VULVODYNIA

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Vulvar Pain and Comorbidities

Data from 1183 Cases
The VU-NET Study

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1183 patients with vulvar pain were evaluated from December 2016 to November 2018 in 25 Italian Centres.
VULVAR PAIN: THE REVEALING SCENARIO OF LEADING COMORBIDITIES IN 1183 CASES

Graziottin A., Murina F., Gambini D., Taraborrelli S., Gardella B., Campo M. Vu-Net Study Group

The bar chart illustrates the distribution of BMI categories among patients. The categories are:

- Severe underweight: 0.2%
- Visibly underweight: 1.7%
- Slightly underweight: 10.2%
- Ideal weight: 72.3%
- Overweight: 12.4%
- Obesity I class: 2.9%
- Obesity II class: 0.2%
- Obesity III class: 0.1%

The chart shows that the majority of patients fall within the ideal weight category, with severe underweight and obesity III class being the least common.
Number of previous partners

- 1 partner: 43%
- 2-5 partners: 53%
- 6-10 partners: 3%
- >10 partners: 1%
Vulvar vestibulitis / Provoked vestibulodynia:
vestibular erythema & muscle contraction

A.Graziottin, 2019
Role of levator ani hyperactivity: the "myalgic pelvic floor"

**Co-morbidity:**
- Sexual: INTROITAL DYSPAREUNIA/Coital pain
- Uro-gynecologic: LUTS!
- Proctologic: CONSTIPATION

**Alerting symptoms**
- Pain at tampon insertion
- Vaginal dryness/dyspareunia
- Lifelong obstructive constipation
- Irritative bladder symptoms
- Sex-associated cystitis

Bertolasi et al., 2004; Bergeron et al., 2001, 2002; Glazer et al., 1999; Graziotto et al., 1999, 2004; McKay et al., 2001, Barlow et al., 2004, 2006, Graziotto & Giovannelli 2006, Graziotto, 2020

Vulvar Pain

How to describe the vulvar lesions in the perineal context.

Clinical history

- WHEN did the vulvar pain begin?
  - In childhood: any trauma, unintentional or intentional (abuse, FGM)

- After puberty:
  - after 1+ antibiotic treatment: CANDIDA!
  - after the first intercourse: Vaginismus!
  - after a contraceptive pill: hyperactive pelvic floor & vaginal dryness
  - after partner change: genital dimensions

Graziottin & Murina, Vulvar Pain from childhood to old age, Springer 2/2017
Vulvar Pain

How to describe the vulvar lesions in the perineal context 2.

Clinical history

- **WHEN** did the vulvar pain begin?

- After delivery: 23% have vulvar pain & dyspareunia persisting 18 mths after delivery

- After the menopause: Genitourinary Syndrome of Menopause (GSM), lichen sclerosus

- After medical treatment: iatrogenic - surgery, chemio, radiotherapy, laser: too deep, with neurologic damage

- After onset of neurological diseases: Multiple sclerosis: 62.9% dyspareunia

Graziottin & Murina, Vulvar Pain from childhood to old age, Springer 2/2017
Vulvar pain & HYPERACTIVE PELVIC FLOOR: 
coital pain ("introital dyspareunia") 
bladder and rectal comorbidities

**BLADDER**
- Urge incontinence
- Giggle incontinence since childhood
- Post-coital cystitis 24-72 hours AFTER intercourse
- Bladder Pain Syndrome

**RECTAL**
- Obstructive constipation since childhood
- Hemorrhoids & rhagads
- Dyschezia (if comorbidity with endometriosis)

A. Graziottin, 2020
Diabetes prevalence in Italian population is 5.3% of the total population (16.5% among people aged 65 and over). ISTAT, 2017.
WHY is the GENETIC VULNERABILITY to DIABETES so IMPORTANT?

- It triples (OR=3.0) the vulnerability to recurrent CANDIDA vaginitis
- Aberrant Immuno-reaction to Candida triggers the vulvar inflammatory process leading to vulvar vestibulitis/PV
- It justifies the recommendation for healthier lifestyles:
  - to AVOID sugar foods with glucose and saccarose
  - to do daily aerobic exercise (brisk walking, 30-45')
  - to maintain normal body weight
  - to reduce the vulnerability to the metabolic syndrome

Vulvovaginal CANDIDA = inflammation due to an "aberrant adaptive immune response"

Vaginal infiltration of polymorphonuclear neutrophils (PMNs) in women with symptomatic infection

Vaginal smears of healthy women after inoculation of Candida in the vagina (Papanicolaou staining).

(A) Women who got a symptomatic infection.
(B) Women with asymptomatic Candida colonization.

Infection = result of an innate aberrant immune response
### Clinical History

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent candida</td>
<td>27.3%</td>
</tr>
<tr>
<td>Constipation</td>
<td>23.5%</td>
</tr>
<tr>
<td>Anxiety</td>
<td>15.0%</td>
</tr>
<tr>
<td>Urogynecological surgery</td>
<td>12.7%</td>
</tr>
<tr>
<td>Sleep disorders</td>
<td>11.7%</td>
</tr>
<tr>
<td>Dyspareunia</td>
<td>11.1%</td>
</tr>
<tr>
<td>Dysmenorrhea</td>
<td>10.7%</td>
</tr>
<tr>
<td>Fissures / Hemorrhoids</td>
<td>10.0%</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>10.0%</td>
</tr>
<tr>
<td>Food allergy</td>
<td>0.1%</td>
</tr>
<tr>
<td>Premenstrual syndrome</td>
<td>0.8%</td>
</tr>
<tr>
<td>Muscle pain (e.g., Fibromyalgia)</td>
<td>0.8%</td>
</tr>
<tr>
<td>Low back pain</td>
<td>0.5%</td>
</tr>
<tr>
<td>Menstrual headache</td>
<td>0.4%</td>
</tr>
<tr>
<td>PMS</td>
<td>8.9%</td>
</tr>
<tr>
<td>Headache</td>
<td>18.0%</td>
</tr>
<tr>
<td>Menstrual Headache</td>
<td>7.7%</td>
</tr>
<tr>
<td>Candida</td>
<td></td>
</tr>
<tr>
<td>FSD</td>
<td>43.4%</td>
</tr>
</tbody>
</table>

