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Review

Abdominal adhesions: A practical review of an often overlooked entity

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HIGHLIGHTS

- Abdominal adhesions commonly form after intra-abdominal surgery, radiation, and inflammatory processes.
- In a subset of patients, adhesions lead to problematic symptoms such as abdominal pain, bloating, and bowel obstruction.
- Symptomatic adhesions (i.e. adhesive disease) can be diagnostically elusive and thus under-recognized by physicians.
- Adhesive disease often requires multimodal evaluation; in select patients, operative intervention can be diagnostic and therapeutic.

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ABSTRACT

Formation of intra-abdominal adhesions is a common consequence of abdomino-pelvic surgery, radiation therapy, and inflammatory processes. In a small but clinically significant proportion of patients, adhesive disease may develop, wherein adhesions lead to a variety of chronic symptoms such as abdominal distension, pain, nausea, and abnormal bowel movement pattern which can be daily, intermittent, or episodic. Due to the chronic and troublesome nature of these symptoms, adhesive disease may be life-altering in many patients, particularly when not recognized and appropriately addressed, as is the case not infrequently. In addition, there is a paucity of literature regarding the evaluation and management of patients with suspected abdominal adhesive disease. Therefore, in this concise review, we provide a clinically practical synopsis of the etiopathogenesis, symptoms, differential diagnosis, evaluation, and treatment of abdominal adhesive disease.

Contents

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1. Introduction

Abdominal adhesions are fibrous bands that span two or more intra-abdominal organs and/or the inner abdominal wall (i.e. peritoneal membrane) which typically form after abdominal surgery. Adhesions may also form secondary to inflammatory conditions of the abdomen in the absence of prior abdominal surgery or as a sequela of abdomino-pelvic radiation. Although the majority of patients with intra-abdominal adhesions remain asymptomatic, a clinically significant subset of patients will develop "adhesive disease", a symptomatic state ranging from mild and/or vague to highly distressing and even life-threatening symptoms [1,2].

Considering the fact that adhesions have no characteristic laboratory features and are not readily visible by currently available imaging methods, many cases of adhesive disease will go undiagnosed for prolonged periods of time, causing medical providers to find themselves in a diagnostic and therapeutic quandary. Patients, consequently, after extensive non-diagnostic testing and empiric treatments, may not only experience protracted symptoms and adverse medical outcomes, but can also suffer from significant emotional distress or demoralization, which in turn may be misdiagnosed as depression, anxiety, or a functional bowel disorder.

In this focused clinical review, we discuss the etiopathogenesis, symptoms, differential diagnosis, evaluation, and multi-modal management of abdominal adhesions and adhesive disease.

2. Etiolopathogenesis of adhesions

The mechanisms of adhesiogenesis are not well understood but are believed to involve mesothelial surface disruption with subsequent fibrinocoagulative and inflammatory signaling processes [3]. Etiologic causes of adhesions can generally be organized into the following categories (in addition to congenital adhesions, which are not discussed herein):

1. Post-surgical: Nearly 90% of abdominal adhesions form as a result of prior abdominal surgery, primarily laparotomy (i.e. open surgery) and to a much lesser extent laparoscopic surgery [4,5]. In one study, intra-abdominal adhesion formation was noted intraoperatively in 95% of patients who had previously undergone laparotomy [6]. The indications for the initial laparotomy in said study were broad, ranging from gastrointestinal (GI) tract malignancy, benign small bowel disease, complicated appendectomy, cholecystectomy, hysterectomy, or ectopic pregnancy. The extent of adhesions seemed to correlate with the severity/extent of the underlying initial process. Fortunately, the incidence of significant adhesions has decreased considerably in the era of laparoscopic surgery, with approximately only about 5% of such cases subsequently developing adhesive disease.
2. Post-inflammatory or infectious: Endometriosis and pelvic inflammatory disease are the most common etiologies of non-surgical adhesions in women. Other etiologies affecting either sex include diverticular disease (particularly of small bowel), Crohn's disease, and abdominal tuberculosis (in endemic areas).
3. Post-radiation: Abdominopelvic radiation used for treatment of a variety of malignancies, including gynecologic, prostatic, rectal, or lymphoproliferative diseases, can cause adhesions as a late sequela, the severity of which depends on the anatomic extent of the area treated, the degree of dose fractionation, and the total dose of radiation [7]. Post-radiation adhesions can be particularly challenging to manage due to their extent and density and the compromised nature of the underlying tissues (e.g. chronically ischemic or friable).

