




A Patient-Centered Approach to Vernal Keratoconjunctivitis (VKC): A Podcast

Ann Cathrine Larsen · Marie Louise Roed Rasmussen 

Received: October 13, 2023 / Accepted: February 15, 2024 / Published online: March 4, 2024
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ABSTRACT

Vernal keratoconjunctivitis (VKC) is a rare yet severe form of allergic conjunctivitis predominantly affecting children, mainly boys, with a global prevalence and a higher incidence in certain geographical regions. The disease is characterized by seasonal exacerbations. VKC presents with ocular surface inflammation leading to various distressing symptoms such as itching, redness, mucous discharge, and pain. The disease primarily manifests bilaterally, though it may initially appear unilaterally. If left untreated, VKC can result in corneal complications, including shield ulcers and vision impairment, affecting daily activities and psychosocial well-being, especially in children. The diagnosis of VKC involves identifying key clinical findings on the ocular surface such as Tranta dots, giant papillae, or shield ulcers.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s40123-024-00909-y>.

A. C. Larsen · M. L. R. Rasmussen (✉)
Department of Ophthalmology, Rigshospitalet-Glostrup, University Hospital Rigshospitalet, Valdemar Hansens vej 1-23, 2600 Glostrup, Denmark
e-mail: marie.louise.roed.rasmussen@regionh.dk

M. L. R. Rasmussen
Department of Clinical Medicine, University of Copenhagen, 2100 Copenhagen, Denmark

Management follows a stepwise approach, including anti-allergic eye drops, steroid eye drops, and topical medications like cyclosporine, which may take up to 3 months to show efficacy. Allergic sensitization, often to inhaled allergens like pollen and house dust mites, is associated with VKC in half of the cases. Understanding and managing these allergies through measures such as avoidance, sensitization control, and co-treatment of associated conditions like asthma and rhinoconjunctivitis are essential in VKC management. Atopic keratoconjunctivitis (AKC), a related condition associated with atopic dermatitis and asthma, shares similarities with VKC but typically affects young adults. However, there is an observed spectrum between the two diseases, indicating similar treatment strategies for both. VKC treatment requires a patient-centered approach, involving informed and supported parents, considering economic factors due to costly eye drops, and ensuring accessibility and practicality of treatment, especially in children. A multidisciplinary team collaboration, including ophthalmologists, pediatricians, and dermatologists, optimizes patient care. The rewarding aspect of VKC treatment lies in witnessing children regain their quality of life, overcome vision challenges, and thrive in their daily activities. In conclusion, understanding VKC, its associated allergies, and employing a comprehensive, patient-centered approach are crucial in managing this challenging condition,

particularly in children, to enhance their vision and overall well-being.

Keywords: Vernal keratoconjunctivitis; Pediatric ophthalmology; Shield ulcers; Giant papillae; Stepwise therapy

Key Summary Points

Vernal keratoconjunctivitis (VKC) is a severe conjunctival and corneal disease in mainly children and young people.

Untreated VKC has a severe impact on the patient's quality of life.

VKC treatment follows a stepwise approach, considering medicine availability and price.

With timely and sufficient treatment, it is a disease where you as a doctor are able to transform a life.

DIGITAL FEATURES

This article is published with digital features, including podcast audio, to facilitate understanding of the article. To view digital features for this article, go to <https://doi.org/10.6084/m9.figshare.25189493>.

TRANSCRIPT

ACL: Hello and welcome to the *Ophthalmology and Therapy* podcast on vernal keratoconjunctivitis a patient-centered approach. My name is Ann Cathrine Larsen. I'm a consultant at the department of ophthalmology at University Hospital Rigshospitalet, in Copenhagen, Denmark. I'm joined by Marie Louise Roed Rasmussen. She's an associate professor and senior consultant at the department of ophthalmology, Rigshospitalet, also Copenhagen, Denmark.

MLRR: Hello.

ACL: Today we'll be discussing vernal keratoconjunctivitis in children. We will discuss briefly what type of eye disease this is, how it affects daily living, how to treat it with a patient-centered approach. To start, what is vernal keratoconjunctivitis and especially who is affected by this disease?

MLRR: Vernal keratoconjunctivitis is a rare but severe form of allergic conjunctivitis that affects mainly children. Eighty percent of the kids have a debut before the age of ten, mostly in the 3- to 6-year-old period and it's a disease that mainly affects boys. Boys are affected three to four times more often than girls. We see vernal keratoconjunctivitis globally, but it's most commonly observed in the Mediterranean region, the Middle East, Africa, Central America, the Indian subcontinent, and less frequently in northern Europe, North America, and Australia. We know that vernal keratoconjunctivitis is more prevalent in patients with a family history of atopy, but an actual genetic component has not been identified [1–7].

