Slide 1

Abdominal Pain : Four Unusual Cases

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Slide 2

Slide 3

Abdominal pain

- We will discuss what causes abdominal pain.
- Approaches to assessing abdominal pain
- We will then look at unusual causes of pains that illustrate some of the previously discussed points.

Slide 4

What causes abdominal pain?

- The neurological basis of pain is at the level of the pain receptors of the GI tract.
- Pain receptors respond to both mechanical and chemical stimulation.

Slide 5

Mechanical stimuli

- Stretch is the major mechanical stimulus.
- Colonoscopy is a great example. We are all experts at what causes pain here. Looping, bowel distention, etc.
- Other mechanical stimuli include torsion, contractions, or compression.
- Mechanoreceptors are located on the serosal wall, in the mesentery, and within the walls of the hollow viscera.

Slide 6

Chemical Stimuli

- There are also receptors that respond to chemical stimuli and these are found in the mucosa.
- Chemical stimuli include histamine, serotonin, bradykinin, prostaglandins, substance P.
- Triggers for these substances may include: inflammation, ischemia, and ingested products.

Slide 7

- Once again, we are all intuitively familiar with how chemical stimuli cause pain in the UGI tract. Why do pts with gastroduodenal ulcers have pain? We biopsy, clip, APC the mucosa and the pt feels nothing.

Slide 8

- The answer is probably related to the inflammation of the gastric or duodenal wall with an ulcer present. This inflamed mucosa in the presence of acid, pepsin, bile causes pain mediated by some of the chemicals mentioned previously.

Slide 9

- Why we have pain with stimulation of these mechanical or chemical receptors is the million dollar question and really not within the scope of this talk, but the type of stimulation and the brain's interpretation of those nociceptive inputs are important in a pt's perception of pain.

Slide 10

Processing of pain signals

- How a pain signal is processed by the CNS is important.
- As we all know, the threshold for perceiving pain from visceral stimuli varies greatly. Our IBS pts tend to be much more sensitive to our endoscopic procedures than others. Experiments where balloon inflation in the GI tract have shown IBS pts feel painful distention at a lower distention pressure vs controls.
- Psychological factors

Slide 11

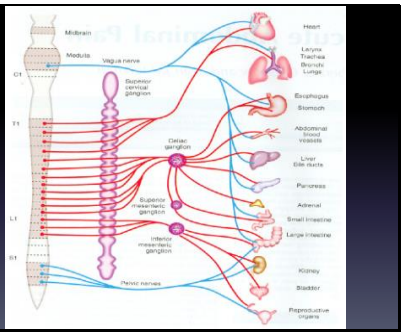
Localization of pain

- The localizing of pain is not very precise but there are some principals.
- 1) GI sources of pain are usually perceived in the midline. It appears that there is bilateral innervation of GI organs. Gallbladder and right and left colons have predominant innervation on one side.
- 2) Pains that are lateralizing arise from organs that have one sided innervation, kidneys, ureters, ovaries, etc.

Slide 12

- 3) Visceral pain is usually perceived in the spinal segment at which visceral afferent nerves enter the spinal cord.
- For example

Slide 13



Slide 14

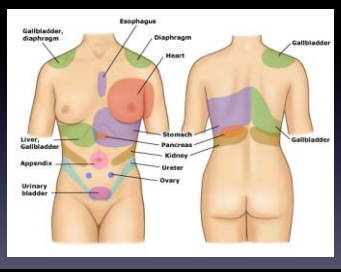
Referred pain

- We are all familiar with this concept where pain originating from a visceral organ is perceived at a site quite distant from that organ. Example, coronary ischemia presenting with arm or jaw pain or gallbladder pain in the scapula.

Slide 15

- Referred pain is usually located in the cutaneous dermatomes sharing the same spinal cord level as the visceral inputs

Slide 16



Slide 17

Extra-abdominal causes of abdominal pain

- Occasionally, the source of abdominal pain is not really coming from the abdomen. Herpes zoster causes a neuropathic pain at the dermatome of the affected nerve. If this is a thoracic dermatome, there will abdominal or chest pain noted before the zoster rash becomes present. There can be fever, abdominal pain that can mimic cholecystitis.

