CASE #1

D is a 13 year old female who is here today with her Mom A May 27, 2015 to better understand treatments for her symptoms of unwanted and unrelenting "feelings".

D began having symptoms of "feelings" around age 6 in the 1st grade. D recalls beginning to cross her legs to help relieve the "feelings" symptoms of PGAD in the third grade around age 9.

D and her mother do not recall any direct injuries to her genital area.

D was diagnosed with anxiety disorder in kindergarten. D was diagnosed with ADHD in 2nd grade. Daphne was first treated with Stratera for ADHD.

CASE #1

D states she is currently taking 1 mg once a day of Paxil, which has helped lower her unwanted “feelings” symptoms to a 2/10. D states that on bad days she would have ‘the feeling’ up to 6 times a day.

D’s symptoms seem to worsen with anxiety and stress.

D just began to swim on the swim team. D recently had episodes lasting up to an hour. D states that Paxil has not affected the duration of her episodes.

D states that excitement causes her to have “the feeling”.

CASE #1

A states D discovered “the feeling” and began masturbating in the first grade.

D is able to relieve the "feeling" by crossing her legs tightly - A states that in general Daphne would masturbate about 3 times/day.

With anxiety D increases her masturbation to 4-5 times a day.

D started Paxil for her anxiety which has helped with her PGAD symptoms. On Paxil D has returned to masturbating 2-3 times a day.

CASE #1

The MRI of the sacral spine S2 to rule out a Tarlov cyst was negative.

CASE #1

PREVIOUS TESTS

Test	05/21/15	Units	Range
Calculated Free Testosterone [SDSM code]	0.126	ng/dL	0.6-0.8
Testosterone, Total, Serum	9	ng/dL	<41
Thyroid Stimulating Hormone (TSH)	1.96	uIU/mL	.5-4.30
Estradiol, Serum (Oestradiol, E2, 17-beta Estradiol, E-17)	37	pg/mL	19-144
Dihydrotestosterone (DHT)	pending	ng/dL	112-955
Progesterone	<0.5	ng/mL	<1.0
Sex Hormone Binding Globulin (Testosterone-estrogen Binding Globulin; TeBG), Serum	48	nmol/L	12-150
Luteinizing Hormone (Lutropin), Serum	2.1	mIU/mL	1.9-12.5
Follicle-Stimulating Hormone (FSH, Follitropin), Serum	4.9	mIU/mL	2.5-10.2

DIHYDROTESTOSTERONE,
LC/MS/MS <5 L 5-46 ng/dL

This test was developed and its performance characteristics have been determined by Quest Diagnostics Nichols Institute, San Juan Capistrano. Performance characteristics refer to the analytical performance of the test.

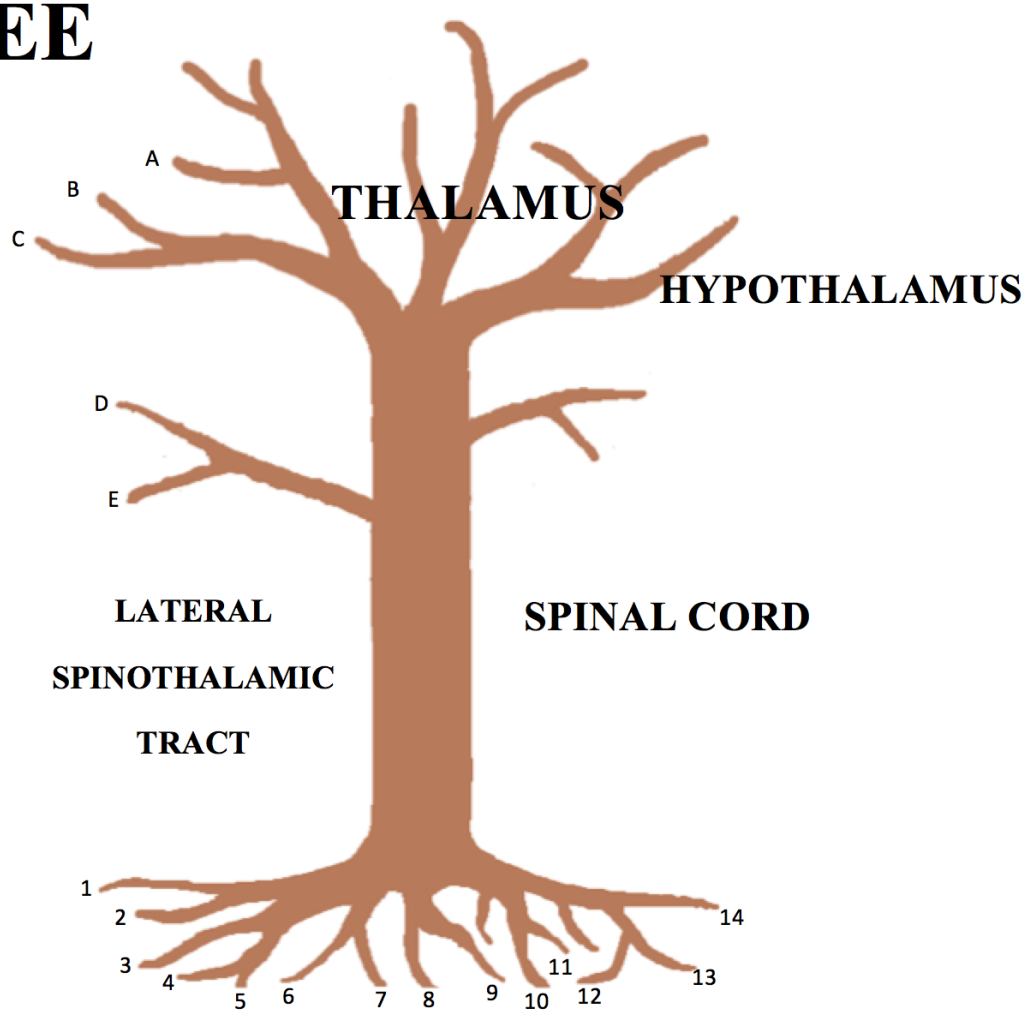
PGAD TREE

Brain Central Nervous System Causes

A. Central dysregulation problem (from abrupt withdrawal of previous SSRI use)
B. Tumor/Mass/Cyst/Aneurysm in Brain
C. Cerebral Vascular Accident

Spinal Cord Central Nervous System Causes

D. Tumor/Mass/Cyst/Aneurysm in Spinal Cord
E. Herniated Disc



Peripheral Genital Pathologies –
Sacral Root S2, S3, S4 - Causes

1. Altered pre-menopausal hormone integrity – hormonally mediated provoked vestibulodynia
2. Altered menopausal hormone integrity – vulvovaginal atrophy/genitourinary syndrome of menopause
3. Increased nerve fiber density - genetic susceptibility leading to elevated levels of nerve growth factor substances
4. An injury to, or irritation of, the pudendal nerves that transmit pain and other sensations
5. Abnormal response of tissues to Candida infection, or recognized allergies or non-specific allergies
6. Dermatologic conditions: lichen sclerosus or lichen planus
7. Vulvar granuloma fissuratum
8. Peri-urethral glans pathology
9. Clitorodynia
10. Pelvic congestion syndrome
11. Arterio-venous malformation
12. S2 Tarlov Cyst
13. High tone pelvic floor dysfunction

It is probable that PGAD exists because of:

1) **excess sensory information passing from a number of peripheral genital (S2, S3, S4) pathologies or brain or spinal cord central nervous system pathologies that pass along the spinothalamic tract to the thalamus and then to the hypothalamus**
2) **decreased inhibition of the excess information along the lateral spinothalamic tract, thalamus, and hypothalamus**

Local to vestibule estradiol 0.02%/testosterone 0.1% in methylcellulose BID

Tramadol – normally 50 mg tablets

compounded into 5 mg tablets

Zolpidem – normally 10 mg tablets

compounded into 0.5 mg tablets

CASE #1

D is a 13 yo female with a history of PGAD that presents for VAT.

At her last visit, she was noted to have erythema at the introitus and pain mainly in the vestibule. Her mother, A, had applied the testosterone/estradiol cream everyday from May until August 2015.

A did note that her pain improved while applying the cream.

They stopped in August because D became increasingly uncomfortable with her mother applying the cream.

A states that her PGAD has been worsening—previously she had occasional flares with back to back occurrences, but now having flares everyday.

We discussed at length neuroproliferative vestibulodynia and treatment options. She is currently using tramadol 5mg at 0800, 1200, and 1600, which has helped (she has gone from flares 5 x a day to 2 x a day).

She also takes Paxil 1mL (10mg/5mL) QHS. Daphne is tearful and “does not want anyone to touch it down there.”

CASE #1

D and her mother agreed that D would undergo a VAT today.

D was put in the lithotomy position. We then outlined the vestibule with a sterile marking pen. Next we applied BLT cream to the outer vestibule and let D sit for 3-5 mins so the numbing could take effect.

We then applied the BLT a 2nd time moving further into the vestibule but staying outside of the hymen and let her sit for another 3-5 mins.

We then applied the BLT cream directly to the vestibular glands staying outside of the hymen and let D sit for another 3-5 mins.

After this we performed Q-tip testing of the vestibular glands and D was pain free from 1, 3, 9 and 11 o'clock. D still had pain at 5, 6 and 7 o'clock. We reapplied additional BLT cream to the areas with remaining pain and let D sit for another 3-5 mins.

CASE #1

On Q-tip test again D was pain free in all vestibular glands and no longer had any PGAD and her PGAD had been very bothersome all morning.

D was almost euphoric at this point asking if this is how "normal people" feel.