**References:**

FEMALE SEXUAL FUNCTION

BIOLOGICAL Factors

MOOD
Body Image
Body Feelings

SEXUAL DESIRE & CENTRAL AROUSAL

ANDROGENS
ESTROGENS PROGESTINS

RISOLUTION & SATISFACTION

GENITALS FEEDBACKS PLEASURE

ORGASM

GENITAL AROUSAL & LUBRICATION

Estrogens & topical androgens

Past and recent CLINICAL HISTORY

IBS: 28.0%  8.8%
Constipation: 23.5%  14.0%
Dyschezia: 11.7%  11.0%
Hemorrhoids: 10.7%  10.0%
Abdom Pain: 10.7%  10.0%
Food allergies: 10.1%  1-6%
Total: 94.7%
Rec. Cystitis = 19.5%
Post-coital C = 17.9%
Total = 37.4%
The exciting NEW perspective.

There is a BRAIN in the GUT!

Why is it important for the gynecologist?

It has emotions: «gut feelings»; memories; it suffers from negative biological and psychological events.

- Is it our «unconscious brain»?
- What is its role in our health?
- and in our behaviour?

Modified from V. Stanghellini
The two BRAINS

The Enteric Nervous System (ENS): «the little brain»
1st brain from the evolutionary perspective
it mediates emotions, mood, immunity, pain

The Central Nervous System (CNS)
«the big brain»
It coordinates and commands the neurovegetative, affective, cognitive and motor systems

A. Graziottin, 2020
Human brains connections

The big brain, CNS

The little brain, ENS

BRAIN-GUT AXIS

GUT-BRAIN AXIS

Courtesy of V. Stanghellini
GUT BRAIN: "triumvirate"

- ENTERIC NERVOUS SYSTEM (ENS)
- MICROBIOTA «a real ORGAN per se»
- BOWELS

A.Graziottin, 2020
1. The Enteric Nervous System (ENS)

Auerbach, 1862
Meissner, 1857

1 x 10^6 neurons (exp. animals)
5 x 10^8 neuron (human ENS)
1 x 10^10 neurons (human CNS)

Courtesy of V. Stanghellini

Human gut MICROBIOTA

Nature 2012, ‘The Fellow Travelers’ Human microbiome project

(=10x our total cell number)

- 3.3 million genes = microbiome
  vs.
- 23,000 genes = human genome

- 9 divisions of bacteria
  (mainly Bacteroides and Firmicutes)

GENES ARE PLANS INFORMATION POSSIBILITIES

Modified from V. Stanghellini 2018
A. Graziotton, 2020
Diseases associated with dysbiosis:

- Parkinson
- Infertility
- Obesity
- PCOS
- Chronic Pelvic Pain
- IBS
- IBD

- Multiple sclerosis
- Chronic fatigue syndrome
- Non-alcoholic fatty liver disease
- Atherosclerosis
- Idiopathic thrombocytic purpura
- Obesity
- Insulin resistance/type 2 diabetes mellitus
- C difficile infection
- Irritable bowel syndrome
- Inflammatory bowel disease
3. The BOWEL and the colonic wall: from a selective frontier to the leaky gut syndrome
Increased gut permeability 
NEURAL 
HYPERSENSITIVITY 

FIBROMIALGIA 
IBS 
ANORECTAL PAIN 
BLADDER PAIN SYNDROME 
ENDOMETRIOSIS 
COITAL PAIN 
VULVODYNIA 
INFERTILITY 

CHRONIC PELVIC PAIN!

Modified from V. Stanghellini, 2019

Grazzetti A. Chronic pelvic pain: a clinical perspective
In: Di Renzo G.C., Obstetric and Gynecological Women's Health: Prevention and Safeguard, Springer Verlag 2020
CONCLUSIONS 1.

Vulvar Pain is highly prevalent
(15% of women in the lifespan)

Comorbidities are significant

The VU-NET projects highlights key vulnerabilities and the need of a closer collaboration between different specialists to offer women more effective multimodal treatments.

Graziottin A. Chronic pelvic pain: a clinical perspective

Graziottin A. Murina F. Gambini D. Taraborrelli S. Gardella B. Campo M. Vu-Net Study Group
Vulvar pain: the revealing scenario of leading comorbidities in 1183 cases
In women with Vulvar Pain, Gynecologist should ACTIVELY investigate:

- Family history for diabetes

**Key comorbidities:**
- lifelong or acquired introital dyspareunia: check the tonus of the pelvic floor
- Female Sexual Dysfuntions: check libido, arousal / lubrication, orgasm
- recurrent Candida: investigate diabetes & pelvic floor!
- recurrent cystitis: look for hyperactive pelvic floor
- IBS & abdominal brain: look for dysbiosis
- constipations: evaluate the pelvic floor & diet
- food allergies: evaluate disbiosis, IBS
- headache

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