Signa Vitae

EDITORIAL

Nonspecific abdominal pain: Do I have to allocate a specific diagnosis for every patient?

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Abstract

Acute abdominal pain is one of the most common chief complaints in the acute setting all over the world. The definitive diagnoses of these patients vary depending on age, gender, geographical and sociodemographic characteristics *etc*. Apart from these, aging of the population, obesity, advanced diagnostic imaging modalities and changes in nutritional habits also have an impact on the rates of specific diagnoses. On the other hand, nonspecific abdominal pain constitutes almost half of all visits due to acute abdominal pain in the acute care setting. This phenomenon is the main differential diagnostic problem in the management of these patients because missing a life-threatening condition can cause enormous medicolegal problems for the caregivers. Certain diagnostic scoring systems have also been developed to facilitate recognition and management of these conditions. This article aims to review the entity and underline the challenges it can bring to the scene.

Keywords

Abdominal pain; Nonspecific abdominal pain; Diagnosis; Differential diagnosis; Radiological evaluation; Diagnostic score

Acute abdominal pain (AP) is one of the most common complaints seen among patients in the emergency departments (ED) and other acute care units. Recent broad-based, cross-sectional studies pointed out these visits accounted for around 6% to 10% of all ED census [1, 2]. The objectives of this manuscript is to highlight the mechanisms of abdominal pain, underline the current status of rational approaches to diagnose and manage patients with AP in the acute setting with the emphasis on general diagnostic pathways to predict operative interventions and recognition of nonspecific abdominal pain (NSAP).

Around one third-to one half of patients with abdominal pain (AP) admitted to hospitals do not receive a significant diagnosis, and thus these patients are diagnosed with NSAP. Broad studies cited that NSAP constitute 30% to 51% of all visits due to acute AP in the acute setting [3, 4]. This phenomenon is closely linked to age, sex and historical features of a given patient. For example, as age progresses, certain diseases such as biliary system diseases, malignancy, ischemic bowel disease, and intestinal obstruction take predominance as etiologies of AP. In general, definitive diagnoses comprise acute appendicitis (AAp) (28%), biliary system diseases (10%), acute gynecological diseases (4%), intestinal obstruction (4%) in this context. A Greek study investigated the evaluation processes and final diagnoses of the patients presented with acute AP in the ED and disclosed that the percentage of NSAP (cited as patients who had "no final ED diagnosis") was reported to be 13.6% [5]. While 37.5% of the patients were admitted

to the hospital, acute gastroenteritis and acid-peptic diseases constituted more than 25% in this case series.

The mechanisms and pathogenesis of AP: International Association for the Study of Pain (IASP) classified pain into three major classes—nociceptive pain, neuropathic pain and inflammatory pain [6]. While nociceptive pain is the sensation that begins with the stimulation of nociceptors and ends with treatment, neuropathic pain is pain that occurs in the nerves as a result of trauma or a metabolic disease such as diabetes, which is directly affected by pain sensors.

In humans, nociceptors are the undifferentiated terminals of the thin myelinated (A-delta) and unmyelinated C fibers. A-delta and C fibers are responsible for the transmission of pain. A-delta fibers transmit sharp, initial pains; C fibers, by contrast, transmit dull or burning pain.

To be more specific, the classification of AP is dichotomous: Visceral and somatic.

Visceral pain is a type of pain originating from the internal organs. This type of pain is ill-defined, not well localized, is felt in a wide area, and its changes are also felt much slower than somatic pain. C fibers are unmyelinated nerve fibers which are responsible from slow (no faster than 2 m/s) and dull pain sensation originating from tissues. With these features, it can cause pain to be felt away from the diseased or inflamed organ. This phenomenon is linked to the large extent of ascending and descending (afferent or efferent) nerve fibers from the spinal cord, innervating the viscera. The degree of pain generally does not match the severity of organ injury. Visceral

pain is often associated with marked autonomic phenomena, including pallor, profuse sweating, nausea, gastrointestinal disturbances and changes in body temperature, blood pressure and heart rate. It can also produce strong affective responses and leads to sensitization of somatic tissues.