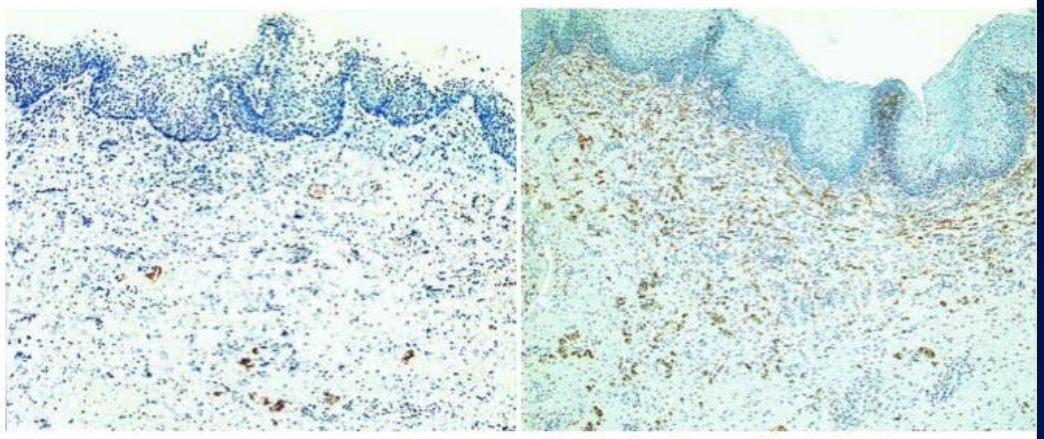
She said her body was so relaxed and she had never felt this way.

Her mother said she was walking and able to move in ways that normally she can not as she always walks like her muscles are so tense.

D's response to the VAT was very positive.

Neuroproliferative Vestibulodynia

S-100 Immunostain

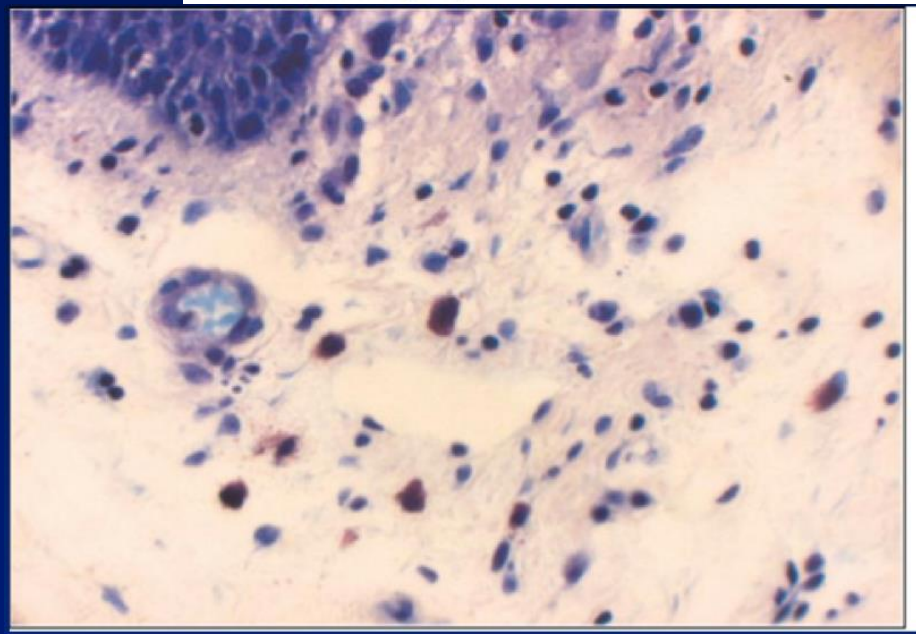


29-year-old control

Only a few nerve cell bundles are detectable (×25)

Patient with vestibulodynia

Abundant proliferation of nerve fibers (×25)



Involvement of Heparanase in the Pathogenesis of Localized Vulvodynia.
Bornstein, Jacob; Cohen, Yitzhak; Zarfati, Doron; Sela, Shifra; Ophir, Ella

International Journal of Gynecological Pathology. 27(1): 136-141, January 2008.
DOI: 10.1097/pgp.0b013e318140021b

FIG. 1 . A x600 Giemsa stain depicting the mast cells subepithelially in a specimen from localized vulvodynia.

Neuroproliferative Vestibulodynia

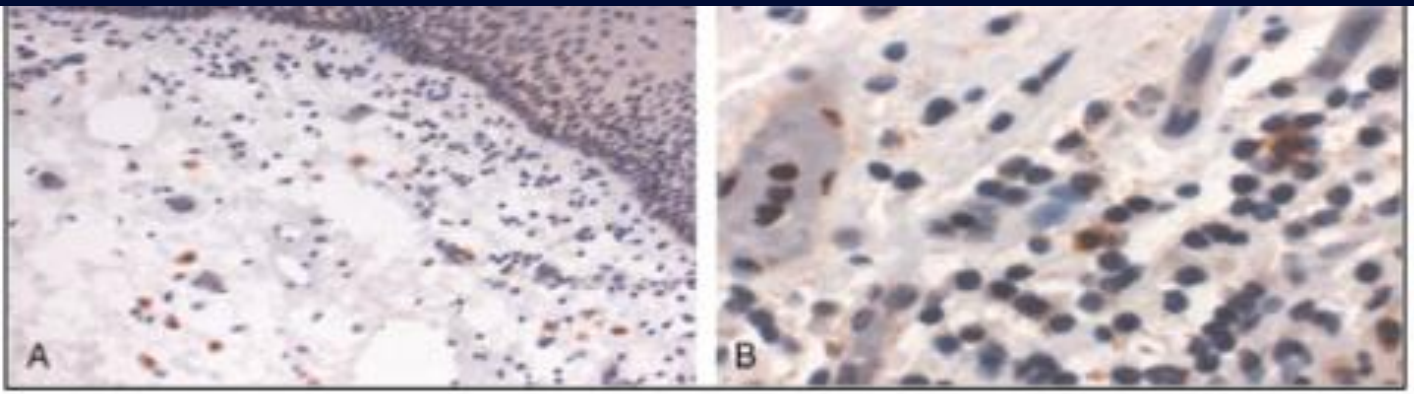


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FIG. 2 . A x400 (A) and x600 (B) CD117 (C-kit) stain depicting mast cells. They are located subepithelially, among other inflammatory cells, in a specimen from localized vulvodynia.

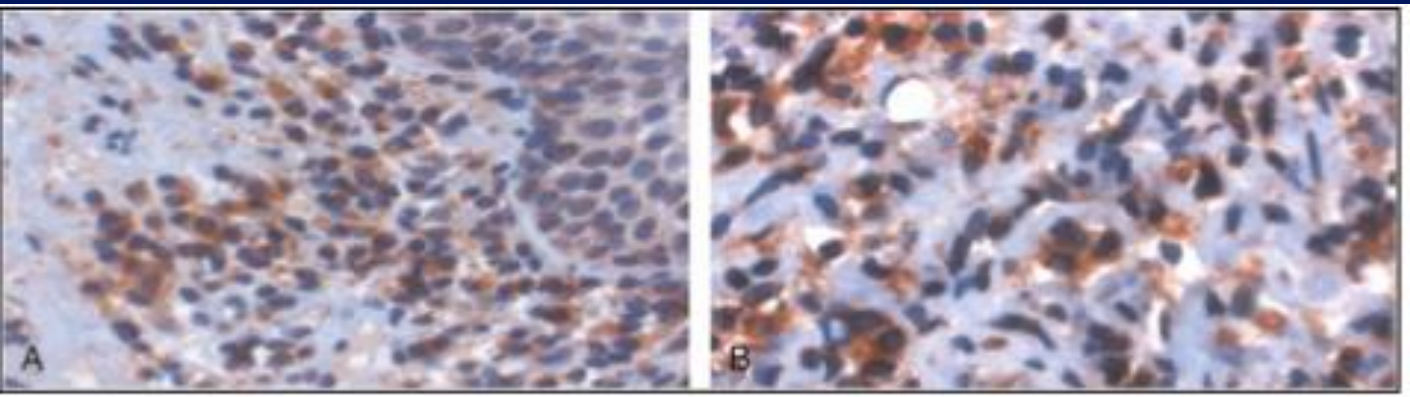

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FIG. 3 . Heparanase expression. x400 (A) and x600 (B). Positive cytoplasmatic staining is seen in the subepithelial layer, close to the epithelial basement membrane.

Neuroproliferative Vestibulodynia

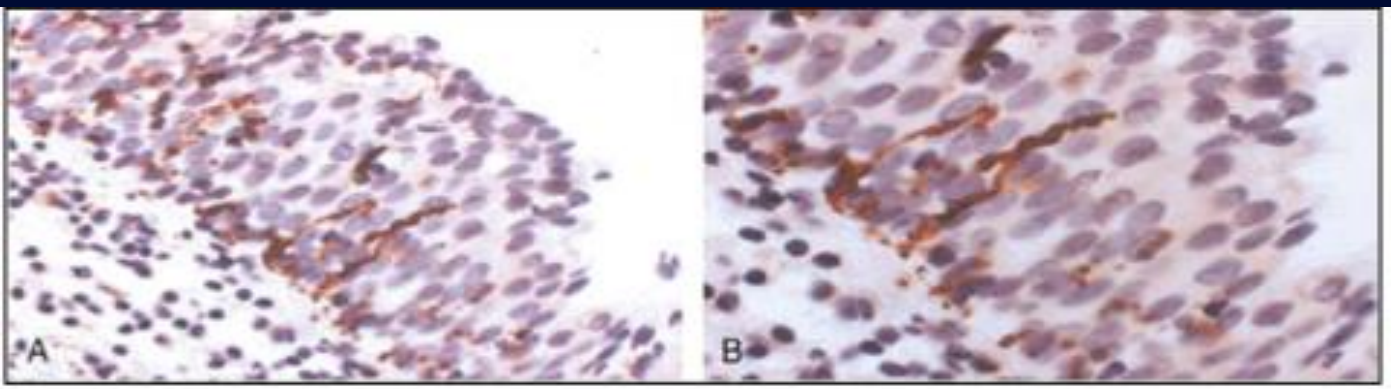

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FIG. 4 . x400 (A) and x600 (B) staining for PGP 9.5. The nerve fibers are seen intruding into the epithelium to more than half its depth.

