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The Mysteries and Challenges of Treating Mild Cervical Dysplasia

You are listening to ReachMD XM 160, the Channel for Medical Professionals. Welcome to Advances in Women's Health. I am Dr. Lisa Mazzulo, you host, and with me today is Dr. Enrique Hernandez, Chairman of Ob/Gyn and Director of the Division of Gynecological Oncology at Temple University in Philadelphia. We are going to be discussing today some of the challenges of mild, moderate, and severe cervical dysplasia in the clinical care of our patients that are female.

DR. LISA MAZZULO:

Welcome Dr. Hernandez.

DR. ENRIQUE HERNANDEZ:

Good morning.

DR. LISA MAZZULO:

So, cervical cancer has been #2 cause of death of women around the world, makes all practitioners want to try to prevent their patients from getting it. So, may we let's start with a little bit of how you recommend screening patients who may have had a history in the past of mild dysplasia?

DR. ENRIQUE HERNANDEZ:

Well, a patient that has had a history of mild dysplasia in the past we follow a little more closely than patients that has had history of completely normal Pap smears. So, the patient with a history of dysplasia in the past, mild or otherwise, I will recommend that she has a Pap smear at least once a year, and that's where the patient that had that in the past and it has been clear, I mean that the subsequent followup has been normal, and then from then on, follow up will be a little bit closer, at least once a year.

DR. LISA MAZZULO:

What if you have a patient who has had a history of may be of year of low grade or mild dysplasia and their Pap smears continue to

come back low grade 6 months or year or later, what would you suggest in the management of that kind of patients?

DR. ENRIQUE HERNANDEZ:

Well, if except for adolescence and adolescence it's now defined by the American College of Ob/Gyn and by the American Society of Colposcopy and Cervical Pathology, as a woman that is younger than 21 years of age. Except for that group, if a woman has a Pap smear that shows mild dysplasia and in Pap smears, is a little bit different, they actually call it a low-grade squamous intraepithelial lesion or LSIL for short. In that patient a single Pap smear of LSIL, requires that patient to be examined under magnification using equipment that is called a colposcope. So, have to undergo a colposcopy that would examine the cervix under magnification to try to identify if indeed LSIL is all they have.

DR. LISA MAZZULO:

And when in the first system switched from the mild dysplasia to the low-grade squamous intraepithelial lesions, why do you think they change the nomenclature?

DR. ENRIQUE HERNANDEZ:

To better align with the natural history of the disease. When you have an LSIL and that is confirmed on biopsy, but you really seen is viral infection of the human papilloma virus, in reality you are not seen yet a neoplastic change. Once you go to a high-grade lesion, an HSIL or moderate-to-severe dysplasia that's the patient where the virus is produced in a neoplastic change.

DR. LISA MAZZULO:

Do you think that this new Bethesda system is more helpful in clinical guidance for these patients?

DR. ENRIQUE HERNANDEZ:

Oh, it's much better. The Bethesda system has developed over a number of years, actually now over a decade, which initially the Bethesda system was just to have a uniform nomenclature for reporting Pap smears. Now, as of 2006, it also includes a better defined evidence based guidelines on how to manage these patients.

DR. LISA MAZZULO:

And you are talking about the ASCCP guidelines from last year?

DR. ENRIQUE HERNANDEZ:

The ASCCP guidelines that actually the meeting was in the Bethesda in September of 2006. The guidelines got published throughout 2007 and eventually they published from guidelines booklets and CDs and DVDs, those were published over the end of 2007.

DR. LISA MAZZULO:

And most of these guidelines are suggesting that with HPV testing you may be able to follow, for example, someone with atypical cells a year later instead of 6 months which is what we are used to do.

DR. ENRIQUE HERNANDEZ:

That is correct. So, if you a have a patient whose Pap smear is negative, for example, but you chose also to do HPV testing and that's only recommend for women over the age of 30 because in the younger women, the prevalence of HPV is so high that doing HPV testing is not going to be helpful, but if the Pap smear is negative and the HPV is positive, then you can repeat the HPV test in 1 year and the reason for the 1 year is the medium time of the time when 50% of patients have an initial infection with HPV that will clear the infection, it's 8 months. So, you don't want to repeat it too soon because it will be again positive.

DR. LISA MAZZULO:

In going back to mild dysplasia as we were talking before, what you think the role of HVP typing is in that particular patient population?

