strauss MD⁶ and David BenEzra MD PhD²

Departments of ¹Dermatology, ²Ophthalmology, and ³Microbiology, Hadassah University Hospital and Hebrew University-Hadassah Medical School, Jerusalem, Israel

⁴Jerusalem District Health Office, Jerusalem, Israel

⁵Government Central Laboratories, Ministry of Health, Jerusalem, Israel

⁶Maccabi Health Services, Jerusalem District, Jerusalem, Israel

Key words: onchocerciasis, onchodermatitis, eye manifestations, Ethiopian immigrants, Israel

Abstract

Background: Onchocerciasis results from infestation by the nematode *Onchocerca volvulus*, and is characterized clinically by troublesome itching, skin lesions and eye manifestations. Since 1992, approximately 9,000 immigrants have arrived in Israel from the Kuwara province of northwest Ethiopia where the prevalence of onchocerciasis is particularly high.

Objectives: To determine whether onchocerciasis is the cause of cutaneous and ocular symptoms among recent immigrants from the Kuwara province in Ethiopia

Methods: We examined 1,200 recent immigrants from the Kuwara province residing at the Mevasseret Zion immigration center outside Jerusalem. Among them, patients with cutaneous signs suggestive of onchocerciasis underwent a skin-snip biopsy and a thorough eye examination.

Results: In the detailed skin examination performed in 83 patients, the most common skin finding was chronic papular onchodermatitis, found in more than 46 patients (55%); depigmentation and atrophy was found in 13 (15%) and 12 (14%), respectively. In 40 patients (48%), living microfilaria were detected in their skin snips. Of the 65 patients who underwent a thorough eye examination, 45 patients (66%) had ocular complaints. Corneal abnormalities were found in 55 of the 130 eyes (42%), active anterior segment intraocular inflammation and live microfilariae were found in 4 eyes (3%) and lens changes in 16 eyes (1%). Eleven eyes (9%) showed retinal or choroidal changes.

Conclusions: Skin and eye manifestations associated with onchocerciasis are prevalent among symptomatic Ethiopians who immigrated to Israel from the Kuwara province.

IMAJ 2003;5:485-488

certain locations [2]. Therefore, many cases of onchocerciasis should be expected among the recent immigrants from the more endemic areas for the disease.

Onchocerciasis results from infestation by the nematode *Onchocerca volvulus*, which is transmitted by bites from infected *Simulium* blackflies. Clinically, onchocerciasis is characterized by troublesome itching, skin lesions and eye manifestations. Skin lesions are non-specific and present as acute and chronic dermatitis, vitiligo-like hypopigmentation, atrophy, or subcutaneous nodules [3]. Onchocercal ocular disease can manifest in various ways and includes periorbital nodules, itching, erythema, photophobia, corneal scarring, anterior segment intraocular inflammation (or uveitis), glaucoma with eventual visual field loss [4], and posterior segment intraocular inflammation [5,6]. Although chronic and of low grade, the ocular infestation and intraocular inflammation induce visual impairments and can lead to manifest blindness during the second and third decades. This specific type of visual loss has been coined "river blindness." Diagnosis is usually made by superficial skin biopsies or skin snips, in which microfilariae can be seen by microscopy, or by their direct observation within the eye by slit-lamp examination.

In 1999, 1,200 recent immigrants from the Kuwara province settled in the Mevasseret Zion absorption center outside Jerusalem. On the initiative of the Maccabi Health Services, all patients with cutaneous complaints suggestive of onchocerciasis underwent skin biopsy and a thorough eye examination. Our findings are presented here.

Patients and Methods

Patients

All Ethiopian immigrants residing at the Mevasseret Zion absorption center underwent a general health examination upon their arrival in Israel, including physical examination, Mantoux, chest X-ray, and serologic tests for bacterial and viral infections. None of the immigrants was recognized to be suffering from onchocerciasis during this initial examination. Patients who subsequently complained of itching or skin rash were referred by their family physician for a dermatology consultation during the period January 2000 to August 2001. Patients with clinical skin findings suggestive of onchocerciasis were biopsied by the skin-snip method and were

For Editorial see page 522

Over 80,000 Ethiopian Jews have immigrated to Israel during the years 1985-2001. Though the vast majority of these immigrants originate from villages in the Gondar province in western Ethiopia, close to 9,000 of the most recent immigrants come from the Kuwara highland in northwest Ethiopia. In their review of the health profile of the immigrants from Gondar, Nachmias et al. [1] reported 26 cases of onchocerciasis. The prevalence of onchocerciasis varies with geographic location and appears to be particularly high around the Blue Nile Valley in northwestern Ethiopia, reaching 84% in

referred for an eye examination with the specific aim of diagnosing onchocerciasis-related eye abnormalities.