Characteristic	Score (0–3)						
	Localized Vulvodynia			Control			
	Mean ± SD	Median	Range	Mean ± SD	Median	Range	2-Sided *P**
No. mast cells (Giemsa stain)	2.14 ± 0.378	2.0	2–3	0.14 ± 0.378	0.0	0–1	0.001
Heparanase expression	2.71 ± 0.488	3.0	2–3	0.14 ± 0.378	0.0	0–1	0.001
Subepithelial innervation (PGP 9.5)	2.0 ± 0	2.0	2–2	0.71 ± 0.488	1.0	0–1	0.001
Intraepithelial innervation (PGP 9.5)	2.0 ± 0	2.0	2–2	0.14 ± 0.378	0.0	0–1	0.001

*Wilcoxon rank sum test (Mann-Whitney *U* test).

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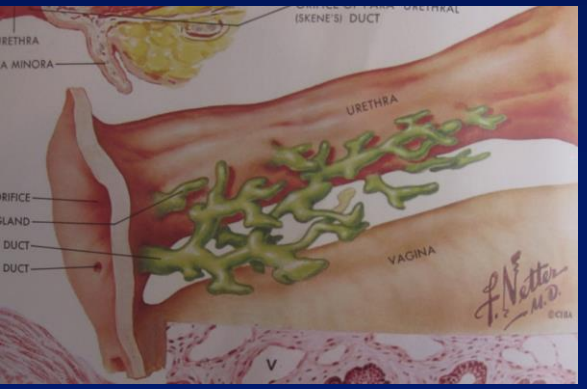
TABLE 1 . Comparison of semiquantitative scores in localized vulvodynia and controls

Neuro-Proliferative Vestibulodynia




9/29/09
4/27/10
3/14/13

CASE #2

S is a 20 year old female here today November 11, 2015 with her Mom K to obtain a diagnosis for her complaints of constant awareness of her urethra, and to better understand the treatment options available to her for this symptom.

S states that prior to age 15 she did not feel any constant awareness of her urethra. S states she used to be an avid runner and is now no longer able to run because of her condition - constant awareness of her urethra. S states she feels awareness increase from the vibrations in a car. S rates her bother from the constant awareness to be 10/10. S states she is currently taking naltrexone, Topamax, and Tizanidine to treat the constant awareness. S states she worked with a physical therapist, AS for about 4 weeks. S states she participated in a neurostimulator trial - that was unsuccessful. S was presumed to have interstitial cystitis.

S states she has sensations of awareness are likely similar to arousal and that the arousal and awareness give her the urge to urinate.

CASE #2

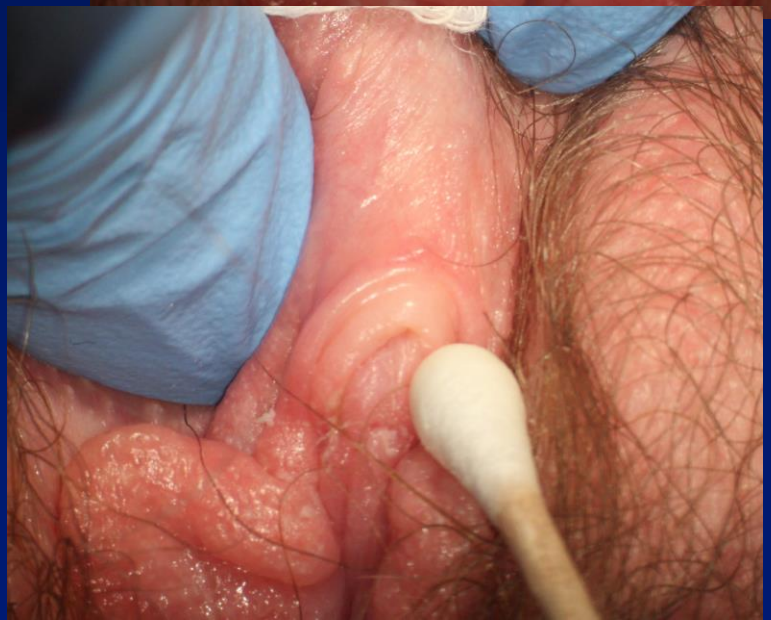
PREVIOUS TESTS

Test	10/23/15	Units	Range
Vitamin D 25-OH Total	22.1	ng/mL	30-100
Thyroid Stimulating Hormone (TSH)	.46	uIU/mL	.45-4.12
Testosterone, Total, Serum	<20	ng/dL	<20-73
Prolactin	8.3	ng/mL	2.1-47.6
Sex Hormone Binding Globulin (Testosterone-estrogen Binding Globulin; TeBG), Serum	54	nmol/L	10-50
Follicle-Stimulating Hormone (FSH, Follitropin), Serum	2.7	mIU/mL	3.0-8.1
Luteinizing Hormone (Lutropin), Serum	1.8	mIU/mL	1.8-11.8
Progesterone	2.2	ng/mL	<.1-.3
Estradiol, Serum (Oestradiol, E2, 17-beta Estradiol, E-17)	60	pg/mL	27-122
Dihydrotestosterone (DHT)	12.8	ng/dL	2.4-20.8
Calculated Free Testosterone [SDSM code]	0.26	ng/dL	0.6-0.8

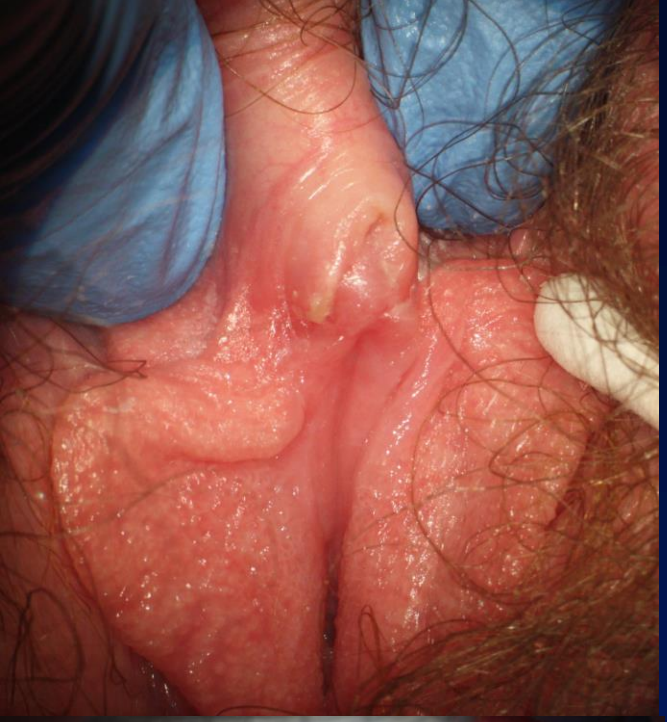
CASE #2

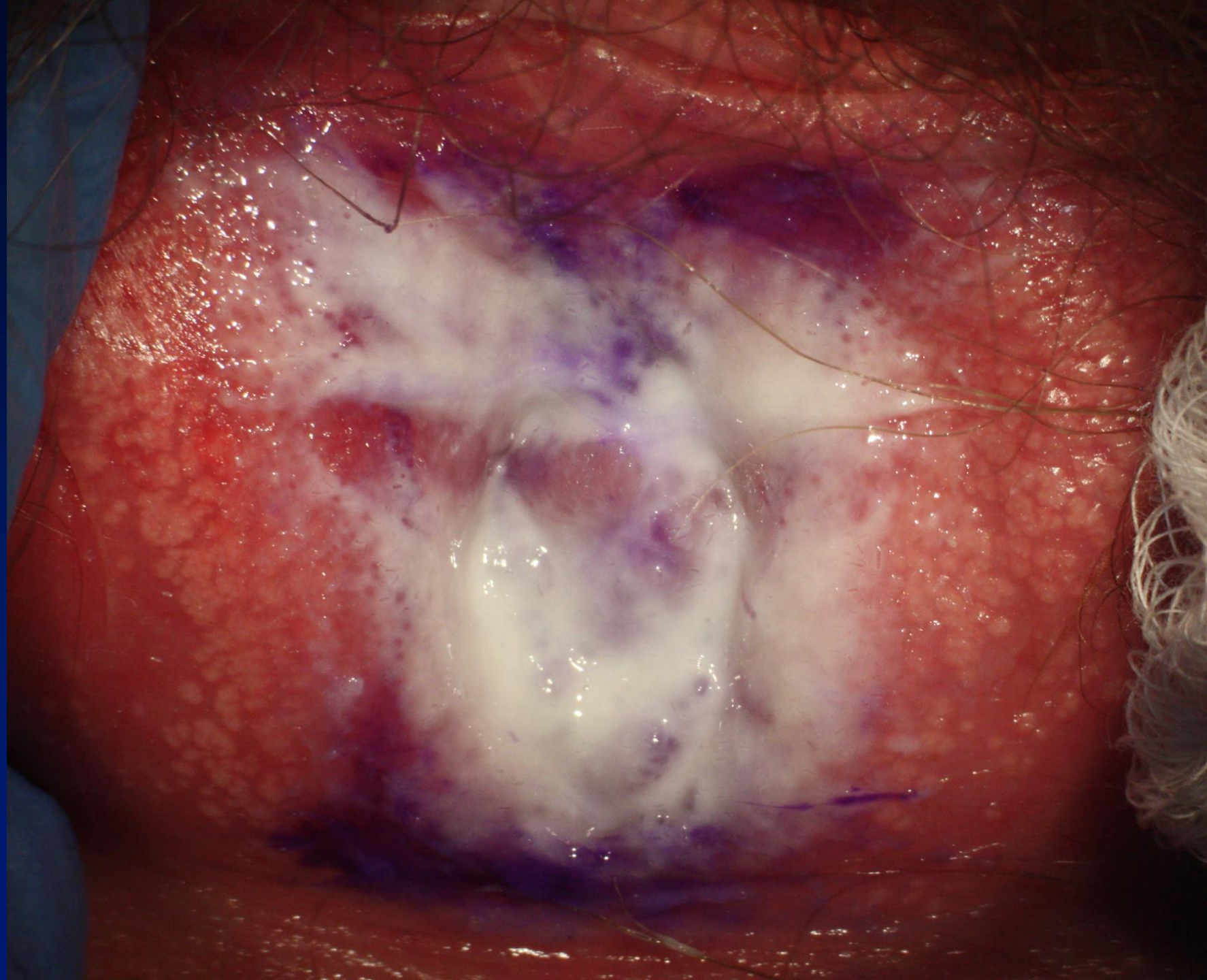
The MRI of the sacral spine S2 to rule out a Tarlov cyst was negative.

