



GLOBAL INTERSTITIAL CYSTITIS,
BLADDER PAIN SOCIETY

GIBS Newsletter

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Playful Immune System and Bladder Pain Syndrome - NOT ANYMORE

“
*"Some people think;
that to be strong is to
never feel pain.
However, in reality, the
strongest people are the
ones who feel it,
understand it, and
accept it."*
”

The quote is so true for all, who are suffering from Interstitial Cystitis/ Bladder Pain

Syndrome (IC/BPS). Where the whole world is celebrating Christmas and New year, welcoming everyone gracefully with love and affection, however, nothing has changed for the patients suffering from IC. Their life is the same, full of stress, sorrow and, unhappiness. Their life is miserable with huge chunk of medication, embarrassment and struggle to survival.

Here is a story from Professor Vik Khullar, a professor of urogynecology at St. Mary's Hospital and Queen Charlottes Hospital and Imperial College, London. His lecture was based on mast cells, histamine and bladder pain syndrome. He focused on fibromyalgia, a condition in which pain evolves in all four quadrants of the body and axial skeleton and in particular it involves 11 out of 18 tender points through the body.



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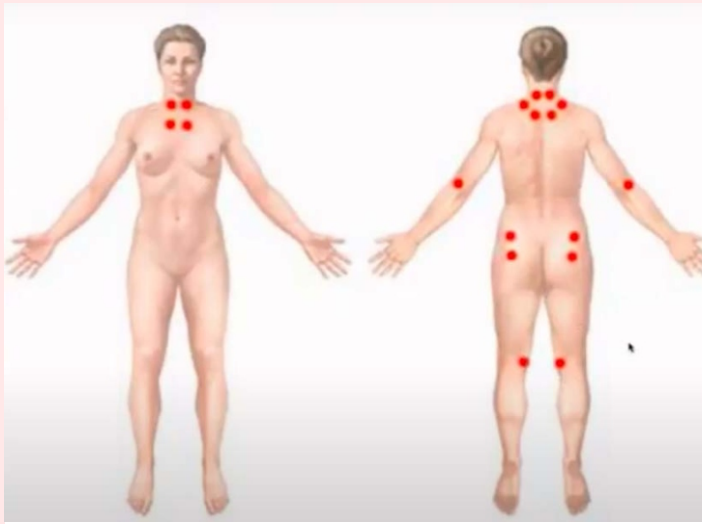


Fig. 1. 18 Tender Points (Out of these 18 tender points, 11 is involved in causing pain)

The tenderness generally is noticed due to amplification of pain signals. He showed the different sites where the pain occurs in the body and the association of the sites to bladder pain syndrome. Hence, such patients exhibit problems of irritable bowel, pain of the musculoskeletal system and, joint problems. BPS is a condition, associated with abnormal central nervous system processing of pressure and visceral sensations. These abnormal processing are associated with motility disorders of the abdominal viscera (irritable bowel) and sleep disorders. Prof. Vik mentioned about different disorders which are related to the He showed the interaction between different bacteria and mucosal-innate immune system and if a patient exhibits a perfect response i.e. not too strong or not too weak then, the urine infection can be cleared from the system very easily. He also pointed out the role of immune system and the bacteria in the human body. If the immune system is weak or absent the bacteria will stay and the person will have lots of bacteria in the urine, however, will not show any urinary symptoms and this would be due to a weak immune system. This mode of response is very commonly seen in elderly patients.

The last group of patients are, the ones who have severe immune response exhibiting lots of inflammation, lots of remodelling and a thick bladder wall due to edema.

The prime role of the immune system is to keep disease out of the body and every human being is assigned with the innate immune system which is developed from birth and involves the first line of defence i.e. the skin or the epithelium and the second line of defence are the innate immune cells which have a non-specific reaction to bacteria, viruses and even temperature changes. There's no memory response, however, there is a memory in terms of if an infection has occurred in the bladder then the cells from the immune system are in the tissues already and this produces a tissue memory.