Somatic pain, on the other hand, is transmitted by fibers (peripheral nociceptive nerves). originating from almost all tissues. Primary afferent fibers, (i.e., unmyelinated C-fiber and myelinated $A\sigma$-fiber) remain silent during homeostasis in the absence of pain and are activated when there is a potential of noxious stimulus. Somatic pain extends along sensory fibers while visceral pain is conducted via autonomic fibers. Somatic pain is initially felt as sharp, then there is burning or throbbing sensation as the response is modulated. In contrast, visceral pain arises from visceral nociceptors that converge on the same neurons in dorsal root ganglions that receive somatic input. This is the reason why this type of pain is poorly localized, dull and painful with marked autonomic activation. These sensations can then turn into sharp, localized, reflected pain.

For example, AAp mostly causes periumbilical pain from visceral origin. This pain sensation originates from visceral afferents that supply the small intestine and enter the spinal cord at the T10 level by passing through the celiac ganglia and splanchnic nerves. This input sensitizes the dorsal horn in T10, resulting in sensitization of all dorsal horn nociceptive neurons and ultimately pain perception in the T10 dermatome. As appendicitis progresses, the pain is localized in the right lower quadrant as the inflammation engulfs the parietal peritoneum with the same nerve supply as the upper dermatome, which is termed as somatic pain.

In general, acute AP is essentially triggered by irritation of the parietal peritoneum. It is also provoked by infection, chemical irritation (like spilled bile, faeces or urine into peritoneal cavity), and/or trauma.

When the inflammatory process expands and eventually irritates the peritoneum, the somatic component is activated and the pain is much better localized by the conscious patient. It is often described by patients in the form of severe "sharp" pain. Typically, this course is observed in pathologies such as AAp and acute cholecystitis, which are in direct contact with the peritoneal lining.

Age and sex: Two important factors for the definitive diagnosis of AP are age and gender. Peptic ulcer, gastritis, urinary stone disease and AAp are more common causes of AP encountered in men, while NSAP, biliary tract diseases, functional bowel disorders including Irritable Bowel Syndrome (IBS), urinary tract infections (UTI) and pelvic inflammatory disease (PID) are predominant in women.

The female-to-male ratio in those considered to have NSAP is around 2.4 to 3 in some studies [7, 8]. The average age is between 38 and 41. 90% of patients with NSAP recover in the first few weeks or remain asymptomatic, up to 10% may have some disease, for example, 1/3 of them develop AAp. In the doctorate thesis study conducted in Izmir/Turkey, it is shown that 46% out of 684 AP patients were discharged from the university-based ED with the diagnosis of NSAP. Of note, 9% of them were re-admitted within the first 3 days and there were several patients with de novo diagnoses of acute abdominal conditions [9].

Differential diagnosis (DD) of NSAP: Before diagnosing a patient with NSAP, serious causes of AP which mandate emergency surgical intervention must be excluded from the long list of differential diagnoses (DD). A significant decline in the rate of NSAP has been marked with the increased accessibility of laboratory and radiological modalities within the last decades, especially after 1990s.

Unlike many entities presenting to outpatient clinics and those admitted to the wards, the origin of acute AP is difficult to diagnose provided with the complexity and closeness of the structures in the abdomen. Nonetheless, giant advances have occurred in recent years related to the diagnosis and treatment of patients with acute AP. Computed tomography (CT), magnetic resonance imaging, and most importantly, bedside, point-of-care procedures like ultrasonography (USG) have been developed and expedited diagnostic and therapeutic methods of the patients with AP. Point-of-care ultrasonography (POCUS) represents a revolution in practical and rapid imaging and diagnostic decision making. A recent meta-analysis disclosed that USG showed significant accuracy of diagnosis in patients with suspected AAp (the diagnostic odds ratio was 6.88 (95% Confidence Interval (CI) 1.99–23.82)) [10]. This modality can be complemented with CT, laboratory adjuncts and other necessary investigations tailored for the patient. Such an integrated approach creates an expedient path to the operation room in most cases within the context of acute AP (e.g., ectopic pregnancies, aortic catastrophes, visceral perforations *etc.*).

Likewise, extraabdominal causes have the potential to precipitate the symptomatology attributed to abdominal conditions. Extremes of ages, pregnancy, conditions with immune deficiency, usage of certain drugs complicate the diagnostic processes and represent substantial challenges for the caregivers in establishing diagnosis and starting due management.