CASE #2



CASE #2





PGAD TREE

Brain Central Nervous System Causes

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B. Tumor/Mass/Cyst/Aneurysm in Brain
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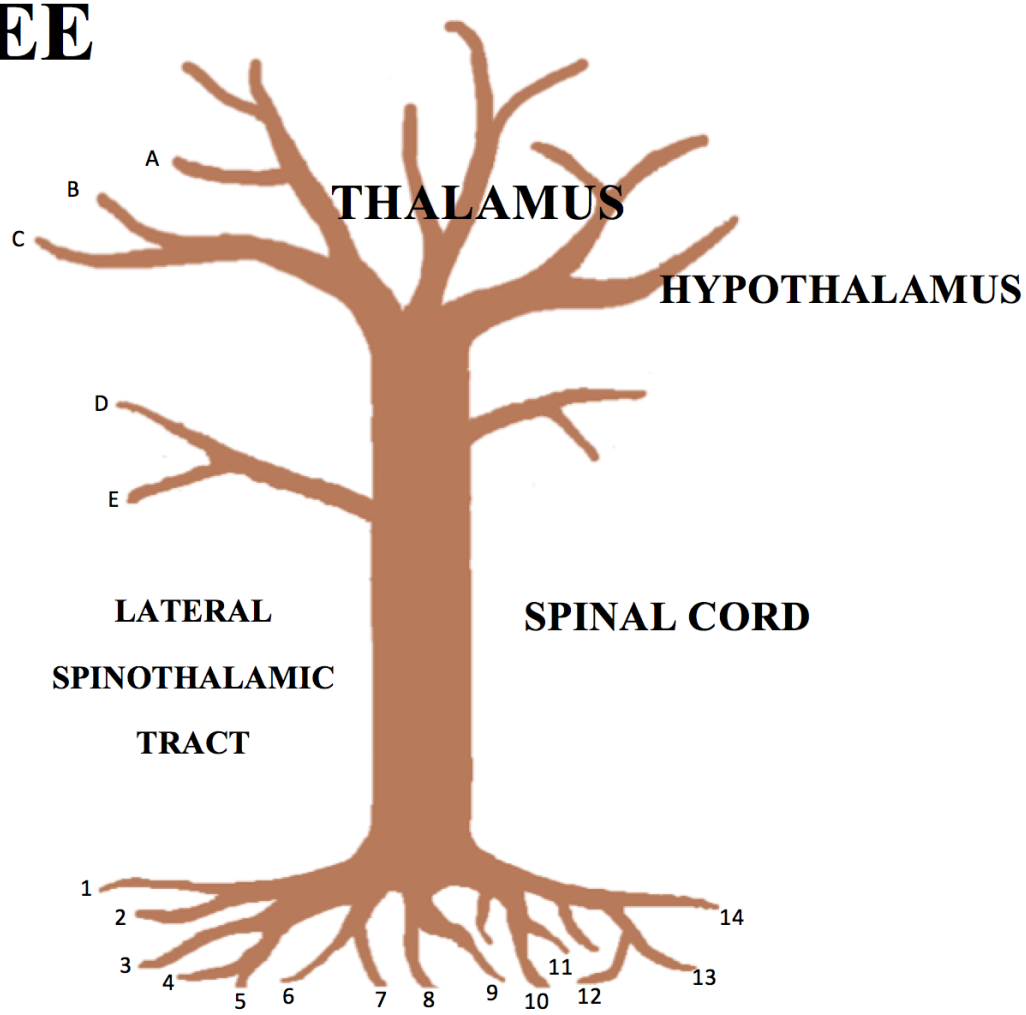
Spinal Cord Central Nervous System Causes

D. Tumor/Mass/Cyst/Aneurysm in Spinal Cord
E. Herniated Disc



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7. Vulvar granuloma fissuratum
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12. S2 Tarlov Cyst
13. High tone pelvic floor dysfunction

It is probable that PGAD exists because of:

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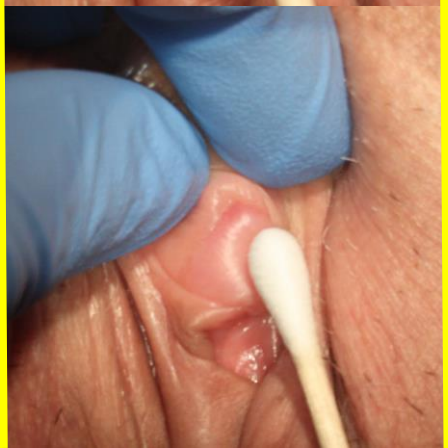
2) **decreased inhibition of the excess information along the lateral spinothalamic tract, thalamus, and hypothalamus**