In terms of Adaptive immune system which is antibodies, this type of immune response is very specific. There's a memory response and this can occur throughout the body. The mast cells activate the sensory nerves by releasing histamines and this lowers the threshold of the sensory nerves. The mast cells also release 25 other inflammatory chemicals leading to increased permeability of blood vessels leading to increased edema and erythema leukocytes migration to the tissues, so they have multiple actions and they release leukotriene 4 and lots of other different histamines.

The other part of the innate immune system is the complement system, where the system consists of C3 and C4, and if the mannose binding lectin is bound to an invader, it activates the complement system, hence the splicing of C2 and C4 is noted. The reduction in C2 and C4 indicates that the system has been activated and the divided C2 and C4 attach together and they themselves divide the C3. This indicates that at each stage they get amplified. The mannose binding lectin is found on the fimbriae on the E.coli. The white blood cells and its podocyte attaches to the mannose binding lectin receptor on the bacteria and hence, it can pull the bacteria in and carry out phagocytosis (engulfment).

What it means in terms of Painful Bladder Syndrome???

Women with joint hypermobility in a study group of 667 women showed that 40% of the

women had reduced level of diamine oxidase. Diamine oxidase is the prime enzyme to destroy histamine and the study showed that 40% of the patients can't have cured foods, fermented products (Cheese). The study showed that 35% women had reduced mannose binding lectin, hence they don't initiate a good complement response. In other terms their complement response system is poor if they have a bladder infection.

It was also found looking at the bladder wall, that the number of mast cells with CD 117 stain and those greater than 28 mast cells per square millimeter which is a normal value was evaluated. It was found in 40% of the women that there were increased number of mast cells i.e. above the normal values, in the tissues due to chemotaxis or increased apoptosis. Most of the patients of this 40% had normal levels of diamine oxidase that could destroy histamine. Hence, the patients had excess mast cells and were overproducing the histamine.

Genes that connect all of the above factors together!!!

Joint hypermobility is very common in fibromyalgia, irritable bowel syndrome and endometriosis. If joint hypermobility is considered, then the alpha-trypsin gene which is associated with fatigue, fibromyalgia, irritable bowel and skin rashes. However, association of this particular gene to bladders were completely ignored. It was found that increased level of serum trypsin was associated with more copies of the alpha trypsin gene, and their treatment essentially were

antihistamines i.e. type 1 and type 2 antihistamines.

Following is the treatment modality for increased mast cells in the bladder...

1. Avoidance of consumption of mast cell liberators. Eg. Cumin, chilli, citrus, tomato, aubergine, chocolate, gluten
2. Intake of Vitamin C, 500 mg twice a day
3. Intake Anti-histamine Type-1 eg. Loratadine, 10 mg twice daily
4. Intake of Anti-histamine Type-2 eg. Famotidine, 40 mg once daily
5. Intake Ketotifen 1 mg at night

Conclusion

Bladder pain is a part of systemic reaction to bacteria by the immune system leading to pain. 40% may have low diamine oxidase (histamine intolerance) and have excess mast cells in the bladder. 20% may have elevated levels of both diamine oxidase and excess mast cells. Hence, these patients tend to present the symptoms at an early age of life, during puberty or as soon as their period starts. They exhibit problems of feeling ill, problems with swallowing or digesting food.

Patients who have reduced diamine oxidase activity or mannose binding lectin exhibit more episodes of urinary tract infections or inflamed bladders, secondary to the abnormal innate immune system. Though diet being the key, the main treatments are antihistamines and the mast cell stabilizers. These key points must be a point of focus in future.



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The Blog is written by : **Dr. Sapna Biswas** [Scientific Writer-GIBS]
while it was presented by me at GIBS 2022 7th Annual Conference on IC/BPS.
- Dr. Vikram Khullar

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