Demographic and Clinical Characteristics of Patients with Nutcracker Esophagus

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ABSTRACT

Objective: This retrospective study was designed to investigate the demographic and clinical characteristics of 77 patients diagnosed with nutcracker esophagus (NE).

Materials and Methods: The medical records of patients with NE who were followed up at a single center between 2000 and 2020 were collected and analyzed.

Results: The average age of the patients was 52.5±15.7 years; 43 (55.8%) were male and 34 (44.2%) were female. Dysphagia was the primary symptom in 49 patients (63.6%) and noncardiac chest pain (NCCP) symptoms were prominent in 28 patients (36.4%). Esophageal manometry results according to the presenting symptom indicated that the median amplitude was 210 mmHg (min–max: 190–270 mmHg) in those with prominent NCCP and 215 mmHg (min–max: 190–310 mmHg) in those with prominent dysphagia, with no statistically significant difference between the groups (p=0.19). The mean lower esophageal sphincter pressure (LESP) of the patients was 25 mmHg (min–max: 10–80 mmHg). While the pressure was normal in 55 patients (71%), was elevated in 22 patients (29%). Comparison of the LESP results revealed that the distal esophageal amplitude (DEA) median was 220 mmHg (min–max: 190–310 mmHg) in patients with normal LESP and 210 mmHg (min–max: 190–250 mmHg) in those with a high LESP. Normal or high LESP was not associated with high DEA (p=0.57).

Conclusion: Patients with NE may present with a variety of symptoms. The presence of reflux should be investigated and symptomatic treatment should be applied.

Keywords: Distal esophageal amplitudes, nutcracker esophagus, reflux

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INTRODUCTION

Nutcracker esophagus (NE) is a disorder characterized by peristaltic high-amplitude contractions in the distal esophagus. It is also called hypertensive peristalsis or spastic nutcracker (1, 2). The pathogenesis is still unknown, though several theories have been proposed. An imbalance between stimulant and inhibitory neurons of the esophagus (3), abnormal autonomic innervation of the esophagus with a hypercholinergic outcome (3, 4), thickening of the esophageal muscular layer (5, 6), or induced hypertensive contractions due to gastroesophageal reflux disease (GERD) have all been suggested as causes of the disease (7, 8). It has also been shown that acute stress can cause high-amplitude contractions in the esophagus (9).

Patients with NE may present with dysphagia, noncardiac chest pain (NCCP), or retrosternal burning sensation symptoms (2, 10). Although it was first described in 1977, the question of whether or not NE is a true esophageal motility distortion or a manometric marker in patients with NCCP is still a subject of debate (1, 11, 12). In one study, NE was reported in 48% of NCCP cases (13). High-amplitude contractions of the esophagus in patients with NE are thought to be the primary cause of the symptoms of atypical chest pain and/or dysphagia. Some studies have reported that the symptoms observed in patients with NCCP are not correlated with high-amplitude contractions (14), and it has been noted in other research that though the amplitudes of contractions decreased to normal values with treatment (calcium channel blockers, nitrates, botulinum injection, etc.), symptoms did not improve (8, 14, 15).

Patients suffering from NE may seek medical care with complaints of dysphagia, as well as complaints of retrosternal burning sensation, chest pain, or reflux. This study examined the demographic and clinical characteristics of patients with NE, as well as the esophageal motility, upper gastrointestinal endoscopy, and ambulatory pH monitoring results of patients diagnosed with NE in the motility laboratory of a single hospital.

MATERIALS and METHODS

Ethics Approval

The study was approved by the ethics committee of Ankara Yüksek Ihtisas Training and Research Hospital on January 17, 2018 (no: 29620911).

Participants

The motility records of patients diagnosed with NE in the gastroenterology motility laboratory and the digital electronic records of the hospital were retrospectively reviewed. The demographic characteristics, complaints upon admission, esophagogastroduodenoscopy findings, 24-hour pH monitor, and esophageal motility results for each NE patient were evaluated.

Patients under the age of 18, those with esophageal cancer, esophageal strictures, a neurological motor disease that may affect esophageal motility (myasthenia gravis, amyotrophic lateral sclerosis, cerebrovascular sequelae, etc.), a history of esophageal surgery for any reason, a total gastrectomy, or conditions that may affect esophageal motility (lung cancer, Nissen fundoplication for reflux, etc.) were not included in the study.

Manometric Protocol

Esophageal motility was assessed using conventional esophageal manometry (Dentsleeve; Dentsleeve International, Mui Scientific, Mississauga, Ontario, Canada). Conventional manometry uses an 8-channel polyvinyl catheter with a Dent sleeve. The catheter is placed in the lower esophageal sphincter (LES) and sensors evaluate LES relaxation and pressure. The Dentsleeve feature allows for an average analysis of data over an area of 6 cm. The first distal channel is placed in the stomach, and the second Dentsleeve channel is inserted into the LES. The third channel is located 5 cm proximal to the LES, followed by the fourth and fifth channels at 2 cm intervals, and then the proximal esophagus is evaluated from other channels at 5 cm intervals. Each channel is perfused with 0.5 mL/min of distilled water with a system of low compliance pneumohydraulic capillary perfusion. In all, 8 channels are connected to external transducers that provide output to a computer-based analysis system.

