19

A 40-Year-Old Man from Togo With Subcutaneous Nodules and Corneal Opacities

GUIDO KLUXEN

Clinical Presentation

History

A 40-year-old man from Togo presents to a local clinic. He has noticed changes in both of his eyes over the past 4 years. There are no visual disturbances, but he is worried: In his village there are adults in each family who have turned completely blind after their eyes had shown features very similar to the changes he has noticed in his own eyes.

He has also observed some painless bumps under his skin which have developed over the past two decades. The patient also complains of suffering from intense itching of his skin that keeps him awake at night.

The patient has always lived in a village in the savannah near a fast-flowing river. He reports that small biting flies are common near the river.

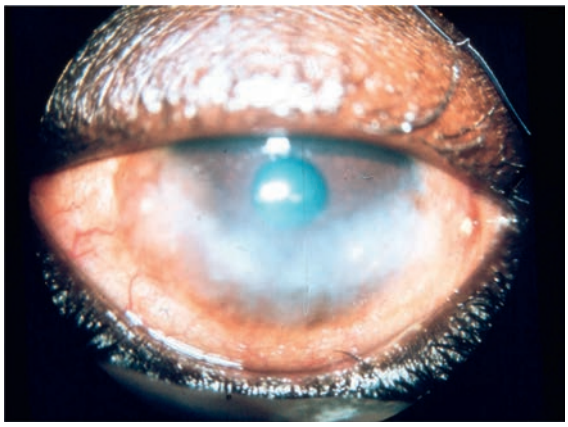
Clinical Findings

There are opacities in the cornea of both eyes. The patient's left eye is shown in Figure 19.1.

The skin appears atrophic in some areas (thinning with loss of elasticity), and there are multiple scratch marks. Subcutaneous nodules are palpable in various regions of his body, especially over bony prominences like the ribs (Fig. 19.2), iliac crest, femoral trochanters and on the head. The nodules are firm, non-tender and measure 1 to 3 cm in diameter.

Questions

1. What is your most important differential diagnosis?
2. What investigations would you like to carry out?



• **Fig. 19.1** The patient's left eye showing corneal opacities. (Courtesy H. Trojan)

• **Fig. 19.2** Subcutaneous nodule over the costal arch. (Courtesy H. Trojan)

Discussion

The patient presents with a triad of corneal opacities, skin changes and subcutaneous nodules. He comes from a village in the North of Togo, located close to a rapidly flowing river. Many adults in the village are blind.

Answer to Question 1

What is Your Most Important Differential Diagnosis?

The clinical triad of ocular changes, itchy dermatitis with atrophy of the skin and subcutaneous nodules in a patient from rural Togo makes onchocerciasis (river blindness) the most likely differential diagnosis. A fast-flowing river is the preferred breeding site for *Simulium* blackflies, which transmit the disease.

The picture of his left eye shows keratitis semilunaris, a form of band-shaped sclerosing keratopathy commonly seen in onchocerciasis. The central and upper parts of the cornea are initially clear, but may become affected as the disease progresses.

Subcutaneous nodules can resemble lipomas and cysticerci of *Taenia solium.*

Pruritic dermatitis may also be caused by scabies or be seen in papular pruritic eruptions associated with HIV infection. In patients from West Africa, infection with *Mansonella streptocerca* can also cause pruritus. Chronic dermatitis can also be seen in yaws, leprosy, mycotic infections and eczema.

Answer to Question 2

What Investigations Would You Like to Carry Out?

The patient's presentation appears very typical for onchocerciasis. In an endemic, resource-limited setting his diagnosis would most probably be made on clinical grounds alone. Skin snips taken from the vicinity of a subcutaneous nodule may show microfilariae of *Onchocerca volvulus.*

Slit-lamp examination of the eyes may reveal microfilariae in the anterior chamber of the eye and in the cornea. Nodulectomy of subcutaneous nodules may show adults of *O.* volvulus, but this is not routinely done.

Serological tests were less useful in patients from endemic areas in the past, because antibody test results lacked specificity and were not clearly linked to clinical disease.

However, serological tests which detect IgG4 responses to *O. volvulus* antigen (OvAg) and the recombinant Ov16 antigen are recommended by WHO. In case of a positive result it is recommended to continue ivermectin therapy.

