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Tick inoculation in an eyelid region: report on five cases with one complication of the orbital myositis associated with Lyme borreliosis

Wszczepienie kleszcza w rejonie powieki oka – przedstawienie pięciu przypadków z komplikacją w postaci zapalenia mięśnia ocznego spowodowanego boreliozą

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Summary: Purpose: To determine the frequency and dependence of Lyme borreliosis after tick infestation in the eyelid region.
Material and methods: Five patients after tick inoculation were investigated by immunofluorescence assays for IgM and IgG antibodies to Borrelia burgdorferi. One positive test was followed with an enzyme immunoassay and immunoblot (a two step system). Ophthalmologic evaluation of myositis was supported with MRI, laboratory, and internal clinical investigations.
Results: Four children showed negative Borrelia serology after a bite from a tick. In one case the left abducens nerve palsy was found, which was diagnosed in MRI as a thickened left lateral rectus muscle. The diagnosis of myositis with positive Borrelia burgdorferi serology was consistent with Lyme borreliosis. Other laboratory examinations were negative. The symptoms were reduced after treatment with ceftriaxon.
Conclusions: Lyme borreliosis was found in one in five patients after tick infestation in the eyelid region. Antibiotic prophylaxis against Lyme borreliosis with ampicillin is recommended for children after a tick bite.

Słowa kluczowe: kleszcz, powieka oka, borelioza, zapalenie mięśnia ocznego.
Key words: tick, eye-lid, Borreliosis, ocular myositis.

The incidence of Lyme borreliosis (Lyme disease) in Niedersachsen is estimated to be 0,5 per 1000 cases of people bitten by ticks (1). 18 cases of serologically confirmed Lyme borreliosis in second and third stages of the disease, with different ophthalmic and neurological symptoms, have been registered in our clinic since 1988 (2,3,4). The transfer of Borrelia burgdorferi (Bb) to the mammalian host is transmitted mostly by ticks (in Europe through Ixodes ricinus). However, a few hour survival of Bb was found in other biting insects, like for example, mosquitos and flies (1). According to Liebisch (5), tick bites in head of animals are concentrated in the regions around ears and eyes. Our data for humans is in agreement with this observation. Here we describe five patients that were bitten by ticks in the eyelid area. We also address the question: how often and when these bites lead to the infection with Bb in eyelids?

Material and methods

We have treated 5 patients from tick bite in eyelid area since 1989. Four of them were children of between 3 to 10 year-old. After application of the local anesthetic ointment with 2,5% lidocain and 2,5% prilocain (Emla Astra® Zeneca), ticks were removed. In case 3 the head of a tick was removed with a sterile needle. Case 5 comprised a 78 year-old man, who removed a big tick by himself and we removed the holdover of the head. All children took the prophylactic treatment for three weeks after the tick bite with antibiotics: amoxicillin 50 mg/kg weight/per day. Serological tests for Borrelia burgdorferi with the immunofluorescence assay (IFA) for IgM (1:48 normal titer range) and IgG antibodies (1:32 normal titer range), were carried out for cases 1-3 one and six months after tick bites. In cases 4 and 5, an additional, more sensitive and specific enzyme immunoassay (EIA) for Borreliosis (with a normal titer range for the IgG antibody at 1:160) was also carried out. We have used a "two step system" (6) that included EIA and immunoblot for IgG antibody (positive by recognition minimum of two of five proteins 20, 24, 35, 39, 88 kDa) in the positive EIA test in case 5. All immunological investigations were carried out in the same laboratory in Bremen (6). Standard ophthalmological tests were performed for all patients. Additionally, an MRI, internal, neurological examinations, and a Hess screen investigation for paretic strabismus were carried out for patient 5, with the diagnosed orbital myositis. This patient was cured after the daily intrave-

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nous 2 g ceftriaxon (Rocephin®, Roche) for 3 weeks and with 60 mg prednison/day for a week.

of the IgG antibody for Bb was negative in the EIA test after 6 months.