After 8 hours of fasting, the manometric catheter was inserted nasally into the stomach. Gastric basal pressure was measured. Following that, the catheter was withdrawn at 1 cm intervals, and deep inspiration, expiration, and/or dry swallows were performed by the patient to pinpoint the location of the LES. After the sleeve area of the catheter was placed in the lower esophagus, esophageal motor functions were assessed with 10 wet swallows at 20-second intervals. Those with average contraction amplitudes of ≥180 mmHg, peristaltic contractions, and normal LES relaxation in ≥20% of 10 wet swallows in the distal esophagus (3 and 8 cm above the LES) were classified as NE. Those with normal esophageal trunk functions and LES relaxation and a resting lower esophageal sphincter pressure (LESP) <10 mmHg were defined as hypotensive LES, while those with LESP >45 mmHg were defined as hypertensive LES (1, 2, 16, 17).

pH Monitor Protocol

Use of medications that could affect the gastric pH of the patient was terminated 7 days before the procedure and the esophageal manometry was performed after 8 hours of fasting. The distal sensor of the PHI15/PHN15 dual pH catheter (Sandhill Scientific Inc., Highlands Ranch, CO, USA) was placed 5 cm above the LES and 20 cm above the proximal sensor. A pH monitor was used to record findings for 24 hours after the catheter was fixed in the nose, and the presence of distal and proximal reflux was investigated (18).

Table 1. Demographic characteristics	
Male (%)/Female (%)	43 (%55.8)/34 (%44.2)
Esophagitis on endoscopy	
No esophagitis	54 (70%)
Grade A esophagitis	12 (16%)
Grade B esophagitis	8 (10%)
Grade C esophagitis	3 (4%)
Eosinophilic esophagitis	6/77(8%)
Presenting symptom	
Dysphagia	49/77 (63.6%)
Noncardiac chest pain	28/77 (36.4%)
pH monitor findings (n=36)	
No reflux	18/36 (50%)
Pathological reflux in the distal esophagus	6/36 (17%)
Pathological reflux, both distal and proximal	12/36 (33%)
Lower esophageal sphincter pressure (mmHg), median (min–max)	25 (10–80)
Normal (10–45 mmHg)	55/77 (71%)
High (>45 mmHg)	22/77 (29%)

Min: Minimum; Max: Maximum

In the distal pH sensor of the 24-hour pH monitor, those with a total reflux time of >5%, a standing reflux time of >6.3%, a lying reflux time of >1.2%, a longest reflux period of >9.2 minutes, a total number of reflux episodes of >50, >3 reflux episodes longer than 5 minutes, and those with a DeMeester score of >15 were considered distal pathological reflux. Patients with a total reflux of >1%, a standing reflux of >1.5%, a longest reflux of >3 minutes, and a total reflux of >10 were considered cases of proximal pathological reflux (2, 19).

Statistical Analysis

The data were evaluated using IBM SPSS Statistics for Windows, Version 20.0 software (IBM Corp., Armonk, NY, USA). Continuous numerical variables with normal distribution were provided as mean±SD; variables with non-normal distribution were shown as the median and minimum–maximum values. A chi-squared test was used to test the correlation between groups and categorical variables. Normality of distribution of DEA values was verified using the Kolmogorov–Smirnov test. An independent t-test was used to compare the 2 study groups based on the normal distribution of scores and percentages. A p=0.05 value was considered statistically significant.

RESULTS

The results of a total of 77 patients with NE were analyzed retrospectively. The demographic and medical characteristics of the patients are presented in Table 1. The mean age of the patients was 52.5±15.7 years; in the study group, 43 (55.8%) were male and 34 (44.2%) female. Evaluation of the endoscopy results of the total of 77 patients according to the Los Angeles classification (20) showed that 54 had a normal esophagus (70%), 12 patients had grade A

Table 2. Distal esophageal amplitude values

	mmHg, median (min–max)	p
Gender		0.42
Female (n=34)	210 (190–250)	
Male (n=43)	220 (190–310)	
Presenting symptoms		0.19
Noncardiac chest pain (n=49)	210 (190–270)	
Dysphagia (n=28)	215 (190–310)	
Esophageal sphincter pressure		0.57
Normal LES pressure (n=55)	220 (190–310)	
High LES pressure (n=22)	210 (190–250)	

LES: Lower esophageal sphincter; Min: Minimum; Max: Maximum

esophagitis (16%), 8 patients had grade B esophagitis (10%), 3 patients had grade C esophagitis (4%), and 6 had eosinophilic esophagitis (8%). After 28 months of follow-up, 1 patient was diagnosed with achalasia (1.5%). While dysphagia was the primary symptom in 49 patients (63.6%), NCCP symptoms were prominent in 28 patients (36.4%). Ambulatory pH monitor results were available for only 36 patients. Reflux was not detected in 18 patients (50%), there were distal findings in 6 patients (17%), and both distal and proximal in 12 patients (33%). The mean LESP of the patients was 25 mmHg (min/max: 10–80 mmHg). The pressure was normal in 55 patients (71%), but was elevated in 22 patients (29%).