ACL: What does vernal mean?

MLRR: Vernal translates into spring, although vernal keratoconjunctivitis is characterized by exacerbation in the spring and summer months, around 60% of the patients also experienced flare-up in the wintertime.

ACL: So, Marie Louise, is it possible for an adult to have vernal keratoconjunctivitis?

MLRR: It is possible, but it's extremely rare. We have seen publications where they have figured out that it's around 2–3% of the entire population of patients with vernal keratoconjunctivitis who are adults, and therefore this group will not be discussed in this podcast [8, 9].

ACL: What are the typical symptoms of vernal keratoconjunctivitis?

MLRR: Vernal keratoconjunctivitis is characterized by an allergic inflammation on the surface of the eye. In the mucosal lining you can say that it's the backside of the eyelids and the front of the eye, including the cornea, and that gets severe when the mucosa gets irritated. It starts secreting more mucus, it is also swollen, so you see redness, edema, you see a lot of mucus. Often it starts itching and you get a

foreign body sensation within the eye, because of this swelling. It feels like you have something in the eye and if the cornea gets really irritated you get photophobia as well. If you are heavily affected, you will experience pain [2, 7, 10].

ACL: Okay, and what are the typical findings we as doctors see?

MLRR: We see these edemas in the skin around the eye, but we also see a redness. In the skin we see conjunctival hyperemia, which is called when you have redness in the white of the eye. You can see the sticky mucus on the eyelashes, and if you invert the upper eyelid you can see papillae, like dots on the upper eyelids in the tarsal conjunctiva. In these patients these can enlarge so heavily that we call them cobblestone papillae, which means that they are extremely big, like small rocks on the backside, and the mucosa is four to six times as thick as a normal conjunctiva. In the cornea, you see an intense ocular surface inflammation causing small erosions in the corneal surface. We call that superficial punctate keratitis. You see all the blood vessels; normally you won't even see them on the eye, but now they are standing out very clearly like red lines into the cornea because of the pannus formation. We see wounds, corneal ulcers, and these can become quite heavy. In this disease we call them shield ulcers when they are really big. Furthermore, in the area, the thin ring around the cornea we call that the limbal area. We see small white yellow nodules. We call them those Horner Tranta dots and they are a sign of the immune system being extremely active in the area. You need to have one of these three key findings to have vernal keratoconjunctivitis, which means you need to have Horner Tranta dots (these yellowish white nodules around the cornea), you need to have giant papillae, or you need to have a shield ulcer to have the diagnosis of vernal keratoconjunctivitis. But you don't need to have all three; one of them is enough. We see some [patients who] have a disease where they're mostly affected on the upper eyelid [whereas] others are more severely affected on the cornea. Some have a combination of all of it [2, 6, 7, 10–13].

ACL: How frequent are these corneal complications?

MLRR: They are quite frequent. They are observed in around less than half of the patients and, if they're left untreated, they will develop keratitis. They will develop a thinning of the cornea and worst case they will perforate and there will be a hole in the eye. It's an extremely dangerous situation.

ACL: Is it always both eyes that are affected?

MLRR: No, and that's quite interesting because often when the smaller children start out having this disease, we always suspect them to have keratitis because one eye is always worse than the other. Then over time it gradually equalizes out, so both eyes are getting equally affected, but we do have patients where it's only one eye which is really affected, but for the majority, 98%, it's both eyes.

ACL: Do the children usually grow out of vernal keratoconjunctivitis?

MLRR: We say that normally it's a children's disease and when they become teenagers the disease will diminish. For some of these children we see that every summer they are less affected. Mainly from the age of 12/13 years old, they are getting less affected, 14, and then it suddenly almost disappears. It never totally disappears, for many of these children it goes on like allergic conjunctivitis in some way for the rest of their life. So, there will be some symptoms left, but it will diminish in severity quite frequently, and then with some it just keeps going. We can't explain why it has this pattern. There have been lots of theories about sex hormones, that it affects the immune system in some way, but we don't know [2, 6, 7, 10–13].

ACL: So, going on, how does severe vernal keratoconjunctivitis affect daily life?