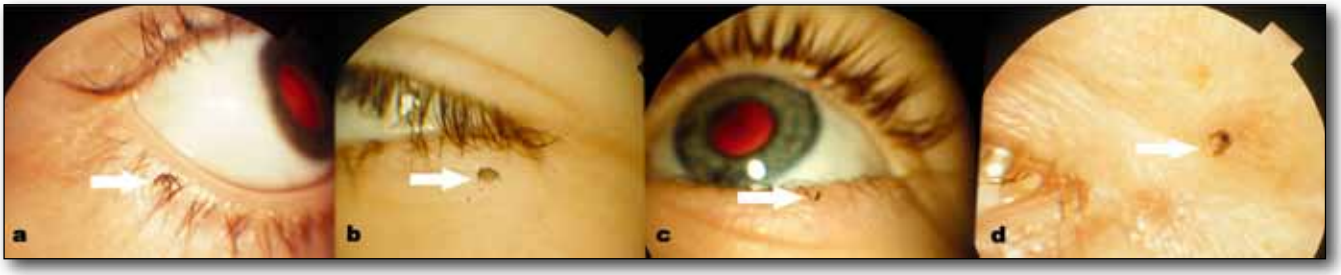

Fig. 1a,b,c,d. Tick infestation in four children in the eyelid region. In case 3 (1c) only a head of a tick was present. In case 4 (1d) a slightly inflammatory reaction was seen around the tick bite

Ryc. 1a,b,c,d. Kleszcze wszczepione w rejonie powiek ocznych u 4 dzieci. W przypadku 3 (1c) pozostała tylko głowa po usunięciu kleszcza. W przypadku 4 (1d) widoczne są zmiany zapalne skóry wokół kleszcza.

Results

Fig. 1 shows all cases of tick bites in children. In three cases (1a, b, c) the tick was localized in the lower lid close to eyelashes. None of these children developed the erythema migrans, typical for the Bb infection. In case 4, of a 7 year-old boy, the tick was situated in the temporal lid angle (1d). We noticed the beginning of an inflammatory reaction. Serological investigation

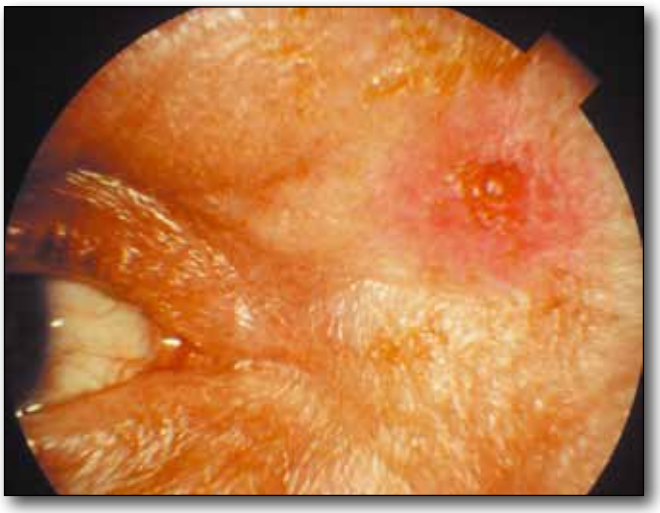

Fig. 2. Heavy local inflammation after a tick removal in the nasal lid angle in a 78 year-old patient (case 5).

Ryc. 2. Odczyn zapalny z rumieniem po usunięciu kleszcza w nosowym kacie powiek u 78-letniego pacjenta (przypadek 5).

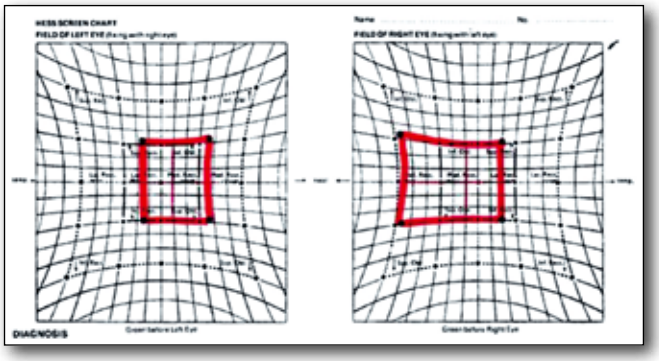

Fig. 3. The Hess screen chart of patient 5 with orbital myositis.

Ryc. 3. Wynik badania na ekranie Hessa u pacjenta z zapaleniem mięśnia ocznego (przypadek 5).