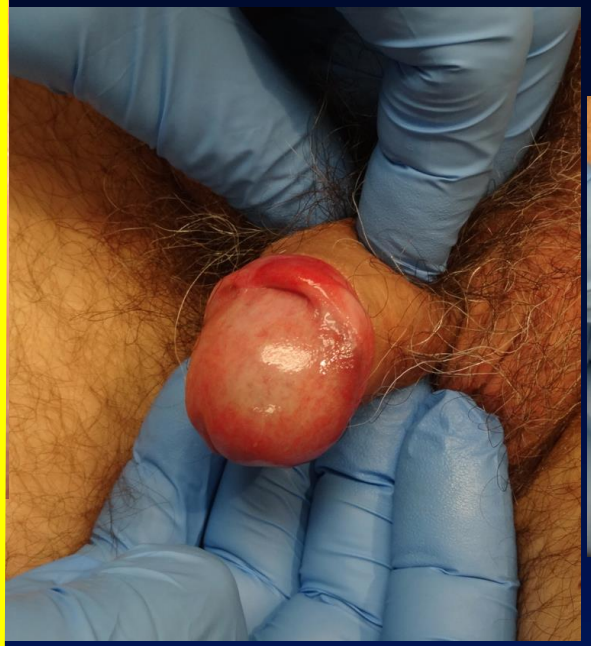






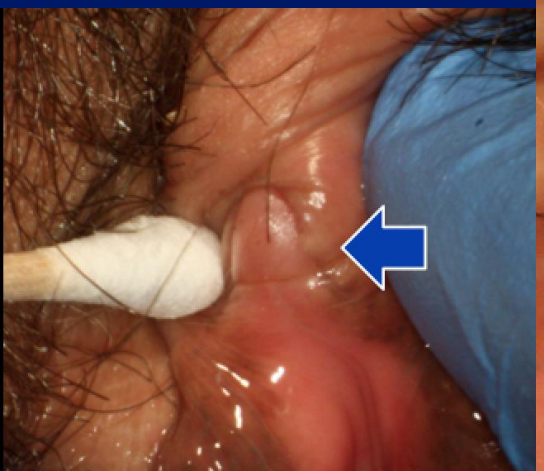



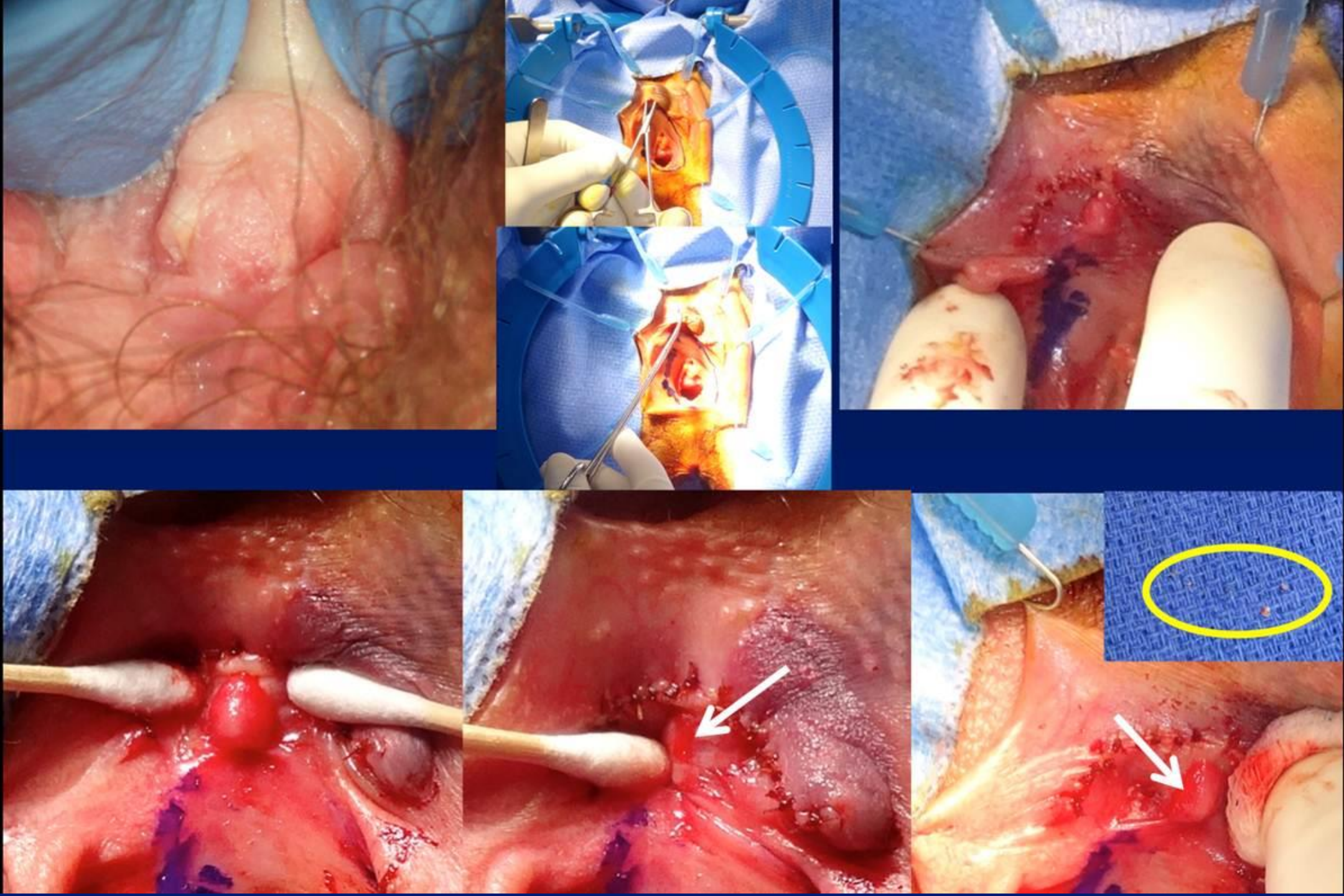










Hormonally Mediated Provoked Vestibulodynia

Treatment:

- Stop hormonal contraceptives
- Systemic testosterone – ideal calculated free testosterone 0.8 ng/dl
- Local to vestibule estradiol 0.02%/ testosterone 0.1% in methylcellulose BID
- Expect no improvement for 6 weeks, 30-40% by 12 weeks

Burrows LJ, Goldstein AT. Vulvodynia. *J Sex Med 2008;5:5-15.*

PGAD MEDS

Here are some of the PGAD meds we discussed

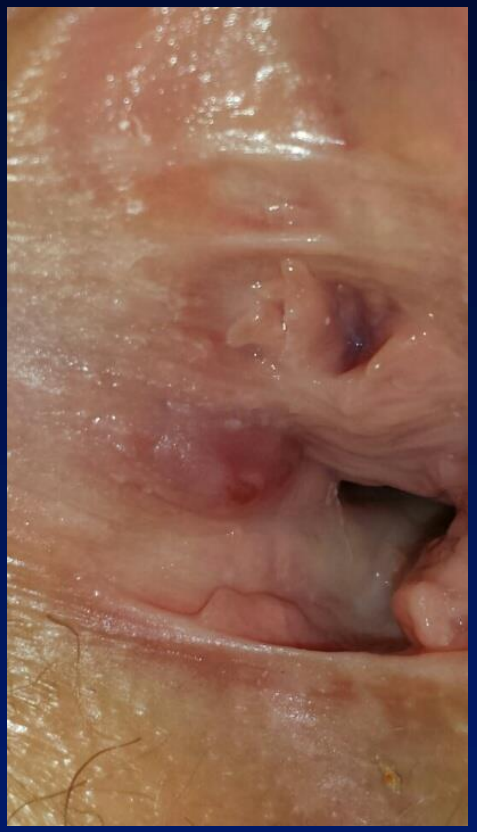
Medication/Supplement	Dosage
Chantix	.5 mg BID - TID
Tramadol	50 mg BID - TID
Clonazepam	.5 mg QD - TID
Lyrica	50 mg TID - QID
Ambien	1 mg TID

CASE #2

Patient is a 32 year-old Caucasian woman who had distressing, bothersome right sided pain during sexual activity and pain during walking

Spontaneously the pain would resolve but hen return every few weeks, seemingly related to her frequency of sexual activity

