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Beyond Dry Eyes: Signs of Sjogren's Syndrome

### SJOGREN'S SYNDROME

You are listening to ReachMD XM 160, the Channel for Medical Professionals. Welcome to medical breakthroughs from the University of Pennsylvania Health System with your host Northwestern University internist, Dr. Lee Freedman.

Even though Sjogren's syndrome is one of the most prevalent autoimmune disorders, is often under diagnosed because the symptoms can mimic certain other conditions. How can we be aware of the warning signs for this sometimes disabling disease? Joining us to discuss Sjogren's syndrome is Dr. Frederick Vivino, clinical associate professor of medicine at the University of Pennsylvania School of Medicine and director of the Penn Sjogren Syndrome Center. Dr. Vivino was also chief of the Division of Rheumatology at Penn Presbyterian Medical Center.

### DR. LEE FREEDMAN:

Thank you for being with us, Dr. Vivino.

### DR. FREDERICK VIVINO:

My pleasure.

### DR. LEE FREEDMAN:

In medical school residency, I was thought Sjogren syndrome is dry eyes and put some drops and then we are done, but it goes beyond that, doesn't it?

### DR. FREDERICK VIVINO:

It was exactly the same with me, but in the last 10 or 15 years, I think physicians are starting to realize that there is significant morbidity and even mortality associated with this disorder.

**DR. LEE FREEDMAN:**

Do we see symptoms beyond dry eyes?

**DR. FREDERICK VIVINO:**

Well we do Dr. Freedman, just like lupus is a systemic disorder, you know, in Sjogren's the immune system targets the exocrine glands and it has the potential to affect virtually any organ system in the body with a notable exception of the heart.

**DR. LEE FREEDMAN:**

Is it something that we would be seeing commonly in our primary care practice?

**DR. FREDERICK VIVINO:**

I think a lot of primary care physicians do see Sjogren's, but because it has such a varied presentation, it is not always recognized. Sjogren's can present with symptoms that may make menopause, it can present with chronic fatigue, it can present with musculoskeletal pain, or it can present with internal organ problems like interstitial lung disease, or renal tubular acidosis, so it really does cause a large variety of problems and sometimes it is difficult for someone to put these seemingly unrelated signs and symptoms together and tie them up in 1 big picture.

**DR. LEE FREEDMAN:**

Very interesting, and do we look for this in the typical rheumatologic patient in the 20s and 30s female.

**DR. FREDERICK VIVINO:**

Well, the typical patient is a peri-menopausal Caucasian female, but you know, as our awareness of the disease increases in our ability to diagnose it improves, we are starting to see cases in younger and younger woman all the time in woman of a variety of racial and ethnic backgrounds in man and in more and more children. So it's really a disease that can affect almost anyone, although classically 90% of the patients are female.

**DR. LEE FREEDMAN:**

And in that postmenopausal range.

**DR. FREDERICK VIVINO:**

That's right.

**DR. LEE FREEDMAN:**

And more white woman.

**DR. FREDERICK VIVINO:**

Yes.

**DR. LEE FREEDMAN:**

I see. In taking the history, you mentioned several things with dry eyes is still one of the cardinal historical features.

**DR. FREDERICK VIVINO:**

Yes. The most common symptoms would be dry eyes, dry mouth, fatigue, and musculoskeletal pain and probably about 80% of the overall patient group presents with the classic sicca syndrome or what we call whole body dryness.

**DR. LEE FREEDMAN:**

Well and that is as I think about patients those are fairly nonspecific symptoms and certainly side effects from many medications give you that dryness, so I guess you really have to have a high index of suspicion.

**DR. FREDERICK VIVINO:**

You really do, and you know as you point out, medicines are far and away the most common cause of sicca symptoms and you can see them with other systemic disorders with some viral illnesses like hepatitis C or HIV with other diseases like hyperlipidemia, sarcoid, amyloid, and with other salivary gland problems. You really have to go through a comprehensive diagnostic evaluation before you can decide whether the patient's sicca symptoms are due to Sjogren's or something else.

**DR. LEE FREEDMAN:**

Are there any things that are helpful on physical examination in patients like this?

**DR. FREDERICK VIVINO:**

Well you know what Dr. Freedman the most striking feature on physical exam is usually the fact that the patients look a lot better than

they feel. Many of them look well. They don't look chronically ill. You know, their friends and families tend to write them off as being hypochondriacs and unfortunately many of them go several years before any one thinks of testing them for autoimmune disease. I think the average duration between the time when symptoms begin and the time the diagnosis is finally made in this country is about 7 years.

**DR. LEE FREEDMAN:**

Wow.

**DR. FREDERICK VIVINO:**

So, early on they can look normal, but of course, you know, you can see subtle signs in the mouth that decrease salivary pool or dry tongue or you can lose the luster of the eye, but it is very easily missed on exam.

**DR. LEE FREEDMAN:**

And I think of in terms of testing, I think of some of the blood work, ANA and certain subtypes of ANA, this ever relate to the underlying pathophysiology and what test should we be ordering?

**DR. FREDERICK VIVINO:**

You know it is an autoimmune disease, so as you point out these patients form a lot of different autoantibodies and just like rheumatoid arthritis and systemic lupus, they can form rheumatoid factor in the blood or antinuclear antibodies and there is actually a lot of clinical as well as serologic overlap with these 2 disorders that are often thought of his cousins to Sjogren's, but the 2 most specific autoantibodies are anti-SSA or SSB, which are also known as anti-RO or anti-La. They are mostly found in Sjogren's to a lesser degree and lupus and we usually do a pretty good job, differentiating between those 2, so if the antibodies are there in the blood that might be the first clue that the patient has Sjogren syndrome.