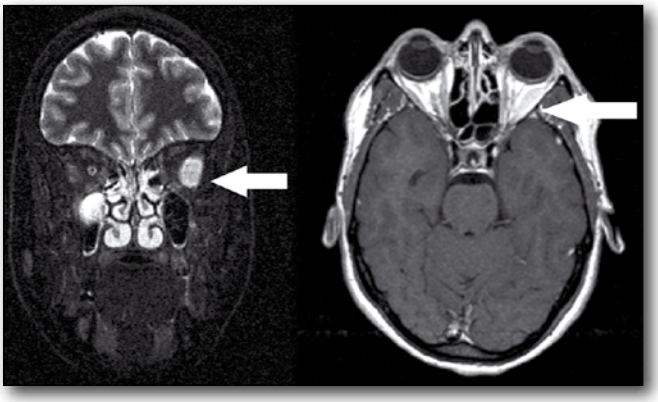

Fig. 4. Vertical and horizontal MRI from patient 5 with orbital myositis.

Ryc. 4. Wertykalny i horyzontalny obraz MRT w przypadku 5.

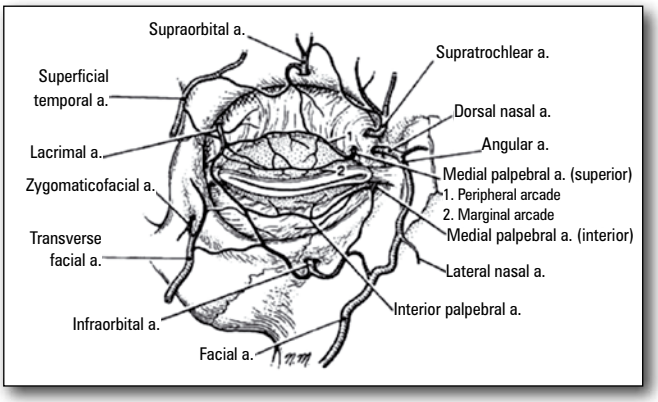

Fig. 5. The vascular supply of an eyelid in man (from Bergin and McCord).

Ryc. 5. Naczynia krwionośne powiek ocznych u człowieka (Bergin i McCord).

Fig. 6a,b. Visible superficial blood vessels in elderly patients with blepharitis.

Ryc. 6a,b. Widoczne powierzchowne naczynia krwionośne u starszych pacjentów z zapaleniem brzegu powiek.

Case	Age	IFA IgM	IFA IgG	EIA IgG	Immunoblot IgG	Other Tests
1	10	1:6	1:8	–	–	–
2	3	Negative	1:4	–	–	–
3	4	1:12	1:4	–	–	–
4	7	1:12	1:16	1:20	–	–
5	78	1:384	1:1024	1:5120	Positive: 20 – reactive 24 – reactive 35 – reactive 39 –non reactive 88 – reactive	ANA 1:20 (neg.) ACE 10U/l (neg.) ANCA 1:20 (neg.) RF 10 in/ml (neg.)

Tab. I. Borrelia serology.
Tab. I. Odczyny serologiczne w boreliozie.

Abbreviations:

IFA: Immunoflurescence Assay, EIA: Enzyme Immuno Essay, ANA: Antinuclear Antibody, ACE: Angiotensin Converting Enzyme, ANCA: Antineutrophil Cytoplasm Antibody, RF: Rheumatoid Factor