3. Symptoms of abdominal adhesive disease

Given the firm and fibrotic nature of adhesive bands, they have the potential to interfere with the normal intestinal motility and transit processes, among other physiologic functions. It remains unknown what proportion of patients with abdominal adhesions become symptomatic (i.e. have adhesive disease, as opposed to solely having asymptomatic adhesions) and in what proportion of such patients symptoms are directly due to the adhesions. Symptoms attributable to adhesive disease are non-specific, and with the paucity of sensitive/accurate diagnostic tests, patients are often undiagnosed. Further complicating the symptomatology and evaluation of adhesive disease is that the location of associated abdominal pain might be referred and thus may or may not correlate with the anatomic area involved by adhesions.

In general, any of the following may be seen in association with/due to intra-abdominal adhesions:

- Chronic (persistent or intermittent) bloating.
- Abdominal cramping and borborygmi.
- Altered bowel habits, including constipation or frequent loose stools (e.g. from development of small intestinal bacterial overgrowth).
- Nausea with or without early satiety.
- Bowel obstruction, which may be transient, partial, or complete (and may cause the aforementioned symptoms).
- Female infertility and dyspareunia.
- Rectal bleeding and dyschezia (i.e. painful defecation) during menses, which typically indicate colorectal involvement of endometriosis [8].

In addition, many patients, particularly if their symptoms are unpredictable, go undiagnosed, and/or without effective treatment, can develop adjustment disorder and demoralization, which may erroneously point toward functional bowel disorders such as irritable bowel syndrome.

4. Differential diagnosis

Given the nonspecific symptoms and clinical presentation of adhesive disease, as mentioned above, the differential diagnosis may become extensive. The diagnostic approach should be stepwise, methodical, and comprehensive, and clinical suspicion should be high in patients with known risk factors for adhesion formation. Considerations include the following:

- Lactose intolerance: Approximately 30–40% of the general population is lactose intolerant; therefore, it is reasonable to start with an empiric trial of lactose-free diet for 7–10 days among those whose primary symptoms are bloating or loose stools. This will help to determine what component of a

patient's symptoms, if any, are lactose-related. If there is, for example, a 25% improvement, then only that percentage of the patient's symptoms are lactose-related; further investigation is thus indicated.

- Medication-induced symptoms: Commonly used medications, such as proton pump inhibitors, calcium channel blockers, anticholinergics (e.g. oxybutynin), and numerous other medications can produce various GI side effects (in particularly bowel habit alterations) in a low but clinically significant subset of patients. If symptoms develop within few weeks of introducing a new medication, or if the patient is receiving a medication known to have GI side effects, then discontinuing that medication for 5–7 days can be diagnostic. If more than one medication is suspected, then only one medication at a time should be stopped, beginning with the most highly suspected.
- Endometriosis: Also called the "great masquerader" [9], this entity should be suspected as a potential underlying cause of abdominal pain among premenopausal women. Symptoms of endometriosis may develop with or without associated adhesions. While some women can be diagnosed on the basis of gynecologic clinical features, others will require diagnostic laparoscopy. Endometriosis can be a cause of dense adhesions, hence leading to what is described as "frozen" pelvis [10].
- Acalculous cholecystitis: The location of pain related to this disorder is typically in the right upper quadrant (RUQ) of the abdomen and is often post-prandial. Imaging findings may be normal (i.e. without gallstones or substantial pericholecystic fluid), but hepatobiliary iminodiacetic acid (HIDA) scan should reproduce the pain upon injection of cholecystokinin, and the gallbladder ejection fraction should be abnormally low (typically below 35%).
- Fatty liver: This condition may be related to obesity (as part of the metabolic syndrome), alcohol, or medication induced. It usually remains asymptomatic in mild cases, but if severe, may present with chronic and vague RUQ abdominal pain which may be intermittent or persistent. The pathogenesis of pain in fatty liver is thought to be related to stretching of Glisson's capsule due to the enlarged liver. The liver function tests can be normal or up to three times normal. Imaging studies on the other hand will show abnormalities such as increased liver echotexture on ultrasound or hypodensity on computed tomography, often with hepatomegaly.
- Other disorders: Atypical presentation of peptic ulcer disease, small bowel strictures, GI tract tumors, small bowel diverticula, Celiac disease, inflammatory bowel disease, chronic mesenteric ischemia, pancreatobiliary disorders (e.g. choledocholithiasis, Sphincter of Oddi dyskinesia), and other disorders such as Porphyria cutanea tarda, can produce symptoms which may mimic adhesive disease and should thus be considered and ruled out. Computed tomography or magnetic resonance (MR) enterography and/or cholangiopancreatography, celiac serologies (e.g. tissue transglutaminaseIgA and IgG) and other laboratory tests (e.g. urine porphyrins), and endoscopy are usually sufficient to exclude the majority of these diagnoses and narrow the differential. Of note, the diagnosis of a functional GI disorder should be one of exclusion, particularly in those with known risk factors for adhesion formation and in whom established criteria (e.g. Rome III) are not clearly met.