DEA comparisons are provided in Table 2. When the DEA of men and women was compared, the median was 210 mmHg (min–max: 190–250 mmHg) in women and 220 mmHg (190–310 mmHg) in men (p=0.42). Comparison of the presenting symptom indicated that the median amplitude was 210 mmHg (min–max: 190–270 mmHg) in those with prominent NCCP and the median amplitude was 215 mmHg (min–max: 190–310 mmHg) in those with prominent dysphagia, with no statistically significant difference between the groups (p=0.19). When compared according to the LESP results, the DEA median was 220 mmHg (min–max: 190–310 mmHg) in patients with a normal LESP and the median was 210 mmHg (min–max: 190–250 mmHg) in those with a high LESP. The LESP measurement was not found to be associated with a high DEA (p=0.57).

DISCUSSION

Evaluation of the results of 77 patients with NE revealed that the majority were men, that roughly half of those who had a 24-hour pH monitor for reflux had pathological reflux, and that reflux was present throughout the entire esophagus in the majority of those with reflux. No correlation was found between DEA level and gender, reflux, or LESP.

NCCP, dysphagia, or reflux might be the primary symptom in patients with NE. One study noted that chest pain was the main complaint in 27 of 28 patients with NE (21). Kamberoglou et al. (11) reported that chest pain was the most common symptom in patients with a high DEA. Agrawal et al. (2) classified 56 patients with NE into 3 groups according to DEA level: group A: 180–220

mmHg, group B: 220–260 mmHg, and group C: >260 mmHg. (2). While the primary symptom was chest pain in all (100%) of those in group C with a high DEA value, in group A it was dysphagia (26%), chest pain (23%), chest burning sensation (23%), and other symptoms, and in group B, 69% of patients complained of chest pain, 19% of cough, and 1% complained of dysphagia and other symptoms. It is interesting to note that the primary complaint of chest pain was observed in all of the group C patients, whereas those with a low DEA had less chest pain and more dysphagia (2). However, no significant correlation was found between the patients' symptoms and their DEA level in other studies (6, 8, 17). For instance, in a study conducted by Richter et al. (19) of patients with NE, no improvement in symptoms was observed despite the decrease in high DEA level to normal with nifedipine treatment (19). In the present study, the primary symptom in patients was NCCP or dysphagia. No correlation was found between reported symptoms and DEA. Similarly, no correlation was found between primary symptoms and reflux.

Some researchers believe that the abnormal motility seen in NE patients is caused by a type of outlet obstruction in the LES. These studies have reported that intrabolus pressure increased and passage of a bolus was impaired in patients with hypertensive LES (22). Orr and Robinson (21) reported that patients with NE had a significantly higher LESP than the normal population. Jiang et al. (23) also found hypertensive LESP in 5 of 13 patients with DEA. Agrawal et al. (2) found that the median LESP was 38.8 mmHg in group A, 33.5 mmHg in group B, and 52.4 mmHg in group C. Only 29% of patients in the present study had a high LESP, leading to the conclusion that a normal or high LESP is not associated with a high DEA value. Mechanisms that play a role in the pathogenesis of NE may be the cause of both high DEA and high LESP.

Fass et al. (8) reported that GERD symptoms are prominent in many NE patients. They reported that chest pain decreased in 83% of patients with NE who were given omeprazole therapy. In another study, Mittal et al. (14) suggested the elimination of GERD before considering a diagnosis of NE. It has also been proposed that NE is an esophageal motility abnormality that occurs in those with GERD (8). While Agrawal et al. (2) detected reflux in 77% of patients with a low DEA (DEA <210 mmHg), they detected reflux in only 19% of patients with a high DEA (>260 mmHg). In another study, it was reported that acid inhibition induced symptomatic improvement in patients with NE but had no effect on motility patterns (8). In the present study, reflux was found in approximately half of the patients who had 24-hour pH monitoring. In addition, in most patients with reflux it was observed that the reflux was present in the whole esophagus, however, in some patients, reflux was only limited to the distal esophagus. No correlation was found between reflux and DEA values.

In some case reports, NE had progressed to achalasia or diffuse esophageal spasm (24–25). One of the patients in the present study was diagnosed with achalasia during follow-up and was treated with 3-cm achalasia balloon dilatation and remained stable. It has also been reported that in some patients, eosinophilic esophagitis may cause motility disorders, such as NE (26–28). Eosinophilic esophagitis was diagnosed during the follow-up of 6 patients in the present study based on clinical, laboratory, and pathological findings.

Limitations

The present study has several limitations. Due to the retrospective nature of the research, long-term follow-up results, the medical treatments administered, and patient response to treatment could not be determined. In addition, 24-hour pH measurements were not performed in the majority of the patients, and therefore the presence of reflux in these patients is not fully known.

CONCLUSION

In conclusion, patients with NE may present with dysphagia, NCCP, or retrosternal burning sensation symptoms. GERD symptoms are also prominent in many NE patients, as seen in the present study. The presence of reflux should be investigated in patients with NE. Symptomatic treatments should continue to be used.

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