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# Achalasia Presenting After Operative and Nonoperative Trauma

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Achalasia has been described following fundoplication and is attributed to vagal nerve damage during surgery. Similarly, other traumatic events to the distal esophagus may be linked to the development of achalasia. Operative and nonoperative trauma as a possible factor in the development of achalasia was studied. A retrospective analysis of patients with achalasia ($n = 64$) at our institution was performed. Collected data included age, gender, symptoms, and history of operative and nonoperative traumatic events. Comparisons were made to a group of patients with similar symptoms but normal esophageal manometry ($n = 73$). Achalasia was diagnosed by manometry in 125 patients over a 6-year period. All patients with complete medical records ($n = 64$) were studied. A history of operative or nonoperative trauma to the upper gastrointestinal tract prior to the development of symptomatic achalasia was present in 16 of 64 (25%). Significantly fewer patients (9.5%) with symptoms of dysphagia, but normal manometry and upper endoscopy, had precedent trauma to the upper gastrointestinal tract ($P < 0.05$). All cases of nonoperative trauma occurred in motor vehicle accidents. Cases of operative trauma included coronary artery bypass surgery ($n = 4$), bariatric surgery ($n = 2$), fundoplication ($n = 3$), heart/lung transplantation ($n = 1$), and others ($n = 5$). Patients with proven achalasia and a history of trauma were more likely to have chest pain (RR, 4.5; $P = 0.012$) but less likely to have regurgitation (RR, 0.51; $P = 0.01$) or nausea/vomiting (RR, 0.0; $P = 0.27$) than those without a history of antecedent trauma. In this series, significantly more patients with achalasia had a history of preceding trauma than did patients with similar symptoms and normal esophageal manometry. Following trauma, patients may be at increased risk for developing achalasia, possibly from neuropathic dysfunction due to vagal nerve damage. Patients with posttraumatic achalasia may have symptoms which differ from those of other achalasia patients.

**KEY WORDS:** achalasia; vagus nerve; motor vehicle accident.

Achalasia is characterized by failure of normal lower esophageal sphincter (LES) relaxation with swallowing, aperistalsis in the body of the esophagus, and normal to increased resting LES pressure. The pathophysiology of achalasia is incompletely understood. Transitions from diffuse esophageal spasm, nonspecific esophageal motor disorders, and gastroesophageal reflux disease to achalasia have been documented, suggesting that these disorders may represent a spectrum of syndromes that have a common pathogenesis (1–7). Causes of secondary achalasia include malignancy, infiltrative disorders (sarcoidosis and amyloidosis), and infection with trypanosoma cruzi (8–13).

Trauma to the gastroesophageal junction may potentially damage the vagus nerve and, thereby, lead to secondary achalasia. Although a few case reports have implicated vagal nerve injury following surgery as a cause of achalasia (14–16), nonoperative trauma has not been

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described in this regard. The purpose of this study was to evaluate the association of trauma, both operative and nonoperative, with the development of achalasia.

## METHODS

Patients diagnosed with achalasia over a 6-year period (January 1996 through December 2001) were identified from manometry logs. The diagnosis was based on incomplete LES relaxation in response to swallowing and aperistalsis in the body of the esophagus. Only patients fulfilling manometric criteria for achalasia with complete medical records were included in the study. Age, gender, symptom type/onset, and history of operative and nonoperative traumatic events to the region of the gastroesophageal junction prior to symptom onset were recorded. Operative trauma included surgery to the chest, esophagus, and/or stomach. Motor vehicle accidents with chest trauma were regarded as nonoperative trauma.

Similar data from a consecutive group of 73 patients without achalasia, as evidenced by normal esophageal manometry and upper endoscopy, were collected for comparison. These patients had undergone esophageal manometry and endoscopy to evaluate dysphagia over the same time period.

Statistical analysis was performed using the Epi Info 6 (Version 6.04) Statistics Program. Numerical results are expressed as mean ± standard deviation. Categorical data are expressed as counts (%). Chi-square (Fisher's exact test when appropriate) and the Wilcoxon two-sample test were used to assess differences between the patient groups. Two-tailed $P$ values less than 0.05 were considered significant.

## RESULTS

Over a 6-year period, achalasia was diagnosed in 125 patients. Of these, 64 patients with complete medical records were included in the study. Characteristics of study patients are summarized in Table 1. There were no significant differences in age, gender, or duration of symptoms between the achalasia and the nonachalasia groups. Of 64 patients with achalasia, 16 (25%) had a history of trauma. Only 7 of 73 patients (9.5%) with dysphagia but normal manometry had such a history (OR, 3.1; 95% CI, 1.1–9.7; $P = 0.016$). There was a strong trend toward an increase in both operative and nonoperative trauma in patients with achalasia compared to the normal manometry group.

TABLE 1. PATIENT CHARACTERISTICS

| | *Achalasia* (n = *64*) | *No achalasia* (n = *73*) | P *value* |
|---|---|---|---|
| Mean age (± SD), years (Range) | 54 ± 16 (21–93) | 45 ± 15 (15–77) | 0.62 |
| Male sex | 27 (42%) | 20 (27%) | 0.069 |
| History of trauma prior to symptom onset | **16 (25%)** | **7 (9.5%)** | **0.016** |
| Operative | 10 (15.6%) | 5 (6.8%) | 0.060 |
| Nonoperative | 6 (9.3%) | 2 (2.7%) | 0.098 |
| Duration of symptoms (years) | 2.5 ± 3.4 | 2.4 ± 3.4 | 0.90 |

*All nonoperative trauma was due to motor vehicle accidents.