The rate of specific diagnoses and need for surgery boost with the advancing age. For example, vascular causes such as aortic dissection, aneurysm and mesenteric infarction have a considerable share of 10% of all AP in people over 65 years of age. Only one tenth of this age group is discharged without provisional diagnosis (i.e., with a preumptive diagnosis of NSAP). Surgical intervention requirement in patients with AP is 33% in those over 65 years of age, while only 16% in the others. In patients around 80 years of age, mortality due to AP is around 7%, which is 70 times higher than that of young adults. In this context, specific diagnoses can be elusive in elderly patients in most clinical scenarios. Diagnostic scores have been launched by researchers to increase accuracy of presumptive diagnoses and minimize the rate of missed or delayed diagnoses. Eskelinen *et al*. [11] disclosed that diagnostic scores formula was superior to both the clinical evaluation (history and physical examination). Employment of diagnostic scores is proposed to be a part of the diagnostic decision-making process in those with suspected AAp and the elderly individuals presented with acute AP.

The overall sensitivity of the clinical history-taking for detecting AAp was 83% (95% CI=72–92%). The five best symptoms of AAp (location of initial pain, location of pain at diagnosis, type of pain, nausea, and vomiting) showed a specificity of 53–90%. More interestingly, some researchers pointed out that diagnostic scores devised to identify NSAP

may be more successful than history taking (symptoms) and evaluation of signs and tests [12]. In receiver operating characteristic analysis, the area under curve (AUC) values for diagnostic scores were found to be as high as 0.87 (95% CI=0.85–0.90) which represented significantly more accuracy than symptoms and signs. Gender, location of initial pain, location of pain on presentation, progression of pain, relieving factors, previous similar pain, vertigo, jaundice, mood, distension, mass, rebound, guarding, murphy, bowel sounds, leucocyte count, urine analysis were found to be contributors in the diagnosis of NSAP.

After all, the most prominent component of the process of diagnosis and management consists of evaluation of the patient with an elaborate history and a thorough physical examination. In other words, a well-received history and a detailed evaluation are mostly sufficient to establish the preliminary diagnosis of around 80% to 90% of the patients presenting with AP. An individualized approach for evaluation will be a major help for the physician which can not only narrow the list of differential diagnosis, but also pave the way to easier access to definitive treatment, preventing unnecessary delays with cumbersome investigations.

The biggest mistake that can be made is to order biochemistry and imaging studies to approach a diagnosis without full history and examination. In this way, a patient who can be diagnosed with myocardial infarction by examining his/her Electrocardiogram (ECG) can even be sent to radiology unit for abdominal CT and his death can be caused. Men over the age of 40 must be thought to have a heart attack until proven otherwise. Always ask for an ECG and assume coronary syndrome. When a presumptive diagnosis is robust and logical, practical interventions can offer shortcuts to treatment: A patient with chronic constipation can be simply relieved by evacuating the fecaloma, instead of being unnecessarily sent for tomography with contrast medium, which will take hours to complete.

An invaluable pearl to keep in mind is not to send the patient home with her/his pain, saying that there is nothing wrong. Most of these prematurely discharged patients will present again with worsening condition mostly in a more complicated clinical picture.

In brief, management of a patient with AP is a real challenge in medicine which requires experience and expertise which are gained in years. A focused history and elaborate examination complemented with well-directed laboratory and radiological adjuncts focusing on the presumptive diagnosis is the most logical approach to expedite management. Beware of unnecessary radiological examination like CT, as it can expose patients and healthcare personnel to unadjusted radiation while increasing waiting times in the acute care areas. Paying attention to some specific clues derived from organized approaches such as scoring systems may help protect the physicians from untoward consequences attributed to misdiagnoses. Scoring systems may help remind the clinician important elements in the history, examination and ancillary tests in the construction of the pathway for the management of the patients with AP, without underestimating the critical value of a thorough evaluation by the experienced physician.

CONFLICT OF INTEREST

The author declares no conflict of interest. Ozgur Karcioglu is serving as one of the Editorial Board members of this journal. We declare that Ozgur Karcioglu had no involvement in the peer review of this article and has no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to YZ.

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