MLRR: If you are really ill of vernal keratoconjunctivitis, the children, when we see these patients in the waiting area, we know already by looking at them how bad it is, because if it's really bad, they come with sunglasses inside. They wear caps. They have their hoodies covering their eyes or they're behaving like they're blind because they don't want to open up their eyes. Parents can tell us stories about living in the darkness because these children won't have the light turned on, so if they're going to go out for dinner, they are going to shut down the light in the entire kitchen or dining area, else

the child won't be able to come out and eat. These kids don't want to go outside, especially when the sun's out. They wake up during the night because it hurts, and they have all these secretions in the eye when they wake up in the morning, and they can't open their eyes. These kids are often called home from kindergarten or from school because adults/ teachers think they have conjunctivitis that will be infectious, or they are in so much pain and suffering that they can't really take part in the activities. Usually, they don't attend any leisure activities. So, it has a significant limit on their daily activities, and it affects the child's psychosocial well-being and diminishes their overall quality of life from the entire family [1, 14–17].

ACL: Okay, so regarding the treatment in a stepwise manner of this disease, what does that mean?

MLRR: We have made guidelines where we tried to make the treatment as less intensive as needed, so we don't want to give children medicine if they don't need it. Both due to the side effects, but also due to cost and the huge thing about compliance when you have ill children, because they can't remember to have eye drops by themselves. There needs to be an adult available to put these eye drops into the eye of the child, and the child might not want the eye drops. So, you really need to be careful about how much pressure you put on these parents to put the drops into the eyes of their children. We often start out by, you can say the lowest level of treatment, is actually to explain what this is all about. Then we are giving anti-allergic eye drops. We give those to all the patients we have in our clinics. There's no side effects to anti-allergic eye drops. We use unpreserved eye drops and then we use artificial tears. For most pediatric vernal keratoconjunctivitis children we are seeing that they need to take the next steps, which is topical corticosteroids. Corticosteroids are always working. Sometimes it's just a matter of how much you are giving, but with corticosteroids and increasing load, you're seeing increasing side effects. So, it's really a balance. We always fear to have a raise in the tension of the eye that's a kind of glaucoma, but that will disappear if we stop giving them these eye drops. Secondly, if

we give corticosteroids over several years the child will develop cataracts, and lots of other side effects. So, we really need to balance the use of corticosteroids compared to the severity of the disease, but it's corticosteroids that actually work when we are in an acute phase. If we can treat the symptoms with corticosteroids for a short period of time, we'll do that. If the child is fine after that they will go on with allergic eye drops and things will be good. However, if they have a constant need of corticosteroids or they are having flare-up every month, we need to use something else. And then cyclosporine can be used. It doesn't have the same terms [mechanism] of action as corticosteroids, it's less potent, but if you use it every day three to four times a day, it can work on the eye as corticosteroids, and it doesn't have the same side effects. It doesn't have the risk of glaucoma and doesn't have risk of severe eye disease. However, it itches, and it gives red eyes sometimes, especially in the beginning. It takes 3–6 months for cyclosporine to work. So quite often, we need to bridge these patients with a combination of both anti-allergic eye drops, corticosteroids, and cyclosporine for quite a long time to get it calm. And then the patients will continue to have cyclosporine and anti-allergic eye drops, but without long-term side effects. That's the main goal of this treatment. However, we hesitate sometimes because cyclosporine is quite expensive [1, 3, 15, 17–19].

ACL: So, what do you do if giving eye drops is not a possibility?

MLRR: Sometimes we have children where it is quite complicated to have so many eye drops, and then we can make a deposit of steroids, it's called Kenalog, and we can put that sub tarsal in the upper eyelid. So, you put them into surgery, put them under general anesthesia and you put medication below the upper eyelid. This will work for 3–12 months and slowly release the medication. It works extremely well. It works within a week and you see an improvement. Often the children are very bad. They come with sunglasses. They have all the symptoms I described. We will put them under general anesthesia and put in Kenalog because then we can start having an examination. We can start talking to the parents and they can start

breathing again, because it has such a huge impact. So, we need to think about side effects, but also about the social well-being of that child. We are always a little fearful that maybe this child would have a raise in [intraocular] tension, and if they do, we need to treat and we need to monitor the pressure in the eye. We need to give eye drops sometimes; we even have some kids who have glaucoma surgery to tolerate the Kenalog. We can treat glaucoma; we can treat cataract. We can't treat a cornea that melts away.

ACL: Okay, what about the association of allergy in vernal keratoconjunctivitis?

MLRR: That's a very frequent question. The parents always come and ask: "What is it that my child is allergic to, why this happening?" We often see there are some allergic manifestations such as asthma or allergic rhinoconjunctivitis and eczema. The children are often sensitized to one or more inhalation allergens if you test them. Among patients where there's no allergic manifestation, they often aren't sensitized if you test them. They have a negative skin prick test, but around half of the patients do have, and that's mostly towards pollen and dust mites.