**DR. LEE FREEDMAN:**

And are there certain other tests you look for leukopenia or other things we might typically see in rheumatologic disorders?

**DR. FREDERICK VIVINO:**

Well, you know, they get pretty much a complete history and physical exam with blood counts and they can have leukopenia and lymphopenia rarely if they can develop kidney disease and renal tubular acidosis, so we get kidney function test, they can get autoimmune liver disease and thyroid problems. So, we send all those tests as well, but when we are specifically interested in Sjogren's, the main objectives are to send the serologic tests and to do test to look for objective evidence of dry mouth and dry eyes.

**DR. LEE FREEDMAN:**

If you are just tuning in, you are listening to medical breakthroughs from the University of Pennsylvania Health Systems on ReachMD, the Channel for Medical Professionals. I am your host, Dr. Lee Freedman and with me today to discuss Sjogren's syndrome is Dr. Frederick Vivino, clinical associate professor of medicine at the University of Pennsylvania School of Medicine and director of the Penn Sjogren Syndrome Center

Dr. Vivino, the tests that objectify dry eyes, dry mouth, can you describe those are these things we can do in the office?

**DR. FREDERICK VIVINO:**

Some of them we can do in the office, so the eyes for example we can do a Schirmer test or we put a little strip of filter paper in the eye and measure tear production within a 5-minute period. At least that is something the rheumatologists like to do. I don't know if you do that in internal medicine, but if not, then the ophthalmologist, especially the cornea specialist can do that test, as well as another test called vital dye staining where they add a drop of vital dye such as rose bengal or lissamine green to the eye and they have the patient blink and they look at the outer surface of the eye under the slit lamp for these little punctate areas of staining with the node areas where the epithelium of the cornea or conjunctiva are damaged or dying due to chronic dryness. So, if the tear production is significantly decreased or you see dry spots on the surface of the eye that can help with the objective documentation of dry eyes. For the mouth, you can measure a salivary flow rate in your office that's called whole mouth on stimulated sialometry and if the Penn Sjogren Center were really in the spit, so a common test that we would ask people to do would be to swallow once and expectorate into a container for 15 minutes and then we weigh the container and are able to measure the amount or volume of saliva produced per unit time, so that can document dry mouth, you can also order salivary scintigraphy, nuclear medicine test that is very similar in technique to a thyroid scan, same isotope, very similar scanning parameters except we look at the glands for uptake resting function and stimulated function and in the old days, not so much any more but occasionally people will order a parotid sialogram, where water soluble contrast dye is injected intraorally into Stensen duct to make a picture of the ductal system of the parotids looking for abnormalities areas where you see stenosis or poststenotic dilatation or microaneurysms, which helps to verify that something is indeed wrong with the salivary glands.

**DR. LEE FREEDMAN:**

So, there is a variety of different things, ophthalmologic things, as well as looking at the salivary glands and the amount of saliva, very interesting. How often is Sjogren's confined to the eyes and mouth versus becoming a more systemic problem?

**DR. FREDERICK VIVINO:**

Well, the systemic and internal organ manifestations occur in about 30% of patients. So, fortunately the majority just deal with dryness, 20-30% have more serious internal organ manifestations, and about 4-5% unfortunately develop non-Hodgkin B cell lymphoma as a long-term complication of this disease.

**DR. LEE FREEDMAN:**

And when it is more localize, I know we do have some very efficacious treatments for this.

**DR. FREDERICK VIVINO:**

Yes, we do, you know there is a plethora of artificial tears that you can use for dry eyes. If you walk into any drug store, you would be

impressed with the number of available products in ocular lubricants for use at bedtime. They are now long acting tear inserts called Lacrisert, a little palate you can put in the eye and you get them started with drop of artificial tears and they provide relief to some patients and about 4-5 years ago, topical cyclosporin ophthalmic solution, 0.05% was FDA approved and is now marketed under the trade name Restasis that is an eye drop that people apply in each eye twice daily, and a treat ocular surface inflammation and it often significantly improves symptoms of dry eyes.

**DR. LEE FREEDMAN:**

My patients who are on that have certainly expressed their pleasure and relief with that. I have occasionally tried to prescribe an artificial saliva and that has not met with as great acceptance, are those used at all?

**DR. FREDERICK VIVINO:**

Well, we still use them Dr. Freedman, but mainly as adjunctive treatments. I think the best treatments for dry mouth now a days are what we called secretagogues or medications that stimulate flow and 2 examples are pilocarpine, which is also known as Salagen that's a natural remedy that actually was originally derived from shrub in South America, that is a cholinergic agonist that stimulates flow. It was FDA approved in 1998 and then 2 years later another cholinergic agonist called cevimeline or Evoxac was also FDA approved, and both of those medications are just approved for dry mouth, but they not only help dry mouth, but other oral symptoms and they can stimulate flow and the clinical experience with these drug suggest that not only are the efficacious for the mouth, but they may help dryness in other parts of the body, as well even though they are not FDA approved for any other indications besides dry mouth.

**DR. LEE FREEDMAN:**

Well, I want to thank very much Dr. Frederick Vivino from the University of Pennsylvania School of Medicine for being with us today and going over Sjogren's syndrome. He reviewed for us the spectrum of symptoms with which you can present and how we might diagnose it and then he has gone over some treatments for this disorder. Thank you, very much for listening.

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