Skin snips

Superficial skin biopsies were performed by a modified skin-snip technique using a 2 mm disposable punch biopsy. The skin was rinsed with chlorhexidine and anesthetized with ethylene chloride topical spray, and the skin snip was obtained by cutting the skin parallel to the epidermal surface. Typically, eight snips were obtained from each patient (shins, femora and hips). The epidermal snips were placed on a slide in a drop of normal saline under a cover glass and examined by binocular (x 4 magnification) and microscopically. Slides in which no microfilariae were detected at the initial examination were kept at 4°C and reexamined 2 hours later. Some of the microfilariae specimens were stained with Giemsa. The species diagnosis of *O. volvulus* was based on typical morphologic characteristics including lack of sheath and nuclei in the tail.

Eye examination

Patients underwent a comprehensive ophthalmologic examination, which included best-corrected visual acuity, slit-lamp examination of the anterior segment, intraocular pressure measurements, indirect ophthalmoscopy of the fundus, and refraction. Patients with abnormal posterior segment findings underwent fluorescein angiography of the choroid and retinal vessels.

Treatment

Patients in whom *Microfilaria* was identified from the skin snips or by eye examination, as well as *Microfilaria*-negative patients with clinically convincing onchodermatitis were treated with 150 g/kg ivermectin. For immediate relief of itching, an intermediate strength steroid cream was also prescribed for local application.

Results

Skin findings

Patient profiles and skin findings are shown in Table 1. Of the 90 patients who were referred for skin-snip examination 83 underwent skin biopsy. Seven patients refused to undergo the procedure. The age range of the patients with skin symptoms compatible with onchocerciasis was 4–80 years (mean 30). The most prominent clinical skin findings were chronic papular onchodermatitis, depigmentation and atrophy. Many patients exhibited a mixed clinical picture consisting of chronic papular onchodermatitis and depigmentation. Except for atrophy, most skin lesions were limited to shins and femora; atrophy was typically located on the lower back and buttocks. Only two patients had palpable subcutaneous nodules (located on the face and scalp). Forty patients (48%) had demonstrable microfilariae by skin snip.

Ocular manifestations

We examined 130 eyes of 65 patients (25 females and 40 males, age range 5–80 years, mean 30 years). All 65 patients also had skin-snip examination. Forty-three patients (66%) had ocular complaints: ocular or periocular itching (49%), visual loss or blurred vision

(11%), ocular pain (3%), and redness (2%). Mean visual acuity was 0.8 and mean intraocular pressure 12 mmHg. Corneal abnormalities were found in 55 of the 130 eyes (42%). These included old scars (35%), subepithelial infiltrates (6%) and corneal haze (2%). Active

Table 1. Patient profiles and skin findings

No. of patients examined	83
Age (yrs)	
Mean	30
Range	4–80
Gender	
Female	44%
Male	56%
Skin findings	
Chronic papular onchodermatitis	46 (55%)
Depigmentation ("leopard skin")	13 (16%)
Atrophy	12 (14%)
Xerosis ("lizard skin")	6 (7%)
Acute papular onchodermatitis	3 (4%)
Subcutaneous nodules	2 (2%)
Lichenoid	1 (1%)
Skin snips	
Positive	40
Negative	43