DR. ENRIQUE HERNANDEZ:

At this point in time, none, because what that evidence base, the research have shown is that if the Pap smear shows LSIL that over 85% of those patients will have oncogenic HPV. So, LSIL is synonymous with having an HPV infection. Now, that is a Pap smear. A certain percentage of patient that have LSIL and a Pap smear, we will actually harbor a high-grade dysplasia when you do a biopsy.

DR. LISA MAZZULO:

How often do you think that happens?

DR. ENRIQUE HERNANDEZ:

Close to about 20 to 30%.

DR. LISA MAZZULO:

And so, in the patients taking back one step, how accurate do you think the Pap smear is a predicting low-grade SIL, for example false positive to false negative.

DR. ENRIQUE HERNANDEZ:

That's a little more harder to answer. I think the way to look at it is that is have an LSIL on the Pap smear, about 20% of them will have a high-grade dysplasia on the biopsy. The other group the majority will have mild dysplasia on the biopsy and still another group will have normal.

DR. LISA MAZZULO:

Do you find at your institution because I find this at my that all have a low-grade Pap smear, but then the pathology will not be using the Bethesda system and it is read as mild to moderate or severe.

DR. ENRIQUE HERNANDEZ:

Yes, because the Bethesda system for LSIL and HSIL is for cytology. For histopathology, we prefer nomenclature is actually CIN 1, 2, and 3 or cervical intraepithelial neoplasia 1, 2, and 3.

DR. LISA MAZZULO:

If you are joining us now, you are listening to Advances in Women's Health. We are speaking to Dr. Enrique Hernandez, the Chairman of Ob/Gyn at Temple University, and we are discussing the challenges of mild and moderate dysplasia.

We were just talking about the likelihood that the Pap smear is accurate for low-grade findings and therefore mild dysplasia except in about 20% of patients who may be upgraded, correct?

DR. ENRIQUE HERNANDEZ:

Yes.

DR. LISA MAZZULO:

So, the question comes, let's say you have a patient with both the Pap smear and colposcopy that is showing low-grade change, how you follow that patient if all of that is consistent with mild dysplasia. When would you see them back again for another Pap smear or colposcopy, I guess is the question?

DR. ENRIQUE HERNANDEZ:

Actually, the important issue here is in the past if a patient had a Pap smear show LSIL and the biopsy and colposcopy show LSIL, that patient and some people will have treated, and treated either with cryosurgery, laser excisional biopsy. Right now, the guidelines are that if the patient has CIN 1, that that patient can be followed with Pap smear every 6 months until you get 2 negatives or HPV testing, HPV DNA testing at 1 year. If any of those come back abnormal again, then they go back to another colposcopy.

DR. LISA MAZZULO:

So, the question is, because we are going away, I think in practice from treating mild dysplasia and instead are watching it, no chance of regressing sounds like it is quite good.

DR. ENRIQUE HERNANDEZ:

The changes of regression of mild dysplasia are higher than 60%.

DR. LISA MAZZULO:

So, to determine the patient that actually requires therapy in low-grade situations or mild dysplasia, how would you determine that patient?

DR. ENRIQUE HERNANDEZ:

So, that patient had initial colposcopy satisfactory or unsatisfactory and the only thing you find on the biopsy is mild dysplasia, and that patient you follow again 6 months later has mild dysplasia again, you are going to repeat the colposcopy, follow that patient again in 6 months, mild dysplasia again, you are going to repeat the colposcopy, and you will continue to do that and the guideline state that at 2 years, then you can opt to treat at that time or continue to follow. It will depend on how the patient feels about the followup.

DR. LISA MAZZULO:

And their compliance, obviously.

DR. ENRIQUE HERNANDEZ:

Yeah. I mean some patients, you know, it is inconvenient for them and they may decide to be treated, but the reality is that if the only thing you find is mild dysplasia, these patients can continue to be followed. There is 1 special group, and if the patients are HIV positive, the HIV patients, those patients once they get LSIL, it never goes away.

DR. LISA MAZZULO:

Hmm. Hmm.

DR. ENRIQUE HERNANDEZ:

And those patients, we will continue to examine and follow right and doing procedures which we did in the past, and we ended up ending up with a hysterectomy and still seen LSIL on their subsequent Pap smears. So, those patients will continue to follow up very closely, but without therapy.