Slide 18

Case History 1

- 39 yo nonsmoking female RN developed acute left lower quadrant abdominal pain after bending to pick up a box. The pain was fairly intense and got slightly worse as the day went on. No fever, chills, N&V, or diarrhea were noted. There was no change in bowel habit. Her LMP was 3 weeks ago. She presented to her PCP the next AM.

Slide 19

PE The pt is afebrile, VSS: her abdominal exam is remarkable for fairly marked tenderness in the LLQ. No distention is noted. There is no rebound tenderness. BS are present.

The presumptive diagnosis?

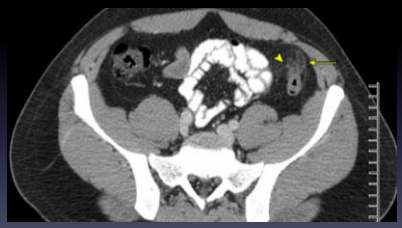
What testing would you consider?

Imaging?

Slide 20

- The PCP ordered an abdominal/pelvic CT as the pt was very uncomfortable, and not improving after 24 hrs.

Slide 21



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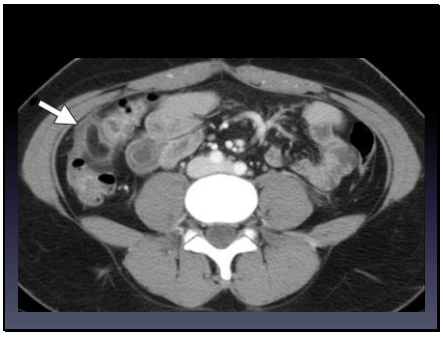

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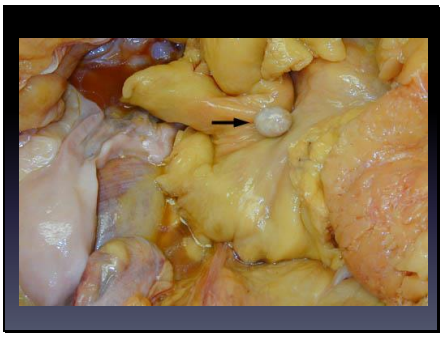
Slide 24



Slide 25

Epiploic Appendagitis

- This is a benign and self-limited condition.
- It occurs when epiploic appendages become twisted with obstruction or thrombosis of a draining vein.
- Usually occurs in decades 2-5; males=females

Slide 26

Treatment

- Supportive only
- NSAID's are very helpful
- Don't operate!
- CT in this case very helpful

Slide 27

Case History 2

- A 22 yo male referred from his college health service. He has had 2 infirmary admissions for abdominal pain, n&v, and diarrhea. The pain is colicky and periumbilical in location. He was treated with iv fluids, anti-emetics and each episode lasted 2-3 days. He had, in fact, had similar episodes dating back to age 16-17. He had a normal colonoscopy and EGD at age 18. He seems to get some prodrome with arthralgias, myalgias, and malaise for a few hours before the abdominal pain begins. His only med is sertraline. There is no FH of IBD or celiac disease. Infirmary labwork included normal CBC, ESR, LFT's, lipase and stool studies.
- What would you do?

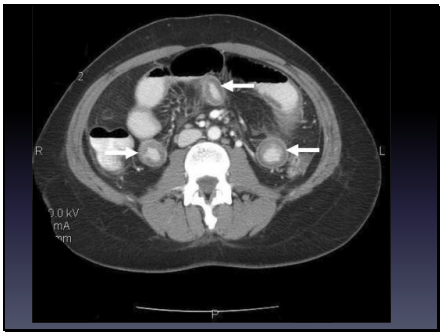
Slide 28

- I repeated labs including celiac serologies, iron serologies and B12. All normal. I thought his sx were small bowel in location. The pt had a small bowel series which was normal.
- ? IBS but sx are so episodic.
- I asked the pt to come to the clinic or ER at the first sign of another attack with a slip for labs, KUB and consideration for CT.

Slide 29

- 2 months later, the pt was hospitalized for 2 days while at home. He again recovered quickly. Labs again normal. CT scanning did show evidence of partial SBO with air-fluid levels and patchy small bowel edema. He followed up with me. Labs were done then.