Table 2. Ocular manifestations in 65 patients

No. of eyes examined	130
Age (yrs)	
Mean	30
Range	4–80
Gender	
Female	25
Male	40
Visual acuity	
Mean	0.8
SD	0.3
Intraocular pressure (mmHg)	
Mean	12.0
SD	2.3
Cornea	
Normal	75 (58%)
Stromal scars	45 (34.5%)
Subepithelial infiltrates	8 (6%)
Haze (nebulae)	2 (1.5%)
Anterior chamber	
Microfilaria & iritis	4 (3%)
Lens	
Opacities	16 (12%)
Retina	
Pigmentary or atrophic changes	11 (9%)
Optic disk	
Normal	119 (92%)
Gliosis	5 (4%)
Temporal pallor	4 (3%)
Myelinated nerve fiber layer	1 (0.75%)
Tilted	1 (0.75%)

anterior segment intraocular inflammation with cells and flare in the anterior chamber were seen in four eyes (3%) of two patients, in whom live microfilariae were observed in the aqueous humor. Lens changes were noted in 16 eyes (12%) and were compatible with age. Eleven eyes (9%) showed retinal or choroidal changes, which were mostly atrophic old scars or pigmentary changes. No signs of active choroiditis were detected. The optic nerve heads were within normal limits in 119 eyes (92%). The 8% of optic nerve anomalies included temporal pallor of the nerve head in 4 eyes (3%), gliosis in 5 eyes (4%), and myelinated nerve fibers and tilted disk in 1 eye each (<1%).

Discussion

Ninety patients fit the criteria for inclusion in this study, but 7 did not undergo evaluation and were excluded. The most common skin finding was chronic papular onchodermatitis, found in more than 46 patients (55%), while depigmentation and atrophy were found in less than 15% and 14% of the patients, respectively. These findings are in agreement with those reported by Hagan [7] in an endemic population in Sudan. It is important to note, however, that many of our patients presented with a mixed clinical picture but were categorized according to the most prominent skin manifestation. The mean age was 30 years, but children as young as 4 years were also affected.

Among patients with clinical findings compatible with onchocerciasis, skin snips were positive in only 40 patients (48%). Skin-snip examination, which is the classic method of determining the prevalence of onchocercal infestation [8], is highly specific but has a low sensitivity in latent or early disease with a light microfilarial load [9]. Alternative diagnostic procedures include immunodiagnosis, which has been made possible by the development of various recombinant filarial antigens [10], and molecular techniques based on the polymerase chain reaction using *O. volvulus*-specific DNA probes [11]. However, these newer techniques have not yet been standardized.

It is important to note that our study was not designed as a survey of prevalence. Therefore, the number of onchocerciasis patients among Ethiopian immigrants from Kuwara province cannot be accurately assessed. Skin-snip positivity ranges between 20 and 83% in endemic areas of northwest and southwest Ethiopia [12,13]. By extrapolation, among the 9,000 newly arrived immigrants to Israel from the Kuwara province, the number of onchocerciasis-affected patients can be estimated at approximately 2,000–7,000 individuals.

The most important epidemiologic and population health aspect of onchocerciasis is the ocular affection. Forty-two percent of the eyes examined demonstrated corneal pathologies. Most pathologies were mild and superficial, with only 11% of patients suffering variable degrees of functional loss of vision. It is difficult to accurately assess the role of onchocerca infestation in the creation of these pathologies, though their characteristic appearance is suggestive of this fact. Anterior uveitis, keratitis, trabeculitis and secondary glaucoma are the most common and more prevalent ocular affections associated with onchocerca and are the main causes for the loss of vision in onchocerciasis. No specific posterior

segment involvement was observed in our cohort of patients, which concurs with previous observations performed in other endemic areas [5]. In the past, parasitic skin involvement and the formation of nodules around the orbits were associated with a higher incidence of ocular affection [5]. In our group of patients in the present study, none had parasitic nodules around the orbits, although a large percentage harbored typical ocular (mostly corneal) lesions. Furthermore, the two patients demonstrating live microfilariae in the anterior chambers of both eyes had no detectable nodules around the orbits and had negative skin biopsies. It is possible that the ocular morbidity in our group of patients is less than expected due to their higher level of skin hygiene, the relative young age of most patients, and potential immigration selection biases.

Repeated doses of ivermectin, 150 µg/kg, constitute the optimal regimen both in terms of microfilaricidal activity [14] and the reconstitution of cellular antifilarial immune response [15]. However, because current treatment protocols relate to patients who live in endemic areas, the optimal dose intervals and the duration of treatment to prevent disease relapse for patients living in non-endemic areas such as Israel remain to be established. Prophylactic antiparasitic treatment might minimize the potential for eventual development of additional ocular complications among this group of patients. Therefore, a careful clinical follow-up of these immigrants is imperative and should be carried out.