DR. LISA MAZZULO:

Especially for both physicians and patients in that situation for sure?

DR. ENRIQUE HERNANDEZ:

Yes.

DR. LISA MAZZULO:

What do you think is a natural progression towards cervical cancer. Do you think that mild dysplasia becomes moderate dysplasia and those some patients end cancer itself?

DR. ENRIQUE HERNANDEZ:

Well, again the volumes for this has become better and better. So, what we know is that mild dysplasia represents an HPV infection. Eventually, proteins that are produced by that HPV infection inhibit too much suppressor genes like retinoblastoma gene and the p53 gene. Once that happens, that's when you have progression to moderate-to-severe dysplasia. Once the gene, the HPV genetic material integrates with the chromosomal material of the genetic material of the hose, then is when you see invasive cancer. So, there is a progression from having HPV infection to having a neoplasia caused by mouth functioning of too much suppressor genes to have an invasive cancer because the HPV, chromosomal, or genetic material has incorporated or integrated to the hose genetic material.

DR. LISA MAZZULO:

So, for the patient who for example is not HIV positive and gets a high-grade SIL Pap smear, that combine some moderate and severe dysplasia, so how do you recommend treating that patient?

DR. ENRIQUE HERNANDEZ:

Oh, that that patient is at risk for progressing to cervical cancer. So, the patient has moderate-to-severe dysplasia. The most common treatment is for them to undergo an excisional biopsy where they remove or would remove the entire transformation zone of the cervix and that's the area that is at risk, the area where the squamous epithelium joins the columnar epithelium and is transforming from columnar to squamous, and most people today will do that using an electrical loop what is called a LEEP or loop electro excisional procedure. You can do it that way, you can do it with a scalpel and people call that a cold knife cone, but for patients that have a focal lesion, a satisfactory colposcopic examination that means that we can see the entire transformation zone with curettings of the curettage of the endocervical canal is negative. That patient could be treated with cryosurgery which is simpler, is an office-based procedure, and cheaper. That patient can also be treated with laser. The laser has become less common because the equipment is more expensive, and people today are not being trained in that modality of therapy. They are being trained on the LEEP rather than laser.

DR. LISA MAZZULO:

Do you expect any new trends in the future or any changes in the treatment recommendations at this time for moderate or mild dysplasia?

DR. ENRIQUE HERNANDEZ:

There will be changes, as some people believe that for a moderate-to-severe dysplasia that you can start doing specific HPV typing and looking at HPV types that are at high risk of progression versus those that are not, and then treating the one that are high risk for progression and observing the one that are not, especially younger nulliparous woman. Because one of the complications of the excisional procedures are complications with future pregnancies.

DR. LISA MAZZULO:

Do you feel there is a difference in those complications, if you do a LEEP versus a cold knife cone?

DR. ENRIQUE HERNANDEZ:

Apparently, no difference. There are differences if you compare the LEEP versus the cryotherapy where you see less complications with cryo therapy. To confuse also even more, there are some patients that have CIN 2 or CIN 3 not treated, and they also have an increased risk of pregnancy complications and that may be all the factors related to that have to do the _____ may be high among patients that have moderate-to-severe dysplasia and so on.

DR. LISA MAZZULO:

Is there some other things we can recommend to people to tell their patients to reduce this risk, would be may be 2 or 3 things you can think of?

DR. ENRIQUE HERNANDEZ:

To reduce the risk of mild dysplasia from moderate to severe also, the one thing that we have today is the HPV vaccine and that's now been recommended to be given to women between the ages of 9 and 26.

DR. LISA MAZZULO:

Is there anything other than the vaccine you would recommend for patients to reduce this risk?

DR. ENRIQUE HERNANDEZ:

Well, the other factors of risks are multiple sexual partners, other factors include smoking that increases the risk of progressing to severe dysplasia or invasive cancer. So, those are things to avoid. So, multiple sexual partners and cigarette smoking.

DR. LISA MAZZULO:

Well, with the cervical cancer being one of the #1 reasons women die in the world and up to 3% Pap smears being mild dysplasia or associated with low-grade SIL and 1% being related to high-grade, this is a significant problem that still has some histories, but hopefully these continued guidelines will be helpful and allow us to take care of our patients best.

Thank you so much to Dr. Enrique Hernandez who has been our guest and we have been discussing these challenges in cervical dysplasia treatment. I am Dr. Lisa Mazzulo.

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