The lifespan of the adult worms is about 12 years. After 10 years, usually no further treatment with ivermectin is required after therapy with a combination of ivermectin and doxycycline, if ivermectin was administered 2 to 3 times every year and if serological tests have turned negative. However, in onchocerciasis-endemic areas new infections are possible. To calculate the probability of a reinfection through an individual black fly with *O. volvulus,* worm-specific DNA (Ov150) is tested by poolscreen in vector samples (black flies) using polymerase chain reaction.

The Case Continued…

The patient was treated with ivermectin (150 μg/kg) STAT which was repeated after 3 months and after 1 year. He also received doxycycline 100 mg/d for 6 weeks (see Summary Box).

SUMMARY BOX

Onchocerciasis

Onchocerciasis ('river blindness') is caused by *O. volvulus,* a filarial nematode. It is transmitted by biting *Simulium* species blackflies, which breed in rapidly flowing freshwater. Adult females of *O. volvulus* lodge in human subcutaneous tissue and shed live microfilariae. Microfilariae migrate through the skin and often into the eyes. Most pathology is caused by immune reactions to dead and dying microfilariae and perhaps to their endosymbiotic *Wolbachia* bacteria. Typical clinical features of onchocerciasis are:

1. Non-tender subcutaneous nodules located mainly over bony prominences
2. Dermatitis, depigmentation of the skin ('leopard skin'), lichenification and thickening of the skin ('lizard skin'), and skin atrophy at times leading to 'hanging groins'. The skin changes may be stigmatizing and the unrelenting itch may cause sleep disturbances, depression and even lead to suicide
3. Ocular changes may present as pear-shaped pupil, punctate subepithelial stromal keratopathy, sclerosing keratitis, iritis, uveitis, 'flecked retina' or scarred choroidoretinal fundus (Hissette–Ridley fundus). Optic nerve atrophy may occur.

Ivermectin is now the drug of choice for individual and mass treatment of onchocerciasis. Ivermectin kills microfilariae but has little effect on adult worms apart from reducing embryogenesis. It has to be given repeatedly throughout the lifespan of the adult worm (10–14 years). For individual treatment, ivermectin is provided as a single dose of 150 μg/kg PO. Treatment should be repeated in 3- to 6-month intervals. In mass treatment programmes it is usually provided annually. Ivermectin should not be given to patients with heavy *Loa loa* infections and microfilarial counts greater than 30,000/mL, because this may result in fatal encephalitis. Ivermectin can also cause significant adverse events in patients with lower microfilarial counts. For regions co-endemic of onchocerciasis and *L. loa*, a mobile phone-based, point-of-care microscopy tool – the LoaScope – has proven helpful to easily identify patients with high parasitaemia of *L. loa* and to exempt them from mass treatment with ivermectin. This technology has increased the acceptance of ivermectin MDA for onchocerciasis and lymphatic filariasis in *L. loa* co-endemic areas.

Ivermectin is contraindicated in pregnancy and in children below the age of five or below a height of 90 cm.

Doxycycline at a dosage of 100 to 200 mg/d for 4 to 6 weeks kills the *Wolbachia* endosymbionts, permanently sterilizes adult worms, blocks embryogenesis and slowly kills approximately 60% of adult worms.

A major breakthrough in the battle against onchocerciasis was the ivermectin-donation programme initiated by the producing company Merck. Large control programmes implementing mass drug administration (MDA) of ivermectin in endemic areas in Africa and South America lead to interruption of transmission of onchocerciasis in many countries.

Elimination of the disease is still on the agenda.

Further Reading

1. Simonsen P, Fischer PU, Hoerauf A, et al. The filariases. In: Farrar J, editor. Manson's Tropical Diseases. 23rd ed. London: Elsevier; 2013 [chapter 54].
2. D'Ambrosio MV, Bakalar M, Bennuru S, et al. Point-of-care quantification of blood-borne filarial parasites with a mobile phone microscope. Sci Transl Med 2015;7(286):1–10.
3. Cantey PT, Roy SL, Boakye D, Mwingira U, Ottesen EA, Hopkins AD, Sodahlon YK. Transitioning from river blindness control to elimination: steps towards stopping treatment. Int Health 2018;10:i7–i13. https://doi.org/10.1093/inthealth/ihx049.
4. WHO. 2017 Onchocerciasis guidelines for stopping mass drug administration and verifying the elimination of human onchocerciasis, Available from: http://apps.who.int/iris/bitstream/handle/10665/204180/9789241510011_eng.pdf?sequence=1.
5. Lawrence J, Sodahlon YK. Onchocerciasis: the beginning of the end. Int Health 2018;10:i1–i2. https://doi.org/10.1093/inthealth/ihx070.