Slide 30



Slide 31

- Labs were sent for C_4 and C1-inhibitor, 2 proteins in the complement cascade. Both levels were markedly decreased.
- He was referred to the Health Service allergist for evaluation for Hereditary Angioedema or HAE

Slide 32

Hereditary Angioedema

- HAE is a disease characterized by recurrent episodes of angioedema without urticaria or pruritus. It can involve the upper respiratory tract, or the gastrointestinal tract.. The swelling is self-limited but laryngeal involvement can be fatal. Prevalence is 1/50,000. M=F. 1st presentation by age 15. Autosomal dominant inheritance.

Slide 33

Angioedema: 3 Types

- Cutaneous swelling, extremities, face, genitalia. No urticaria. Skin is "tight" or "tingling."
- GI tract
- Upper respiratory, especially larynx, pharynx.

Slide 34

Clinical Characteristics

- Attacks are self-limited, often 2-4 days
- May occur weekly or once or twice a year
- There can be a prodrome, and a mottled rash in 25%.
- Laryngeal involvement develops over hours, unlike in anaphylaxis. There is usually a predyspnea phase with a "lump in the throat," then dyspnea follows.

Slide 35

Gastrointestinal Attacks

- There are varying degrees of colic, n&v, and diarrhea. GI sx are seen in most pts with HAE, and will be the major sx in 25%. These pts will be seen by GI. As before, many of these pts have had appendectomies, etc before dx. Physical findings and labs are nonspecific. As in our case, angioedema of the GI tract may suggest the dx but that is also a very nonspecific finding.

Slide 36

Triggers for attacks

- Minor trauma such as dental work, surgery, endotracheal intubation; oral or genital trauma: piercing, GYN or obstetrical events.
- Association with H. pylori, and reduced attacks after eradication of H. pylori
- Hormones and medications. Attacks occur after puberty. Estrogens, tamoxifen, ACEI.

Slide 37

Pathophysiology

- HAE results from an excess of production of bradykinin with levels often 7-fold increased in an attack. Bradykinin is a potent vasodilator which causes the angioedema. Histamine, PG's are not involved. There are actually 3 types of HAE and 85% are Type 1 characterized by deficiency in C1 inhibitor which is critical in regulation of bradykinin production.

Slide 38

Treatment of HAE

- 1) C1 inhibitor concentrate iv for acute attacks. Plasma derived, but recombinant human product becoming available
- 2) Icatibont. A bradykinin receptor antagonist, and can be given sc.
- 3) Ecallontide. A kallikrein inhibitor. Kallikrein is an enzyme which helps produce bradykinin.
- 4) Plasma if above are not available. Little data on effectiveness.
- N.B. Standard treatments for allergic angioedema are not helpful

Slide 39

Diagnosis of HAE

- Since this is a laboratory diagnosis, one must entertain the possibility of the disease to screen for it.

Slide 40

Indications for screening

- 1) recurrent attacks of angioedema w/o urticaria
- 2) unexplained episodes of colicky abdominal pain
- 3) FH angioedema
- 4) unexplained laryngeal edema
- 5) low C_4 levels
- Only one of the above needed

Slide 41

Screening tests

- 1) C_4 The natural substrate for C1 esterase
- 2) C1-INH levels, both antigen and functional levels recommended
- These levels are usually <30% of normal
- Above will diagnose Types 1 and 2. Type 3 is more complicated.

Slide 42

Case History 3

- 26 yo male smoker with a hx of multiple ER visits for abdominal pain. He is c/o intense, diffuse abdominal pain which began in the early AM and initially seemed lower abdominal in location but became more diffuse as the day developed. Again, he has had the same attacks of pain many times and when they occur he is debilitated for 2-3 days. There is no n&v, diarrhea but he thinks he has had fevers at times. There is no prodrome but he seems to know an attack is coming. He had his appendix removed at age 18 when living in Armenia. He emigrated to the USA 4 years ago. He is well between episodes, and works as a machinist. PMH is remarkable for left knee pain and swelling intermittently. Meds: none. NKDA. On PE, T 102.4, P104, BP 120/78. Abdominal exam reveals diffuse, marked tenderness, mild rebound, and mild abdominal distention. BS are diminished. Labs: WBC 13K, Hct 44, ESR 46, LFT's and lipase nl.
- What to do?

Slide 43

- Surgical consultation obtained in ER.
- CT abdomen ordered; CT shows mild ileus pattern without evidence of obstruction, and some free fluid in the pelvis. Liver, pancreas,GB, bowel appear nl.
- GI consultation requested. Observation with frequent abdominal exams, repeat labs recommended.