She went to her local MD who under local anesthesia excised the area of eythema



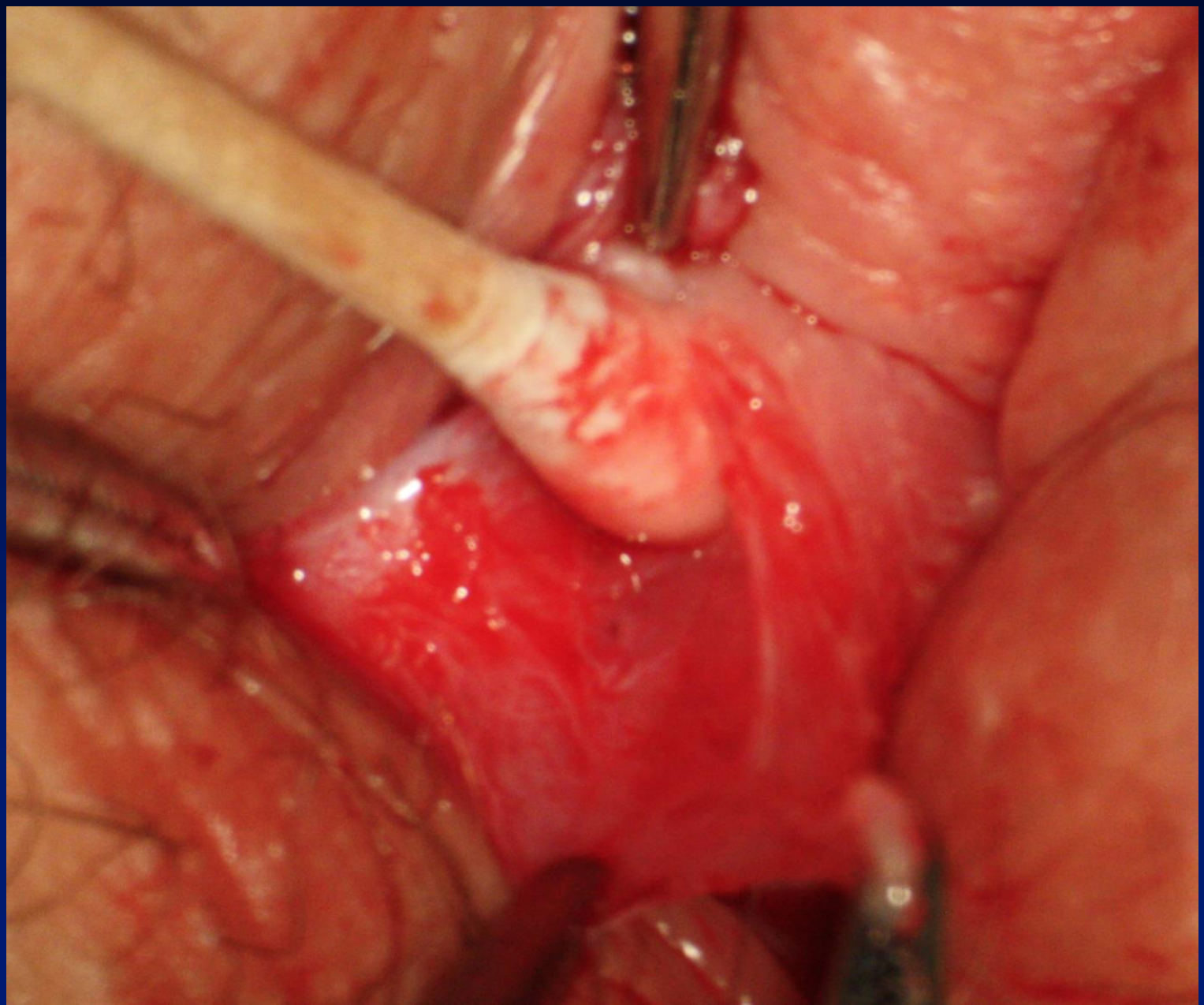
CASE #2

That evening she presented to the ER with acute pain and swelling

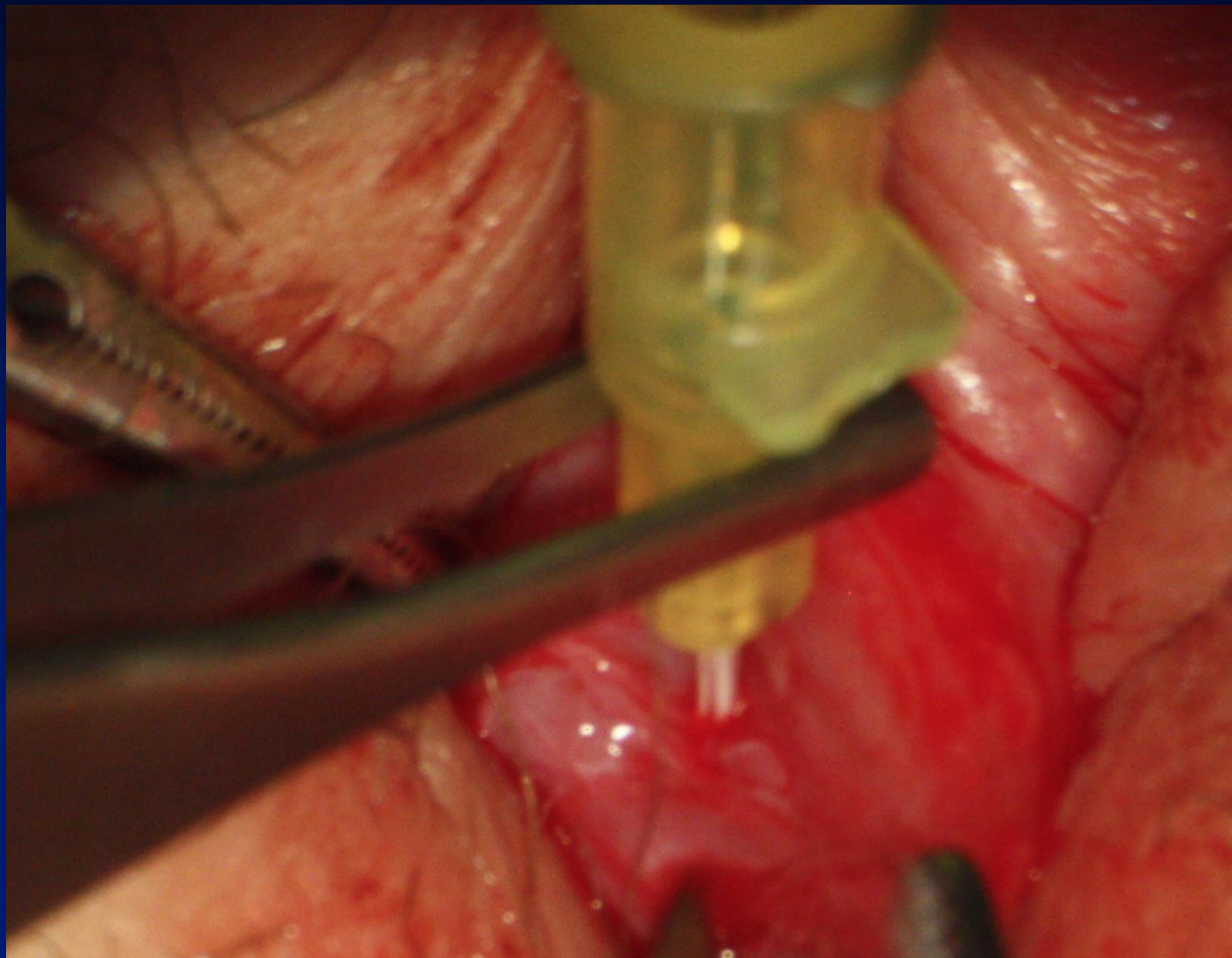
CASE #2

The swelling resolved but the lesion in the right introitus kept returning

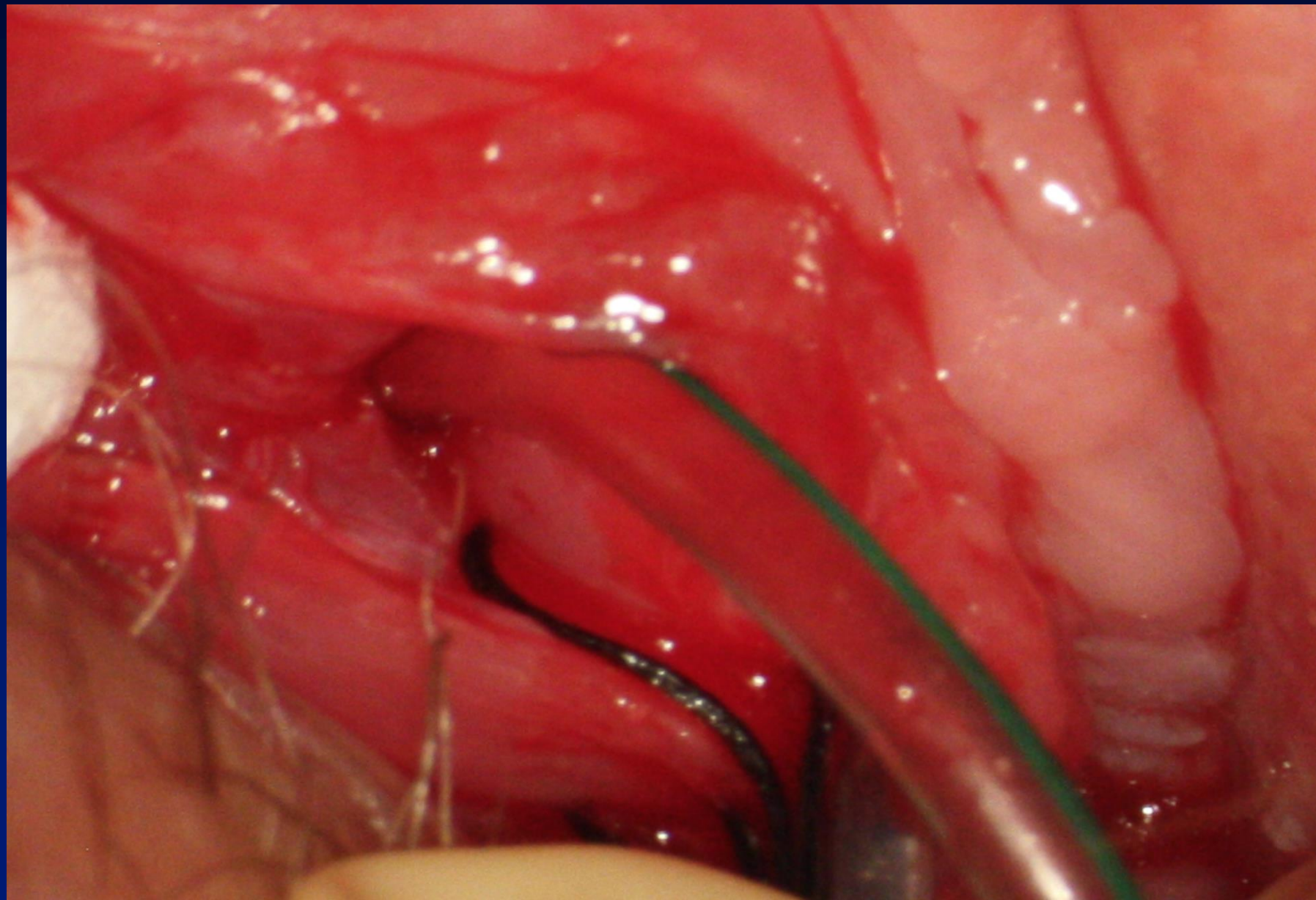
CASE #2



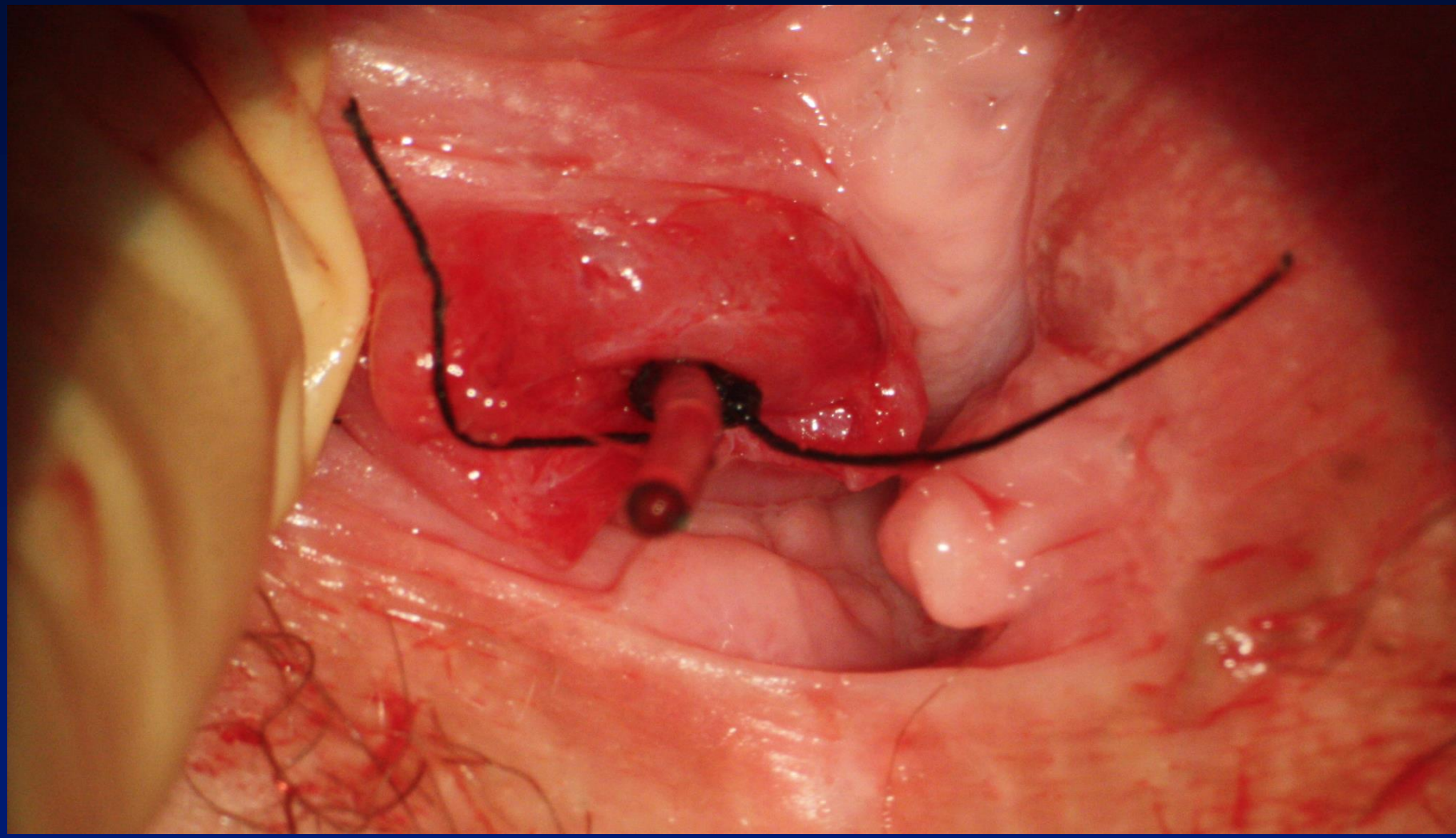
CASE #2



CASE #2



CASE #2



CASE #3

HISTORY OF PRESENT ILLNESS

C is a 39 year-old woman lifelong low sexual desire. C has been on hormonal contraception for 15 years.