5. Diagnostic evaluation of suspected adhesive disease

A history of open abdomino-pelvic surgery, inflammatory disorders, or radiation therapy should be clues to a possible diagnosis of adhesive disease in the presence of the aforementioned symptoms. On the other hand, clinical features such as unexplained weight loss, fever, and night sweats should dissuade against adhesions as the primary etiology. With the exception of increased bowel sounds, tympanism with percussion (when adhesions are obstructive), and tenderness, the physical examination is often unremarkable other than the presence of a laparotomy scar, which again, should serve to alert the clinician.

There are no specific laboratory tests associated with adhesive disease, but such investigations are needed to rule out other entities. For example, an increased C-reactive protein, profound anemia, or serum liver test abnormalities should point toward further evaluation for other etiologies.

Imaging findings are usually non-diagnostic, unless the adhesions have caused acute obstruction. In those who may have had partial/transient bowel obstruction, radiological abnormalities may resolve by the time a patient seeks care or by the time imaging is performed; even when imaging is performed promptly, adhesions as the cause of obstruction are generally difficult to discern (i.e. are not definitively visualized). Nevertheless, as mentioned earlier, abdominal imaging is valuable to rule out other etiologies for a patient's symptoms.

Given the frequently elusive nature of adhesive disease, laparoscopy (and even laparotomy in some instances) with the intention to treat may be necessary in selected patients to facilitate accurate diagnosis and provide treatment, e.g. by performing adhesiolysis (if present). In general, there are four potential scenarios regarding the outcomes of surgical exploration in this setting:

1. Adhesions are lysed, and symptoms resolve.
2. Adhesions as well as an underlying disease process are identified.
3. A completely unexpected disease is identified without adhesions.
4. A normal exam, leading to a diagnosis of functional disease.

There can be benefits with all of these scenarios, such as relieving obstructive adhesive bands, diagnosing a difficult-to-detect disorder (e.g. intra-abdominal endometriosis), or peace of mind in the setting of a normal exam, (i.e. confirmation of functional disorder) [11].

6. Non-invasive management of adhesive disease

There are currently no effective targeted pharmacotherapies for adhesive disease. Empiric and symptomatic treatment such as those available for dyspepsia (e.g. simethicone, proton pump inhibitors, nortriptyline) are often attempted but are of variable efficacy, depending on the extent to which symptoms are attributable to adhesions as well as their severity. Fiber supplementation to treat "constipation" associated with adhesive disease will not produce relief and if anything, may cause more discomfort due to more residue in the setting of mechanical luminal narrowing from adhesions; non-bulking, non-stimulant agents such as polyethylene glycol may, however, be useful (together with low residue diet). For patients with predominantly abdominal cramp-like symptoms, smooth muscle relaxants such as dicyclomine may be worth trialing.

7. Psychosocial complications of adhesive disease

As mentioned earlier, the plurality and unpredictability of chronic symptoms caused by adhesive disease may substantially impact a patient's marital, social, and professional life. The lack of answers is often frustrating, while the fear of the unknown can be

psychologically distressing to the patient and the family members. This may result in some degree of resentment or anger which can be misinterpreted as depression or anxiety disorder, which can be even more detrimental for the patient's mental health and physician-patient rapport. Nevertheless, interventions to help coping and quality of life, such as psychotherapy as an adjuvant approach, are worth discussing and can be of help, as in other chronic GI disorders [12].