Case 5, with a serologically confirmed Lyme disease, had a tick bite in the right upper nasal lid angle area with relatively severe local inflammation (Fig. 2). The patient agreed to a local treatment with the kanamycin ointment therapy, but refused any oral or intravenous antibiosis. Serological tests for the Bb infection showed the IgM concentration at 1:384 and IgG at 1:64 in IFA after 1 month, and therefore the suspected Bb infection was diagnosed. Double vision and pain in the left orbit was observed after four months. Neuro-ophthalmologically, the left abducens nerve palsy was diagnosed and the B-scan orbital ultrasonography was carried out. The Hess screen chart showed a palsy of the left abducens nerve, with typical enlargement of polygon of the right eye and shortened of the left eye from the temporal side (Fig. 3). Internal investigations with diverse laboratory tests did not find any autoimmune conditions (lupus erythematosus, sarcoidosis, and rheumatoid arthritis), any intestinal disorders (inflammatory bowel diseases) or virus infection (herpes zoster). The patient suffered from hypertension and the coronary heart disease. He used two drugs long-term: 100 mg/daily acetyl salicylic acid (Aspirin®, Bayer) and 30 mg/daily (3 pills) nifedipin (Nifehexal®, Hexal). There was a diagnostic dilemma because of an immense enlargement of the left external muscle. Our suspicion of myositis was checked with the MRI. A homogenous thickening, approximately 11x14 mm diameter and 2,2 cm length, was found in the lateral rectus muscle, without any cerebral insult (Fig. 4 and 5). Since a muscle tumor, e.g. sarcoma, was unlikely to happen at the age of the patient, the diagnosis of myositis seems to be relatively sure. The Borrelia serology supported this diagnosis and showed the high IgG concentration in EIA (1:5120) and a positive IgG immunoblot (four of five proteins) 4 months after the tick bite (Tab. I). The therapy with prednison and ceftriaxon was started. Reduction of diplopia was noticed after 2 weeks and all symptoms were reduced after 2 months. The control MRI after 3 months was negative. The patient was without any ophthalmological symptoms in a follow-up, for more than one year.

Discussion

One in five ticks transmitted Bb in our clinical study, which gave 20% probability of infection after a bite by a tick. The data on ticks in Germany give different percentage of Bb in ticks, which is dependent on vegetation (5). The lowest (12%) was found in north Germany (Niedersachsen), the highest (25%) in south Germany (Bayern). Interestingly Bb was found in 97 % in the spittle of Ixodes pacificus, an American species of ticks (5).

A tick bite in the eyelid area appeared frequently in children and old disabled patients in our study. Apparently, thin skin and rich vascular supply are the factors leading to tick infestation in this region (Fig. 6). The best support for our hypothesis could be found in elderly patients with atrophic blepharitis (Fig. 7a, b), with visible vessels through the thinning skin. A few case reports on tick infestation in the eye area have been already published (7), but only this work demonstrates a series of such patients, with one case of ocular myositis, which is a relatively seldom ophthalmologic complication of Borreliosis.

If approximately 12% of ticks in the north part of Germany are infected with Bb (5), prophylactic antibiosis after each tick bite seems to be exaggerated. On the other hand, we should be aware that our serological methods for Borreliosis with the "two-step system" gave specificity between 90-92% (6). It has been shown that Bb could change its surface antigenic expression and can be alive and pass through the cellular immunity (8). Therefore, children should complete an antibiotic therapy with ampicillin, which is efficient for Borreliosis (Tab. II) and has minimal toxicity (9,10). As we have seen in Case 4 small, beginning erythema was noticed around an infested tick. After the removal of a thick, and completion of ampicillin therapy, local inflammation disappeared, and the IgM IFA test was negative and stayed negative for at least 6 months. It should be pointed out that an early increase of IgM antibodies by Borreliosis cannot be positively interpreted without clinical symptomatics, and only IgG antibodies have an increased specificity (1). According to new approach for treatment of Borreliosis in children, the best results will be reached only in an early, localized stage

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Antibiotic	MHK (mg/l)	
	MHK-Bereich	MHK 90
Penicilin G	0.50-0.8	4.0
Oxacilin	0.25-2.0	1.0
Amoxycilin	0.25-1.0	0.5
Mezlocillin	0.25-1.0	0.5
Ceftriaxon	0.03-0.25	0.06
Cefotaxim	0.06-0.25	0.12
Ceftazidim	0.12-0.25	0.12
Cefmenoxim	0.03-0.25	0.12
Cefuroxim	0.12-0.50	0.25
Cefixim	0.12-0.5	0.25
Cefaclor	0.50-16	6.0
Cefadroxil	1.0-64	32
Azithromycin	0.015-0.03	0.015
Clarithromycin	0.015-0.06	0.015
Erythromycin	0.30-0.12	0.06
Roxithromycin	0.015-0.12	0.03
Tetracyclin-HCl	0,25-2.0	1.0
Doxycyclin	0.12-1.0	0.5
Minocyclin	0.12-1.0	0.5
Ciplofloxacin	1.0-4.0	2.0
Ofloxacin	2.0-8.0	4.0
Lincomycin	0.25-1.0	0.5
Imipenem	0.06-1.0	0.25
Chloramphenicol	1.0-4.0	2.0
Cotrimoxazol		>1024
Vancomycin	0.5-8.0	4.0
Aminoglykoside		>32-128
Tuberkulostatika		>2>32