Slide 44

- Day 2. Tmax 101.4. Abdomen is less tender but pt is being rx'd with narcotics. Labs unchanged.
- Day 3.T99. Pt clearly improved, passing flatus. Resumes diet. Discharged at end of day. WBC is nl, ESR 22.
- Diagnosis?

Slide 45

Familial Mediterranean Fever

- Diagnosis is very c/w FMF.
- Condition characterized by fever and serosal inflammation.
- Described primarily in pts of certain ethnic groups around the Mediterranean including Sephardic Jews, Arabs, North Africans, Armenians, Greeks, Turks. Seen in others.

Slide 46

Clinical features

- First attack in childhood, adolescence or young adult. Attacks last 1-7 days.
- Serositis can be seen in different sites, primarily peritonitis, but also pleuritis and synovitis/arthritis.
- Lab markers: inflammation, elevated WBC, ESR, CRP

Slide 47

- Diagnosis is primarily a clinical one: 3 criteria
- 1) Is the history compatible? Other conditions excluded? Ethnic background? FH?
- 2) Responsiveness to colchicine
- 3) Genetic testing

Slide 48

Detailed criteria for the diagnosis of FMF

Major criteria

Typical attacks

1. Peritonitis (generalized)
2. Pleuritis (unilateral) or pericarditis
3. Monoarthritis (hip, knee, ankle)
4. Fever alone

Minor criteria

1-3. **Incomplete** attacks involving one or more of the following sites:

1. Abdomen
2. Chest
3. Joint
4. Exertional leg pain
5. Favorable response to colchicine

Supportive criteria

1. Family history of FMF
2. Appropriate ethnic origin
3. Age <20 years at disease onset

4-7. Features of attacks:

4. Severe, requiring bed rest
5. Spontaneous remission
6. Symptom-free interval
7. Transient inflammatory response, with one or more abnormal test result(s) for the white blood cell count, erythrocyte sedimentation rate, serum amyloid A, and/or fibronogen
8. Episodic proteinuria/hematuria
9. Negative laparotomy or removal of normal appendix
10. Consanguinity of parents

Slide 49

Colchicine

Colchicine used in FMF for 40 years. The only clearly effective Rx. It reduces the frequency and intensity of attacks. If taken chronically, it should reduce both frequency/intensity of attacks.

Slide 50

Longterm complications

- Secondary amyloidosis is actually the major cause of mortality in FMF. Noted in 30% Sephardic Jews and 60% of Turks with FMF before advent of colchicine. Markedly reduced with colchicine.

Slide 51

Why Amyloidosis?

- A condition where abnormal proteins normally soluble become insoluble and are deposited in organs/tissues. Secondary amyloid occurs in chronic inflammatory diseases like RA, IBD, chronic infections. An acute phase reactant called SAA is present in high concentrations and is deposited in organs which are then damaged. Renal disease beginning with proteinuria is the most common manifestion in FMF.

Slide 52

Genetic testing

- The FMF gene was cloned in 1997. One can now test for this gene at 2 labs in the US.
- Gene is autosomal recessive but it appears clear that some pts only have one mutated gene.
- NIH study in 1998: the gene noted in 47/86 pts with generally accepted criteria for FMF with 24 homozygotes and 23 heterozygotes.

Slide 53

Case History 4

- This is a 20 yo female admitted with abdominal pain for 3 days, n&v, mild confusion and weakness of the lower extremities. The pain is mostly periumbilical and increased over the last 12 hours. 10/10.

Slide 54

Patient history

- No significant PMH, s/p appy age 10
- Meds: OCP NKDA
- Recent increase in physical activity with plans for running 10 K
- Recent low carbohydrate diet for weight loss

Slide 55

Physical examination

- P 108 BP 168/98 T99.1, O_2 sat 99% RA
- Mildly confused and agitated
- Abdominal exam diffusely tender w/o guarding/rebound, BS diminished
- Neuro exam, Ox3, decreased strength lower extremities 2-3+/4+, DTR's sl decreased

Slide 56

Initial work-up

- Labs: WBC 11K, nl Hct, nl lipase, LFT's, Beta HCG, and negative urine toxic screen. BUN/creat mildly elevated, Na 125, K 3.0. U/A is nl but very concentrated. The urine was amber in Foley bag in ED.