8. Surgical intervention for adhesive disease

Laparoscopic surgery for treatment of acute bowel obstruction is associated with favorable long-term success rates, with recurrence rates less than those seen with open surgery, typically on the order of 10% based on animal model and human studies [6,13–16]. However results may vary, and some controversy exists regarding the role for surgery depending on the underlying disease and the symptoms present [17,18]. If the pathology is identified to be only a few adhesive bands, laparoscopic surgery may be expedient and highly successful; however, complex, and/or dense adhesions may necessitate a more complicated surgery and may produce less favorable short-and long-term outcomes, since complete removal of all adhesions is high risk and prone to recurrent adhesion formation. Therefore, the severity and extent of adhesions may serve as an important prognostic in determining the surgical outcome. The risk of laparoscopic surgery is higher in the acutely obstructed bowel compared to the elective setting since, aside from the usual complications of urgent surgical intervention, there is increased risk of puncturing the distended bowel, thus requiring potential conversion to open laparotomy, a scenario that has been reported in up to 20% of surgeries for acute obstructions [15].

With respect to elective laparoscopic adhesiolysis, overall outcomes are very favorable [3]. For example, in a study assessing the long-term outcomes of elective laparoscopic adhesiolysis in those with chronic GI symptoms, 70% achieved complete adhesiolysis, and 80% experienced complete resolution of symptoms suggesting that even partial adhesiolysis was effective; also, none of the cases required conversion to open surgery [19]. It has been postulated that partial response may be due to incomplete adhesiolysis or the placebo effect of surgery which wanes over time, while others believe that even partial adhesiolysis can produce sustained response. In another study, 72 patients with chronic abdominal pain underwent surgery and were prospectively followed to assess short- and long-term outcomes [20]. The average operative time was 60 min, and 85% of patients were found to have adhesions, although not all of which may have been necessarily the source of symptoms, while the remainder 15% did not have adhesions. There were 2 conversions to laparotomy, one for intraabdominal bleed and one for urinary bladder perforation. Long term follow-up at 3.7 years showed that 33% who underwent adhesiolysis were totally pain-free, 46% had less pain, and the rest did not experience improvement. In a more recent study, among 52 patients who underwent laparoscopy for chronic abdominal pain, 77% of patients with suspected adhesive disease experienced complete or partial pain relief following adhesiolysis, and there were no operative complications [21]. Despite these and other encouraging studies [22–25], others have had disappointing findings [26], which could possibly be a reflection of patient selection and the amenability of the adhesions to surgical treatment.

It should be mentioned that a variety of techniques have been described to minimize the occurrence of post-operative adhesions [3,27–31]. This is an evolving field, and the implementation of such techniques is encouraged but depends on the particular case and institutional/surgical expertise.

9. Conclusions

Chronic symptoms related to intra-abdominal adhesions are not uncommon, yet accurate diagnosis can be elusive despite extensive testing. Clinicians must keep this entity in mind when evaluating patients with risk factors for adhesions and who present with symptoms that evade clear diagnosis but are compatible with adhesive disease. Ultimately, for many patients, adhesive disease is a diagnosis of exclusion. There are no consensus guidelines on the diagnosis or treatment of adhesive disease, thus the recommendations provided herein in this regard are based on a conglomerate of clinical experience and the limited available published literature.

We believe that diagnostic laparoscopy in the hands of an experienced surgeon is warranted in patients suspected to have adhesive disease and in whom appropriate diagnostic testing (biochemical, imaging, endoscopic) has been unrevealing, particularly if symptoms significantly compromise quality of life and are refractory to conservative, symptom-based therapy. Laparoscopic lysis of adhesions can provide short and long term therapeutic benefits, but patient selection by ruling out other possible entities is essential. The lack of amenability of all adhesions to surgical treatment cannot be overemphasized. Accurate diagnosis, symptomatic treatment, and selection of patients for surgical intervention can be challenging and thus, when facing uncertainty, referral to specialists with experience and expertise in managing adhesive disease is advisable. In such instances, laparoscopy can confirm or modify the diagnosis, change management and outcome, and/or provide peace of mind to the patient, the family, and the treating physician.

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