More than 10 different species of *Simulium* blackflies have been described in Israel [16]. While none of these species has been shown to transmit *O. volvulus*, their potential to serve as vectors remains open. This factor should be taken into consideration when deciding on appropriate measures for controlling the disease in the Israeli population.

Israeli physicians have no experience in recognizing the subtle clinical symptoms of onchocerciasis or in performing the skin-snip examination. This might be the reason why none of our patients was recognized as suffering from onchocerciasis at the initial examination upon their arrival to Israel. The presence of a substantial number of non-diagnosed onchocerciasis patients among Ethiopian immigrants scattered around the country must be assumed. Therefore, the creation of appropriate training programs for a broad group of Israeli health providers geared at performing the relevant diagnostic procedures and providing appropriate treatment and follow-up appears justified.

References

1. Nachmias J, Greenberg Z, Berger SA, et al. Health profile of Ethiopian immigrants in Israel: an overview. *Isr J Med Sci* 1993;29:338–43.
2. Gundersen SG, Schmitt-Lechner A, Bjorvatn B. Onchocerciasis in the Blue Valley of western Ethiopia. *Trans R Soc Trop Med Hyg* 1988;82:122–7.
3. Murdoch ME, Hay RI, Mackenzie CD, et al. A clinical classification and grading system of the cutaneous changes in onchocerciasis. *Br J Dermatol* 1993;129:260–9.
4. BenEzra D. Parasitic ocular infections. In: BenEzra D, Ohno S, Secchi A, Alio J, eds. *Anterior Segment Intraocular Inflammation Guidelines*. London: Martin Dunitz, 2000:75–83.
5. BenEzra D. Diseases of the choroids and anterior uvea. In: Michaelson I.C, ed. *Michaelson's Textbook of the Fundus of the Eye*. 3rd edn. Birmingham: Livingstone, 1980:667–712.

Original Articles

6. Forrester J, Okada A, BenEzra D, Ohno S, eds. Posterior Segment Intraocular Inflammation Guidelines. The Hague: Kugler Publications, 1998:53–5.
 7. Hagan M. Onchocercal dermatitis: clinical impact. *Ann Trop Med Parasitol* 1998;92:S85–96.
 8. WHO Expert Committee on Onchocerciasis. Third Report. Technical Report Series. Geneva: World Health Organization, 1987;152:1–167.
 9. Boatin BA, Toe L, Alley ES, Dembele N. Diagnostics in onchocerciasis: future challenges. *Ann Trop Med Parasitol* 1998;92:S41–5.
 10. Ramachandran CP. Improved immunodiagnostic tests to monitor onchocerciasis control programmes – a multicenter effort. *Parasitol Today* 1993;9:76–9.
 11. Zimmerman PA, Guderian RH, Aruajo E, Elson L, Kubofcik J, Nutman TB. PCR-based diagnosis of *O. volvulus* infection: improved detection of patients with onchocerciasis. *J Infect Dis* 1994;169:686–9.
 12. Zein AZ. The epidemiology of onchocerciasis in northwestern Ethiopia. *Trop Geogr Med* 1986;38:33–7.
 13. Wokneh W, Fletcher M, Olwit GG. Onchocerciasis in field workers at Baya Farm, Teppi Coffee Plantation project, southwestern Ethiopia: prevalence and impact on productivity. *Acta Trop* 1993;54:89–97.
 14. Schulz-Key L, Soboslay PT, Hoffmann WH. Ivermectin facilitated immunity. *Immunol Today* 1992;8:152.
 15. Steel C, Lujan-Trangay A, Gonzales-Peralta C, Zea-Flores G, Nutman TB. Immunologic responses to repeated ivermectin treatment in patients with onchocerciasis. *J Invest Dermatol* 1991;168:581–8.
 16. Friedberg A. Zoogeography of the diptera of Israel. In: Yom-Tov Y, Tchernov E, eds. The Zoogeography of Israel. Dordrecht: Dr. W. Junk Publishers, 1988:277–307.
-

Correspondence: Dr. C.D. Enk, Dept. of Dermatology, Hadassah University Hospital, P.O. Box 12000, Jerusalem 91120, Israel.
Phone: (972-2) 677-7111
Fax: (972-2) 671-3637
email: enk@hadassah.org.il