C is in relationship with B who is concerned for her.

C can achieve orgasm with vibrators. In general she has limited genital sensation.

C has used Cymbalta - she started this 6 years ago.

C has a frequency of intercourse of 3 /week. Currently her interest is 0% that of previous capabilities. Currently her arousal can be 100% that of previous capabilities. She has 0% orgasmic capabilities. She does not have sexual pain.

CASE #3

VALIDATED OUTCOME SCALES

Total Desire Domain score: 1.2.
Total Arousal Domain: 1.2.
Total Lubrication Domain: 6.
Total Orgasm Domain: 1.2.
Total Satisfaction Domain: 3.2.
Total Pain Domain:6.
FSFI score: 18.8.
SDS-R score: 40/52.
PHQ-9 score: 2.

CASE #3

Vulvoscopy was performed with photography. The patients pubic hair was shaved. Her right labia majora was normal. Her left labia majora was normal. The right interlabial sulcus was normal. The left interlabial sulcus was normal.

The clitoris was smaller normal (1/2 size) - mildly atrophic. The clitoral hood was normal. The frenulum on the right side was normal. The frenulum on the left side was normal. The width of the labia was 10 mm on the right and 10 mm on the left. There was 50% resorption of the right minora in the posterior aspect of the vestibule. There was 70% resorption of the left minora in the posterior aspect of the vestibule. Both labia minora did not meet at the posterior fourchette. The urethral meatus was normal. The right ejaculatory duct was not seen in the peri-urethral glans region. The left ejaculatory duct was not seen in the peri-urethral glans region.

The minor vulvar vestibular gland at 1 oclock revealed no erythema and there was 0/10 discomfort to cotton swab testing. The minor vulvar vestibular gland at 3 oclock revealed erythema and there was 1/10 discomfort to cotton swab testing. The minor vulvar vestibular gland at 5 oclock revealed no erythema and there was 1/10 discomfort to cotton swab testing. The posterior fourchette revealed no erythema and there was 1/10 discomfort to cotton swab testing. The minor vulvar vestibular gland at 7 oclock revealed no erythema and there was 1/10 discomfort to cotton swab testing. The minor vulvar vestibular gland at 9 oclock revealed erythema and there was 1/10 discomfort to cotton swab testing. The minor vulvar vestibular gland at 11 oclock revealed no erythema and there was 0/10 discomfort to cotton swab testing. Speculum examination was performed.

Vaginoscopy revealed normal rugae. The color of the vaginal wall was normal. There was normal discharge. The vaginal pH was 4.5 as measured by pH paper. This study revealed mild clitoral atrophy, 50% labial resorption, mild vulvar vestibulitis syndrome or provoked vestibulodynia.

CASE #3

CASE #3

PREVIOUS TESTS

Test	11/13/13	Units	Range
Dihydrotestosterone (DHT)	<5	ng/dL	5-46
Calculated Free Testosterone [SDSM code]	0.339	ng/dl	0.6-0.8
Vitamin D, 25-Hydroxy (25-OH-D)	18	ng/mL	30-100
Thyroid Stimulating Hormone (TSH)	1.05	uIU/mL	0.34-4.82
Testosterone, Total, Serum	22	ng/dL	14-76
Sex Hormone Binding Globulin (Testosterone-estrogen Binding Globulin; TeBG), Serum	42	nmol/L	17-124
Prolactin	12.9	ng/mL	2.8-29.2
Luteinizing Hormone (Lutropin), Serum	31.2	mIU/mL	1.9-12.5
Progesterone	0.9	ng/mL	0.15-1.40
Follicle-Stimulating Hormone (FSH, Follitropin), Serum	16.0	mIU/mL	2.5-10.2
Estradiol, Serum (Oestradiol, E2, 17-beta Estradiol, E-17)	126	pg/mL	19.5-144.2

CASE #3

Testosterone is in the lower tertile. Dihydrotestosterone is low, calculated free testosterone is 3/8th of the ideal value of 0.8 ng/dl

Low 25 OH vitamin D - please consider starting with 5,000 IU cholecalciferol/ vitamin D3 initially

C has the choices of topical daily testosterone, weekly IM injections, 4-6 months subcutaneous pellet

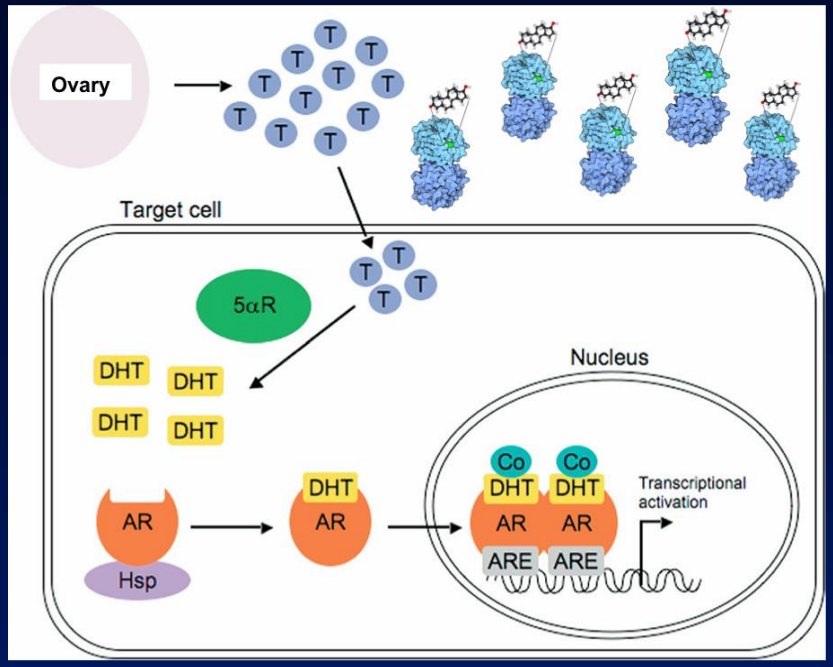
C should consider topical estradiol/testosterone to the vestibule

CASE #3

PREVIOUS TESTS

Test	10/17/14	02/13/14	11/13/13	Units	Range
Calculated Free Testosterone [SDSM code]	3.46	1.01	0.339	ng/dL	0.6-0.8
Dihydrotestosterone (DHT)	47	6	<5	ng/dL	5-46
Testosterone, Total, Serum	192	55	22	ng/dL	14-76
Sex Hormone Binding Globulin (Testosterone-estrogen Binding Globulin; TeBG), Serum	36	32	42	nmol/L	17-124
Progesterone		4.1	0.9	ng/mL	0.15-1.40
Estradiol, Serum (Oestradiol, E2, 17-beta Estradiol, E-17)		42	126	pg/mL	19.5-144.2
% Dihydrotestosterone (DHT), Free			N/A		
Vitamin D, 25-Hydroxy (25-OH-D)			18	ng/mL	30-100
Thyroid Stimulating Hormone (TSH)			1.05	ulU/mL	0.34-4.82
Prolactin			12.9	ng/mL	2.8-29.2
Luteinizing Hormone (Lutropin), Serum			31.2	mIU/mL	1.9-12.5
Follicle-Stimulating Hormone (FSH, Follitropin), Serum			16.0	mIU/mL	2.5-10.2

CASE #3



C started DHT cream and testosterone 2% solution in March and reported for the first time significant boost in her libido.

C reports feeling significantly more aroused, and states that she is experiencing a "normal" 10/10 libido.

C was taking Bupropion, and reports stopping this medication to see the effect on her libido.

She reports a significant decrease in her libido when she was off Bupropion, and is requesting another prescription today.

C reports an increased ability to have an orgasm, but states that she is only able to achieve orgasm with a vibrator.

I counseled C on using amphetamine-dextroamphetamine and Oxytocin Lozenges to improve her orgasm.

CASE #1

Patient is a 31 year-old Caucasian woman who had unrelenting severe pain in the clitoris for 4 days

She is not sexually active

She has not had blunt trauma to the perineum

She is not a bicycle rider and is not a horseback rider

She has no medical history and takes no medication

CASE #1

This is her third episode of acute clitoral pain

She noted spontaneous acute clitoral pain in 2011 and 2013

Both previously resolved over time without intervention

CASE #1

Four days ago, she woke up with the same symptoms of clitoral pain and engorgement – but this did not resolve spontaneously as in the past

She was seen by an MD who was unsuccessful at treating the condition – he attempted direct aspiration at 12:00

The clitoral pain and engorgement was now worse with the intervention

CASE #1

The width of the clitoral shaft was over 2 cms

The prepuce was swollen and the glans was unable to be visualized

There was blood emanating from a previous butterfly needle stick at 12:00 and venous blood was oozing from the area

The clitoral corporal bodies were identified and were palpable as firm and bilaterally quite tender

