

Case report

# Laryngospasm and reflex central apnoea caused by aspiration of refluxed gastric content in adults

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**SUMMARY** Two patients with attacks of choking caused by aspiration of gastric contents in the laryngotracheal tube are presented. One had such severe attacks of respiratory arrest, that tracheostomy was done. The common symptoms of gastro-oesophageal reflux such as pyrosis, acid regurgitation, or retrosternal burning were absent in both patients and upper gut radiological and endoscopic examinations were negative. Histology of the oesophageal mucosa showed a deep chronic oesophagitis, and the 24-hour pH-monitoring of the upper oesophagus showed frequent gastro-oesophageal refluxes. Manometry showed hypotonic lower oesophageal sphincter with marked alterations of peristalsis. In the patient with tracheostomy a 24 pH monitoring of the hypolaryngeal zone showed decreased pH at the time of choking attacks. In the other patient further investigations showed that amyotrophic lateral sclerosis was the cause of the oesophageal motility disorder. An intense antireflux treatment abolished the respiratory attacks in both patients.

Aspiration of gastric contents in the respiratory tree is not rare in patients with gastro-oesophageal reflux. Henderson<sup>1</sup> reported a frequency of 27.9% in a group of 1000 consecutive patients with gastro-oesophageal reflux. In adults the frequent consequence of gastric contents aspiration is represented by broncopulmonary manifestations, as bronchial asthma, recurrent respiratory infections, and chronic bronchitis.<sup>1-5</sup> Respiratory arrest caused by aspiration is observed almost exclusively in infants less than one year old, in whom it is believed to be the main cause of 'cot deaths'.<sup>6-9</sup> This happens even in absence of gross aspiration, being the result of laryngospasm of reflex central apnoea. Respiratory arrest caused by gastro-oesophageal reflux is quite exceptional in adults and may present some diagnostic difficulties.

In this paper we describe two patients admitted to the Emergency Department of the University Hospital for choking attacks caused by functional obstruction of airways at the level of the larynx with

episodes of reflex central apnoea. In one of the patients the attacks were so severe that tracheostomy was necessary. Subsequent examinations revealed that the 'trigger factor' was a gastro-oesophageal reflux with aspiration of the gastric contents in the larynx.

## Case histories

### PATIENT 1

A 57 year old man was admitted to the Emergency Department of the University Hospital for an episode of choking that lasted two to three minutes and relieved spontaneously. The patient was sent to the ORL Department for a full investigation. He had a 15 day history of nocturnal crisis of choking that woke him up suddenly with a sense of 'blocked breathing' lasting a few seconds, followed by non-productive cough rapidly relieved by sitting up. During the day the respiratory crisis with cough and gasp was induced by physical effort, especially lifting weights, trunk flexions, and by the supine position while working. Indirect laryngoscopy revealed a normal larynx except for a mild erythema of the true

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vocal cords which showed normal motility at deep inspiration. Tomography of the larynx showed no morphological alterations of the glottic or hypoglottic regions. Electrocardiography and chest x-ray examination were negative with no signs of pulmonary emboli. Routine examinations were normal, as well as serum calcium and magnesium, and renal function. Endocrinological and neurological examinations did not reveal any alterations and so EEG and TC of the head. Despite the steroid and antibiotic treatment immediately undertaken the attacks of choking continued to appear mainly at night and compelled the patient to remain awake overnight and sit upright, as the supine position triggered the crisis. On the third day of his admission, during a very severe attack of choking, the ORL specialist carried out a tracheostomy. Direct laryngoscopy confirmed the alterations previously observed during the indirect one. After tracheostomy the nocturnal respiratory attacks decreased in frequency and intensity but did not disappear and the patient continued to complain of 'arrest of breathing' and non-productive cough. As the upper x-ray showed some gastro-oesophageal refluxes, the patient was sent to us for further examination. Past gastroenterological history was negative.