ACL: How many are seasonal of these allergies?

MLRR: Mainly around 60%.

ACL: Do you send all your patients for allergy testing?

MLRR: Almost, yes. And I do that because if they have an allergy—and we need to be clear that it's one thing... to have a sensitivity on the skin prick test or have increased IgE in your blood test. That is just that your immune system discovering that these things could be dangerous. But to have a real allergy you need to both have a positive test and react when you are exposed to it. We do see that a lot of these kids they go and have a test and they're not sensitive to any of the things we're testing against. We need to remember that every day we are exposed to more than two million different particles within our daily life, and we are testing for the 10 most frequent. So, there's lots of things we don't know, but we do know that if you test specifically within the tears of the eye,

you'll find a much higher rate of allergies. But that's impossible to do on kids [17, 20–22].

ACL: What are the implications of finding allergies?

MLRR: You can say if you have a suspicion and you know that it's always getting worse in May, June and you suspect grass allergy. It has a relevance because then you can vaccinate against it, but it's a kind of hyposensitization, where you get a small amount of grass every day in a tablet before bedtime and then you can actually diminish the immune reaction to it, and you can get that sort of treatment in Europe for grass, for birch, and now for dust mites. There are other possibilities if you have other specific allergies, but then you need to have a needle with the allergen every week, or second week, and it takes years. So that's long term. Also, if you have a pet, if you have a cat, and you're suspecting that maybe you are allergic to it, you could get rid of the cat. You must clean your house significantly. Or people are thinking about having a dog—it might not be a good idea if they're sensitive to dogs. Secondly, if you know your season you can look it [the pollen count] up on the internet on your mobile phone. You can have the pollen numbers of the day and know when to be more careful. Furthermore, we tell our patients to wash their hands and face if they come in from being outside playing, because then they can wash the allergens away.... If they have asthma or rhinoconjunctivitis, it makes total sense because then you can also treat their nose and their asthma more sufficiently [10, 20, 21].

ACL: Okay, so what about atopic keratoconjunctivitis? How does this differ from vernal keratoconjunctivitis?

MLRR: That's a difficult question. You can say in the literature vernal keratoconjunctivitis is for children and atopic keratoconjunctivitis is for teenagers and younger adults. However, we see a lot of children with atopic dermatitis who come and have a (clinical) picture of vernal keratoconjunctivitis, but they tend not to have the giant papillae, but they have all the symptoms, and you can say in adults they show kind of the same picture with the corneal complications. I wouldn't say it doesn't matter, but it's the same treatment these patients are needing.

For all patients, both the children and the adults with atopic dermatitis, we need to take care of their skin, and we need to give extra attention to the compliance for the patient and the parents because there's so much treatment. They need all the types of ointment on their skin. They need to remember their asthma medication and now they need to remember three different types of eye drops. So, it's a huge task—the parents must take care of all these issues at the same time. We see it more like a spectrum [21, 23, 24].

ACL: So back to normal vernal keratoconjunctivitis. What are the key elements in your patient-centered approach in children?

MLRR: You can't get compliance if the patients and the parents don't understand what this is all about. So, we spend quite a lot of time explaining, why, what, when. There are so many eye drops. They need to understand the side effects. Why can't they just use steroids all the time? What is the economy in this? What is the reimbursement? Why should all drops be unpreserved? Then we give a lot of advice, we have a lot of patient folders now, we have developed that. Then in every consultation we give a plan A. That's the main plan. That's what they need to do and use every day to keep vernal keratoconjunctivitis away. We know many of these patients will have flare-ups, and what are they allowed to do when they have a flare-up? Usually, it's a plan where they can use steroids one or two times a day for a week or maybe 2 weeks, and if that doesn't work, they need to contact us; both so we can follow up on it, but also if we need to measure the eye pressure. Then we are quite available. We are available every day because when these children have a flare-up it's now, it's not in 3 days' time. It's now and the faster we get a plan, they start using steroids, they are diminishing the inflammation, the faster it will go away. And then we have quite a skilled team where we work together with glaucoma specialists. We have pediatric ophthalmologists. We have special opticians, and we have a very good collaboration with pediatrics at other hospitals and dermatologists so we can communicate around the patient and the parents.

ACL: How do you examine these children?

