traités pour une polyarthrite rhumatoïde ou une spondylarthrite [7].

Notre observation permet de répertorier deux cas d’hépatite aiguë associée à l’adalimumab avec des délais de survenu très différents (trois et 15 mois), hépatite non grave mais ayant nécessité l’arrêt du médicament. L’introduction d’un autre anti-TNFα a été un succès pour l’un, non nécessaire pour l’autre. Toutefois les différents cas publiés suggèrent l’absence de toxicité croisée [3–5].

Conclusion

Il importe donc de déclarer ces événements indésirables au centre de pharmacovigilance pour identifier au plus vite une alerte afin d’en protéger au mieux les patients exposés.

Conflit d’intérêt

Aucun.

Références


Nutcracker esophagus: An acid related disease or a primary motor disorder?

Nutcracker esophagus (NCE) is a primary motor disorder, characterized by high-amplitude peristaltic contractions of the distal esophagus [1]. Its pathogenesis and clinical relevance remain unclear. Some authors suggest that it might represent an acid-related esophageal disorder. The association of NCE and gastro-esophageal reflux disease (GERD) is described but the mechanism is still uncertain. The role of acid reflux in the development of non-cardiac chest pain (NCCP) and dysphagia in patients with NCE is controversial. Treatment of this association is difficult. It is based on high dose of proton pump inhibitors (PPI). Calcium channel blockers should be avoided. We report a case of NCE associated with GERD in a man complaining of dysphagia. Our aim was to assess a symptomatic presentation of NCE and point out the necessity to search for an associated GERD to guide the adequate therapy.

Case report

A 65-year-old man presented to our department with complaints of intermittent and low dysphagia, particularly to liquids. He also described vomiting and epigastric pain for the past 2 months. He has no chest pain or heart burn. General state was good. He had no particular medical history. Physical examination was normal. A cardiac cause of the epigastralgia was excluded. Biological test, including lipaemia, were normal. Upper endoscopy revealed an erosive esophagitis (Los Angeles grade A). No hiatal hernia was noticed and gastric mucosa appeared normal. Esophageal and gastric biopsies were non-specific. Esophageal manometry was carried out using the conventional method. Mean distal esophageal peristaltic wave amplitude was greater than 180 mmHg (measured as the average amplitude of ten swallows at two recording sites positioned 3 and 8 cm above the low esophageal sphincter (LES)). LES resting pressure was normal with complete LES relaxation. The diagnosis of NCE was assessed according to the published criteria. Barium swallow showed uncoordinated contractions of the lower esophagus. Twenty-four hours esophageal pH monitoring...
revealed pathologic acid reflux, defined as an intraesophageal pH of less than 4, for more than 4% of the recording time. The patient was treated with full-dose omeprazole (40 mg/day) for 8 weeks before re-examination. Interestingly, the symptoms completely disappeared upon medication with the relief of the dysphagia.

Discussion

The NCE is an esophageal motility disorder characterized by high-amplitude peristaltic contractions in the distal esophagus with a normally relaxing LES. The pathogenesis of NCE is still uncertain. Recent data prove that NCE is related to an excessive cholinergic activity [1]. Intraluminal ultrasound showed that NCE patients have thicker esophageal muscles, both circular muscle (CM) and longitudinal muscle (LM), as compared with normal subjects [1]. High-frequency intraluminal ultrasound has also shown an asynchrony with the peak LM contraction occurring earlier than the peak CM contraction during peristalsis in patients with NCE. The time lag between LM and CM contractions was dose-dependently decreased and reversed by administration of atropine [1]. On the other hand, in normal subjects, edrophonium (acetylcholinesterase inhibitor) induced an increase in both muscle contraction amplitude and duration.

To date most studies about NCE have focused on chest pain rather than on dysphagia. Dysphagia is described in 20—52% of cases [2]. In our patient, dysphagia could be related to NCE or to erosive esophagitis. Dysphagia in NCE patients has been also associated with esophageal diverticula. In Fornari’s study, a significant association between NCE and dysphagia was found independent of GERD [3]. The mechanism of this association is unclear. A high resolution manometric study of NCE revealed that patients presenting with dysphagia have significantly higher amplitudes than patients presenting with other symptoms [4]. Contraction duration and the prevalence of high intrabolus pressure are also significantly increased, suggesting a relationship to outflow resistance. This study also showed that the resting pressure of the LES increases and the proportion of patients with short abdominal LES length significantly decrease with higher amplitudes. These symptomatic and physiologic data suggest that “nutcracker” contraction amplitudes in the distal esophagus have clinical significance. Other studies using impedance-manometry found no consistent abnormality on esophageal bolus transit in NCE patients, suggesting that abnormal visceral sensitivity could play a role on the perception of dysphagia. Other interesting hypotheses in the literature include an outflow obstruction related to LES dysfunction as well as a poorly compliant esophagus due to increased muscle layer thickness. Further studies are needed to clarify such mechanism.

In recent years NCE has been associated with GERD. Increased esophageal acid exposure has been observed in 30—49% of NCE patients investigated with pH monitoring [5]. Acid-related esophageal symptoms have been extensively assessed particularly in patients with NCCP [3,6]. Erosive esophagitis is found in 5—25% NCE patients [7]. These data suggest that acid may play a role in the development of symptoms in NCE [5]. However, this association remains controversial. A recent study identified 16% of NCE patients with a positive reflux symptoms index and normal amounts of acid. Some authors suggest that NCE could be a marker for a subgroup of patients who are different from classic GERD patients, emphasizing the association among NCCP, NCE, and physiologic quantics of acid. Visceral hypersensitivity could be the basis for the symptoms of these patients. In addition, no clinical differences were found in patients with NCE with or without associated GERD [7].

Management of these patients is difficult. Some authors have proposed a therapeutic test in patients suspected of having GERD in association with NCE, reserving pHmetry for another time [2]. However, it seems reasonable to exclude GERD by using pHmetry so as to offer proper treatment. When GERD is present, NCE could be considered as a secondary motility disorder so the treatment is directed toward reflux. Acid-suppressive therapy has provided some benefit. Our observation provides further evidence for a causative role of acid reflux in the pathophysiology of the NCE and, in addition, suggests that effective acid suppression might be a useful therapeutic tool. However, a recent double-blind study could not establish any beneficial effect of PPIs in NCE patients presenting with NCCP [6]. NCE is usually treated with calcium channel blockers. These drugs reduce the LES resting pressure and delay esophageal clearance. These effects would facilitate and/or worsen GERD [7]. In summary, the clinical significance and physiopathology of NCE are increasingly debated. The possible role of acid reflux needs further study.

Conflict of interest

None.

References

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