Tab. II. Antibiotic therapy which is efficient for Borreliosis (Preac-Mursic V., 1992).
Tab. II. Wykaz chemioterapeutyków skutecznych w leczeniu Boreliozy (Preac-Mursic V, 1992).

of erythema migrans in which antibiotics help the local cellular immunity to destroy the bacterium (9). Doxycycline will be chosen for this reason for adults, but amoxicillin will be preferred in young children (9). An interesting question is: for how many hours the Bb from the infectious tick is found in the skin? In experimental animals it takes normally 72 hours after a bite, and not earlier than 2 hours (11). Therefore it seems to be important to remove the tick as soon as possible.

The removed tick can be checked for evidence of Bb (11). For this reason only alive tick should be sent to a parasitic laboratory in a veterinary medicine school (11). Among diagnostic tests for Borreliosis some of them (IFA) are used for prime screening. More sensitive EIA has specificity at 90% and the best of these diagnostic sera reached 100% (Vidas®, bioMerieux)(7). But the specificity of EIA should be proved with the immunoblot test, the so-called "two step system" of serological diagnosis (6). Since these special diagnostic tests are expensive, they should be used only for controls during the course of the disease. The diagnostic problems of Borreliosis are connected with particularly interesting serologic identity of Borrelia burgorferi (Bb). From approximately 150 lipoprotein genes of Bb, some of them protect the bacterium from directly interacting with the environment such as temperature, chemicals, e.g. antibiotics (8). The migration of Bb from first mammalian host (e.g. mice) through a tick to a second mammalian host (e.g. man) creates something like a "life cycle" in which the bacterium undergoes modifications (8). These changes in the population of Bb produce different antigenic expressions and are responsible for persistence of Borreliosis, despite active immune responses against the bacterium. Interestingly, cellular immunity is activated only in the skin by development of erythema migrans; afterwards Bb will be attacked mostly through the humoral immunity. The survival of Bb during persistent infection is possible only through the permanent antigenic adaptation. This feature of Bb is responsible for immense problems in active immunization.

Paretic strabismus with diplopia as a complication of an immunologically assured neuroborreliosis was already described (3,4). Ocular myositis as a sequel of Borreliosis was however found seldom (12,13,14). Only in two publications was the diagnosis confirmed serologically (12,13). A firm proof of a direct involvement of Bb in myositis can be only achieved through the demonstration of the bacterium in the muscle. The evidence of Bb in the muscle biopsy specimens in patients with serologically proven Borreliosis was described by Reimers (14). Visualization of Bb in muscles supports the necessity of a therapeutic use of prednison to achieve the reduction of local inflammatory symptoms (12).

As already shown by us in 1993, the diagnosis of Borreliosis should be established by:

1. Positive specific immunoassays for Bb,
2. Prompt improvement of disease after antibiosis,
3. The absence of an alternative cause of ocular disease after extensive investigation,
4. Endemic exposition (3).

Many clinical reports unfortunately do not conform to this protocol (6), and therefore overdiagnosis of Borreliosis has been reported. A very wide spectrum of ophthalmologic manifestations of Borreliosis is based on many of case reports (2,3,4,12,15,16). Each clinical group has gathered many cases of well-documented Borreliosis, and these clinical studies can extend our diagnostic and therapeutic view of the disease. An example of such a clinical study can be a proof of our suggestion in the case report study that the birdshot retinochoroidopathie may be associated with the serologically confirmed Borreliosis (3). Statistical analysis in 11 cases by Suttorp-Schulten et al. showed Borreliosis in two patients has not confirmed this

interesting hypothesis (17). We should be aware that Borreliosis, as many multisystemic diseases, is responsible for many generic symptoms, and only the best specificity can lead to an ambiguous diagnosis. Thus the best approach and scientific efforts are concentrating today on immunology of the Bb.

Conclusions

Tick infestation in the eyelid region is found mostly in children, and the tick should be removed as soon as possible. While the response of the cellular immunity system (erythema migrans) to Bb is manifested after few days till weeks, we feel that an appropriate antibiotic prophylaxis should be undertaken, before specific IgG antibodies will be found in 3 or more months.

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