There were no masses identified in the corpora cavernosa

CASE #1

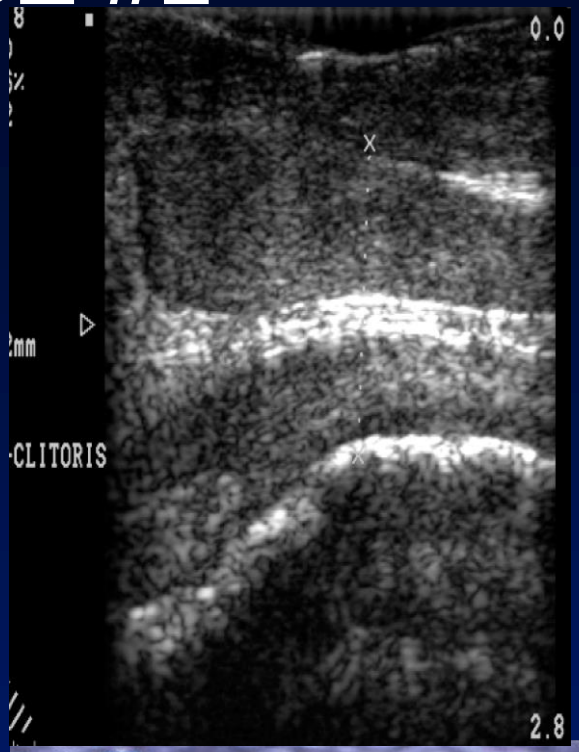
Duplex Doppler ultrasonography –

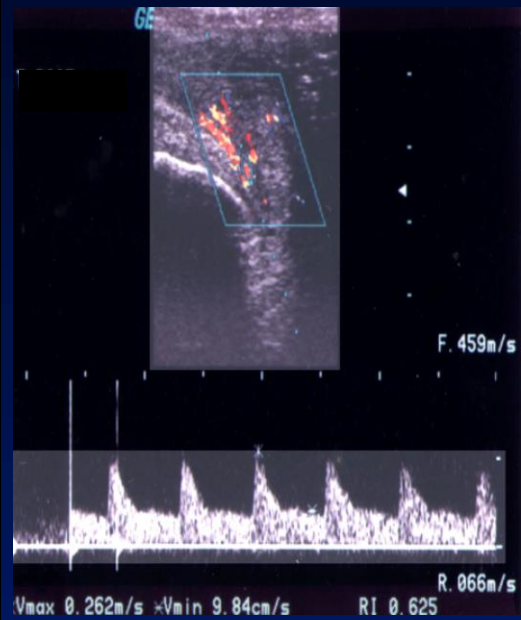
Gray scale studies showed no obvious left corporal fibrosis and no obvious right corporal fibrosis.

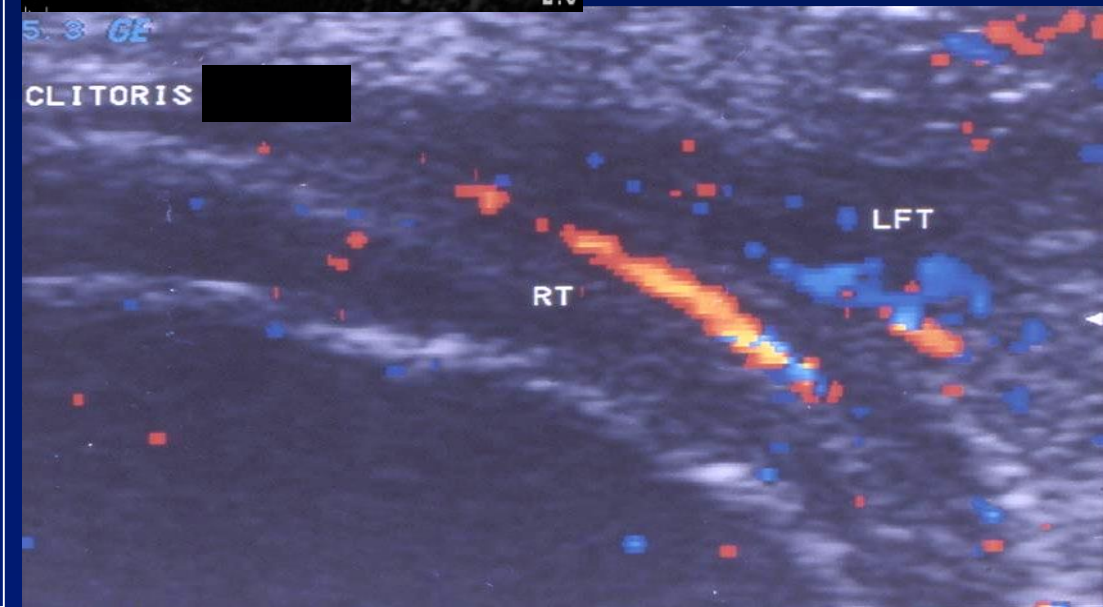
Color duplex Doppler studies showed at baseline the right cavernosal artery peak systolic velocity values were 21.5 cm/s with end-diastolic velocity value of 7.6 cm/sec.

The left cavernosal artery peak systolic velocity values were 26.2 cm/s with end-diastolic velocity values of 9.8 cm/s.

There was no evidence of ischemia or tissue damage or infiltration by metastatic disease.







CASE #1

Treatment options:

1.oral adrenergic agonists such as 12 hour pseudoephedrine - twice daily for multiple days when the onset of priapism is clinically evident

2. direct intracavernosal injection of adrenergic agonists such as 500 ug phenylephrine

3.If recurrent stuttering priapism – surgical shunting

CASE #1

Betadine was applied to the area. A total of 0.5 ml of 1% lidocaine was subcutaneously administered to the 3:00 and 9:00 positions of the mid-shaft of the right and left clitoral shaft

After anesthesia was achieved, direct intracavernosal injection of 0.05 ml phenylephrine (10 mg/ml; 1000 ug = 0.1 ml; 500 ug = 0.05 ml) in 0.3 ml saline - was administered via 31 gauge needle to the right cavernosal tissue

After anesthesia was achieved, direct intracavernosal injection of 0.05 ml phenylephrine (10 mg/ml; 1000 ug = 0.1 ml; 500 ug = 0.05 ml) in 0.3 ml saline - was administered via 31 gauge needle to the left cavernosal tissue

CASE #1

She tolerated the procedure well.

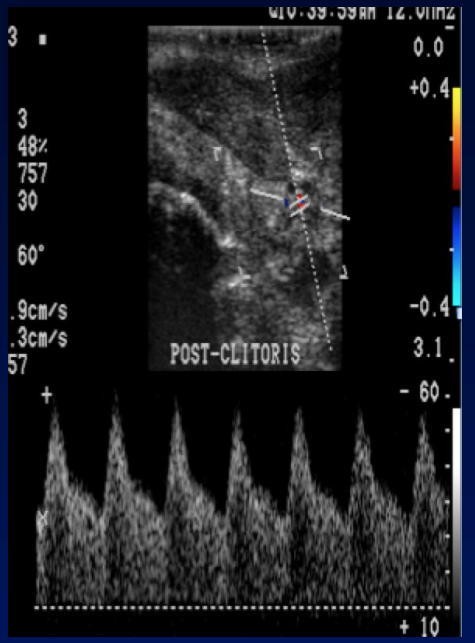
There was immediate shrinkage of the width of the corpora cavernosa.

The new post-adrenergic agonist diameter was less than 1 cm wide.

She felt less tender in the clitoris.

Repeat duplex Doppler ultrasound revealed a post-ischemic hyperemia with cavernosal artery peak systolic velocities greater than 60 cm/sec.

She was advised to ice the area regularly, take opioids for analgesia and to start pseudoephedrine 12 hour - twice daily for 3 days

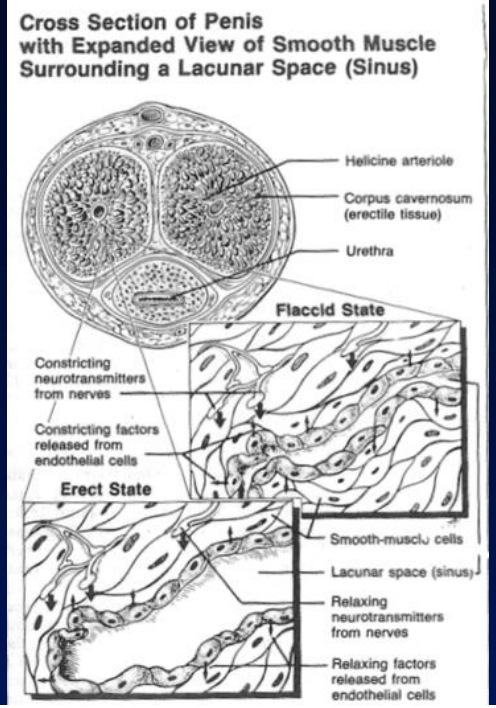


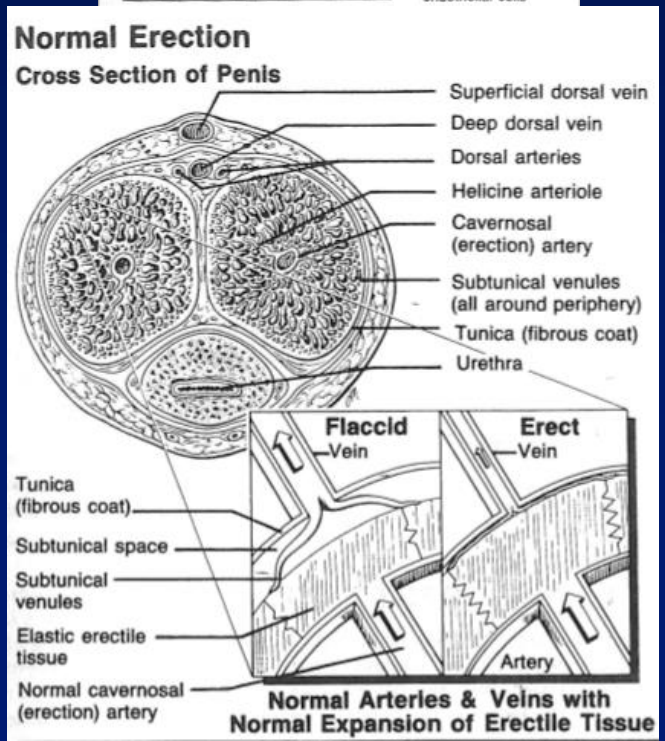
It is hypothesized that idiopathic clitoral priapism is in part a manifestation of the inability of the clitoral corporal smooth muscle cells to contract once relaxed.

This is likely a genetic problem with intracellular calcium returning inside the clitoral cavernosal smooth muscle cells

The inability to get calcium in the smooth muscle cells- maintains compression of subtunical venules and cavernosal engorgement unrelated to sexual stimulation

She has the suspected inability to contract the erectile tissue once relaxed during REM sleep.





Modified Corporal Glanular Shunt with Corporal Snake Maneuver