MLRR: In normal circumstances, we are quite good at getting a look, we don't need to look a long time. Usually, one or two seconds is what we get the first time, but my feeling is that we have improved quite well in that sometimes you can't see a thing and then you need to guess on what the parents tell you. Then you start the treatment in hope that this will improve the situation and ask them to come back in a week's time or two. However, if that doesn't work, we need to put the patients under general anesthesia, and we need to see what's happening. In these cases, we sometimes put in Kenalog. If we invert the eyelids and find out this is vernal keratoconjunctivitis, then we can treat it or we can treat the shield ulcer. Other times we have tried, we put these children under general anesthesia, and then it wasn't vernal keratoconjunctivitis—it was something else. That's also quite important that we need to see what it is. We have the benefit of being mainly two doctors—myself and Ann Cathrine, so we know our patients, we know the parents and that gives quite an improvement in compliance for these kids.

ACL: Marie Louise, what do you think is the most rewarding aspect of treating these children with vernal keratoconjunctivitis?

MLRR: I always get so emotional because it's so great to see these kids coming back without sunglasses. They are smiling. Their eyes are open. The parents are almost crying because now they are finally asleep. The whole family is eating dinner together. The kids are going back to school. So, it's really a transformation in some way where, also over the years, you see these children grow and they are so cool, and some of the kids they are so experienced and they are able to drop their own eyes, and take care of themselves, and that's really fascinating.

ACL: So, have you ever transformed a life?

MLRR: When you attend the American Academy of Ophthalmology, they always talk about, have you ever transformed the life and when you're treating vernal keratoconjunctivitis you are transforming lives. A good example is a boy I followed for the last couple of years. He started out when he was 3 years old coming to the eye department. He had a quite severe keratitis and nobody could see what was actually

happening but we suspected herpes. It was treated and he was dismissed. He came back a year later with a new keratitis on the same eye, the same time of the year in June. Then he was diagnosed with vernal keratoconjunctivitis. At that time when they finally had a look at it, his right eye was okay, but the left eye had a huge astigmatism and a scarring so he wasn't able to see anything. He had a 0.3 vision which is around approximately 30% vision in that eye, and they are patching, they tried various eye drops with steroids, and he became better, but he wasn't really able to see that much. I started seeing him 4 years ago where we started up cyclosporine three times a day. Then he was about to start school, but he was not able to sit inside classes because he was so light sensitive. If you go to a Danish school, you don't have a blackboard anymore, you have modern, electronic active boards. It's like a huge computer screen where the teacher can write on this electronic board inside the classes, and he couldn't look at it and he couldn't stay there. So, we had to give him filtered glasses that had color shifting. After some years on cyclosporine and anti-allergic eye drops, he stopped having flare-ups. His vision improved because the scarring diminished over time. So now he has almost normal vision on that eye. He doesn't need any glasses. You can still see the scarring, that will never disappear, but he has a reasonable vision, about 80% vision in that eye, and he started to do leisure activities. I spent the last 2 years mainly discussing with him and his mom how he can spend more time outside, because he had never been outside when he was a smaller child. He always stayed inside. So, it's a transformation of pushing him into normal, social, physical development. He started playing football now. It's a happy family and a happy boy, so that's really great.

ACL: That's really great. As far as you know are there any new treatments in the pipeline?

MLRR: The short answer is no. I would wish there were.

ACL: What type of treatment would you wish for in the future?

MLRR: I would wish for some sort of long active cyclosporine or if you could have a similar drug, which is not allowed in Europe, [to]

tacrolimus. If it was long lasting so you could give it as a deposit like we do with the Kenalog, or you could put it as a punctal plug. It's always a huge compliance thing to take an eye drop four times a day when you are a child, so normally it doesn't work. So, we can get patients to get an eye drop three times a day. If we could get a drop where it was only one time a day, or you had something which lasts longer that would be amazing. Secondly, I would like to have tacrolimus in Europe. Even though it's not better working than cyclosporine, it could give more competition, and it could also help us because sometimes cyclosporine is out of stock in Europe—we can't get it—and that puts in us in a terrible situation. So, it will be less vulnerable if we had both drugs available.

ACL: Thank you very much for all your great answers, Marie Louise. That concludes my questions.

MLRR: Thank you for your time.

ACKNOWLEDGEMENTS

The podcast transcript has been edited for clarity.

Author Contribution. Marie Louise Roed Rasmussen and Ann Catherine Larson contributed equally to the podcast transcript and recording of the podcast.

Funding. No funding or sponsorship was received for this study or publication of this article.

Editorial Assistance. Christopher Vautrinot, managing editor of *Ophthalmology and Therapy*, provided English language editing of the transcript.

Data Availability. Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Declarations

Conflict of Interest. Author Marie Louise Roed Rasmussen declares to have received

speaker fees for lectures from Santen, and to have received advisory board honorarium from Santen. Ann Catherine Larson has no conflicts in interest to declare.

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