Slide 57

- Head and abd/pelvis CT's are normal
- Pt is pancultured
- Pt is initially admitted to Gen Surgery but after scanning went to Medicine. She is hydrated aggressively with D5NS. Several hours later, she is significantly better. Confusion is gone, lower ext. strength and DTR's normal. Abdominal pain 4/10.

Slide 58

Hospital course

- The patient continued to improve. Her abdominal pain was essentially gone in 2 days. Neuro, ID consultants followed the pt. Initial concern for Guillain-Barre or encephalitis diminished. A preliminary dx was made.

Slide 59

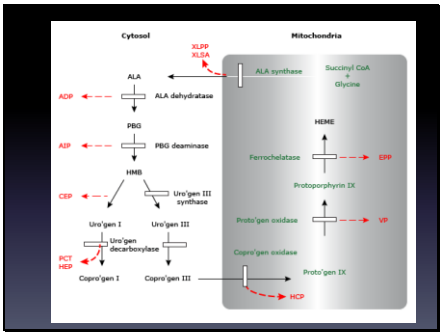
- A preliminary diagnosis of acute intermittent porphyria is made.

Slide 60

The porphyrias

- The porphyrias are metabolic disorders caused by enzyme deficiencies in the biosynthesis of heme. Heme is the oxygen avid component of hemoglobin. There are different porphyrias depending on the inherited enzyme deficiency.

Slide 61



Slide 62

Acute intermittent porphria

- AIP is an autosomal dominant disorder resulting from a deficiency of porphobilinogen deaminase (PBGD).
- AIP symptoms are due to effects on the visceral,autonomic, peripheral and central nervous systems.

Slide 63

Slide 64

- Most pts with this inherited enzyme deficiency never develop symptoms such that they will not have a very recognizable FH and generations are skipped.

Slide 65

Typical presentation

- Attacks are often first noted in the 3rd or 4th decade.
- Attacks develop over hrs to days and last days to weeks.
- Abdominal pain occurs in 85-95% of pts and is the most common symptom. Pain is steady and severe. Ileus and constipation often occur.

Slide 66

- This is a neuropathic mediated disease and not an inflammatory one so there usually is no fever, elevated WBC's, peritoneal signs.
- Urinary retention is common. Dark or reddish urine can be seen.

Slide 67

- Peripheral neuropathy is frequently seen as in this case presentation. There can be chest or extremity pain/numbness/parasthesia as well as motor weakness.
- Autonomic neuropathy effects include tachycardia, hypertension,diaphoresis,tremor.

Slide 68

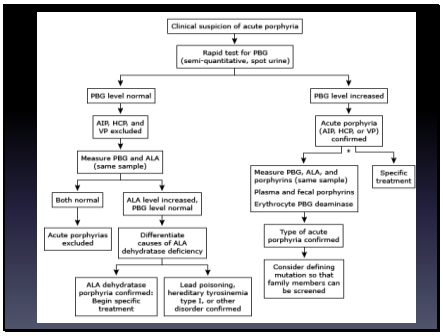
- Neuropsychiatric manifestations are also seen frequently, including restlessness, agitation, anxiety, hallucinations, and change in mental status. Seizures are also seen.
- Repeated attacks can lead to renal disease, chronic hypertension. Transaminases can be elevated.

Slide 69

Diagnosis

- The diagnosis is most easily made during an attack.
- The initial screening test is a spot urine for porphobilinogens. If positive, you have diagnosed an acute porphyria.

Slide 70



Slide 71

Treatment of AIP

- 1) Hospitalization: pain management, iv treatment, observation for repiratory problems
- 2) Carbohydrate loading
- 3) Hemin or panhematin. It binds to albumin and is transported to hepatocytes and reconstitutes the regulating heme pool which turns off synthesis of porphyrin production

Slide 72

Prevention of attacks

- Prevention of attacks is critical.
- 1) cessation of smoking
- 2) avoidance of certain medications, which increase cytochrome p450 enzymes
- 3) endocrine factors: esp. progesterone, testosterone, less so estrogen

Slide 73

Longterm issues

- 1) Renal failure
- 2) Liver disease. Transplantation in setting of frequent attacks. HCC.

Slide 74

- THANK YOU !