TABLE 2. TYPES OF OPERATIVE TRAUMA IN ACHALASIA AND NONACHALASIA GROUPS

| *Achalasia* (n = *10*) | *No achalasia* (n = *5*) |
|---|---|
| Gastric/esophageal surgery ($n = 6$) | Gastric/esophageal surgery ($n = 2$) |
| Fundoplication (1) | Fundoplication (2) |
| Bariatric surgery (2) | |
| Billroth II with vagotomy (1) | |
| Esophageal fistula or perforation repair (2) | |
| Cardiac surgery ($n = 4$) | Cardiac surgery ($n = 2$) |
| Coronary artery bypass graft (2) | Coronary artery bypass graft (2) |
| Heart/lung transplant (1) | |
| Tetralogy of Fallot repair (1) | |
| | Other ($n = 1$) |
| | Thyroidectomy (1) |

Operative trauma (Table 2) for both groups included bariatric surgery, fundoplication, cardiac surgery, and others. All nonoperative trauma events were secondary to motor vehicle accidents.

The predominant symptom of all patients with achalasia was dysphagia (Table 3). Less frequent symptoms included cough, weight loss, regurgitation, chest pain, and nausea/vomiting. Posttraumatic achalasia patients were more likely to complain of chest pain (RR = 4.50, $P = 0.012$) and less likely to have regurgitation (RR = 0.51, $P = 0.010$) or nausea/vomiting (RR = 0.0, $P = 0.027$) than achalasia patients without a history of preceding trauma.

There were no differences in manometric patterns between the groups with achalasia. The time from onset of injury to onset of symptoms ranged from 2 months to 48 years in the nonoperative trauma group and from 1 month to 32 years in the operative group.

## DISCUSSION

This study shows a significant association between achalasia and trauma to the upper gastrointestinal tract. Twenty-five percent of patients diagnosed with achalasia had a history of operative or nonoperative trauma to the chest and/or upper gastrointestinal tract, compared with 9.5% of patients with dysphagia and normal manometry. Furthermore, this study suggests a relationship between achalasia and a prior motor vehicle accident. The heterogeneous postoperative group suggests that achalasia may be an unusual sequela of diverse operations such as Nissen fundoplication, bariatric surgery, and heart/lung transplantation. These observations suggest that in some cases operative and nonoperative trauma may result in

TABLE 3. SYMPTOMS IN ACHALASIA PATIENTS WITH AND WITHOUT A HISTORY OF TRAUMA

| *Symptom* | *History of trauma* (n = *16*) | *No history of trauma* (n = *48*) | *RR* | *95% confidence interval* | P *value* |
|---|---|---|---|---|---|
| Dysphagia | 16 (100%) | 46 (95.8%) | 1.0 | 0.98–1.1 | 1.00 |
| Cough | 2 (12.5%) | 12 (25%) | 0.50 | 0.13–2.0 | 0.49 |
| Weight loss | 6 (37.5%) | 19 (33.3%) | 1.1 | 0.53–2.4 | 0.77 |
| **Chest pain** | 6 (37.5%) | 4 (8.3%) | **4.5** | 1.5–14 | **0.012** |
| **Regurgitation** | 6 (37.5)% | 35 (72.9%) | **0.51** | 0.27–0.99 | **0.010** |
| **Nausea/vomiting** | 0 (0%) | 13 (27%) | **0** | 0–0.65 | **0.027** |

vagal disruption leading to neuropathic dysfunction with the resultant development of achalasia. Prior studies have shown the development of achalasia after Nissen fundoplication and after heart–lung transplantation, both of which may damage the vagus nerve. The mechanism of damage may not be the same as vagal transection.

Vagus efferent fibers, with their cell bodies in the dorsal motor nucleus of the vagus nerve, have a crucial role in initiating and modulating esophageal peristalsis and lower esophageal sphincter relaxation. Pathological analyses of operative and postmortem specimens from patients with achalasia have demonstrated abnormalities of both extrinsic and intrinsic innervation of the esophagus and the LES. The majority of studies revealed a loss of ganglion cells from the dorsal motor nucleus of the vagus and demyelination of the vagal afferent fibers suggesting denervation (i.e., Wallerian degeneration) (17–19).

Neural control of the LES includes cholinergic and nonadrenergic/noncholinergic inhibitory pathways involving nitric oxide, acetylcholine, and vasoactive intestinal polypeptide. Nitric oxide plays an important role in mediating LES relaxation. Nitrergic neurons are present in the dorsal motor nucleus of the vagus, the source of preganglionic motor neurons to the LES (20). Experimental inhibition of nitric oxide produces a picture that manometrically mimics achalasia. An alternative explanation for posttraumatic achalasia might involve nitrergic pathways; by some mechanism, trauma may impair the generation of nitric oxide, resulting in decreased inhibition of the lower esophageal sphincter and an abnormality in sequential relaxation of the body of the esophagus. An association between achalasia and trauma was found, with differences in symptom characteristics between patients with and those without trauma preceding the diagnosis of achalasia. These findings are limited by the retrospective nature of the study and its small sample size. Inclusion of only 64 patients with complete medical records of 125 patients may have introduced a selection bias. Another limitation of this study may be the reliance on chart review to collect data regarding a history of trauma and/or operations. Although most patients are able to recall their operations, they may fail to report involvement in a motor vehicle accident as part of their medical history.

The association of achalasia with prior trauma is intriguing. A history of trauma (operative or nonoperative) may be elicited from a subset of patients who would otherwise have been diagnosed with primary or idiopathic achalasia. A prospective study involving a large cohort of patients at risk for vagus nerve injury (i.e., patients undergoing fundoplication, heart/lung transplantation, or bariatric surgery) is a potential group that could be examined over a prolonged follow-up period. In addition, comparing esophageal manometry and vagal integrity before and after surgery would help us to understand these findings (21–23).

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