Oesophageal manometry performed with a technique previously described<sup>10</sup> showed a very low basal tone of the LOS (4.7 mmHg) and pressure waves with a lower than normal amplitude and sometimes synchronous. Twenty four hour oesophageal pH monitoring<sup>11</sup> with the pH electrode positioned either 5 cm above the lower oesophageal sphincter and just below the upper oesophageal sphincter showed a higher than normal 'total reflux time' (24.5% and 6.8%, respectively), with frequent acid refluxes reaching the upper oesophagus mainly during the night. The diary kept by the patient and the event marker of the pH recorder indicated that the nocturnal respiratory crises were preceded by acid refluxes recorded at the level of the upper oesophagus. The pH electrode was also positioned in the tracheostomy just below the larynx and pH monitoring of the hypalaryngeal lumen was carried out for 24 hours: a drop in pH was observed during a respiratory crisis (Fig. 1). To our knowledge, how-



Fig. 1 Overnight recording from 10 pm to 6 am of the intraluminal pH of the hypoglottic region obtained by means of a pH electrode introduced through the tracheostomy in patient 1. Note the fall in intraluminal pH at the time of the appearance of choking attack (\*) indicating an aspiration of acid material refluxed from the stomach.

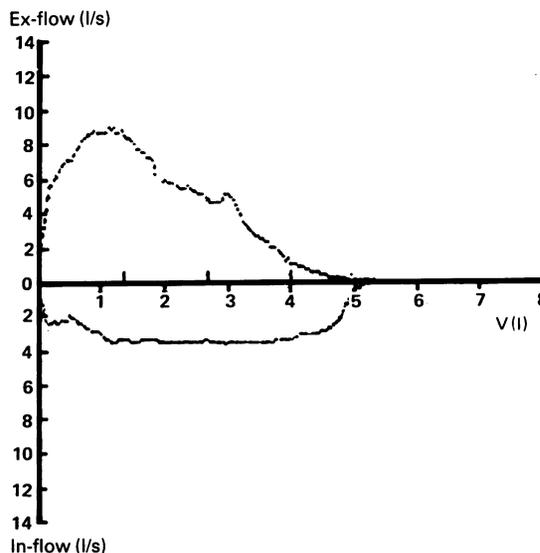


Fig. 2 Measurement of the forced expiratory volume (ex-flow, tracing above the ordinate) and forced inspiratory volume (in-flow, tracing below the ordinate) in the patient 2 at the time of a choking attack. The flattening of the inspiratory flow indicates an obstruction in the extrathoracic airways.

ever, the 24 hour 'hypalaryngeal' pH monitoring has not been carried out to date and parameters useful for establishing the entity of pH drop indicative of acid juice aspiration are not available. Gastric emptying test with a scintigraphic method described elsewhere<sup>12</sup> showed a moderate delay in gastric emptying and some spontaneous gastro-oesophageal refluxes. Endoscopy showed a apparently normal gullet but oesophageal biopsy from the superior third showed a deep chronic oesophagitis. On the basis of these results we conclude that the patient had episodes of aspiration of gastric contents with consequent crisis of laryngospasm and reflex central apnoea, the pathogenesis of which will be discussed in the 'comment' section. The patient was discharged from the hospital with tracheostomy and with a treatment consisting of gastric antisecretory drugs, such as famotidine, 40 mg before going to bed, prokinetic

drugs, as metoclopramide 10 mg before each meal and before sleep, and antireflux drugs, as gaviscon (alginic acid+antacid) after meals and before going to bed. Dietary advice and changes in life style were also prescribed. Clinical controls were programmed every three days and when required. As the respiratory crisis did not reappear and indirect laryngoscopy showed a normal larynx, tracheostomy was closed 20 days after the discharge from the hospital. At the second and six month follow up the patient did not complain of any significant symptoms, and indirect laryngoscopy was completely normal. The 24 hour oesophageal pH metric monitoring carried out after a six months treatment showed a marked decrease of the 'total reflux time' in the lower

oesophagus from 24.5% to 3.1% which is within the normal range.

#### PATIENT 2

A 52 year old man presented at the Emergency Department for an acute respiratory insufficiency with choking, cornage and tirage. He was transferred to the Pneumology Department where respiratory tests carried out immediately showed signs of extratoracic airways obstruction, probably laryngeal (Fig. 2). The patient was then sent to the ORL Department. Indirect laryngoscopy revealed a chronic inflammation of the vocal cords with oedema, while the laryngeal motility was normal. In the meantime, the crisis relieved spontaneously. This respiratory

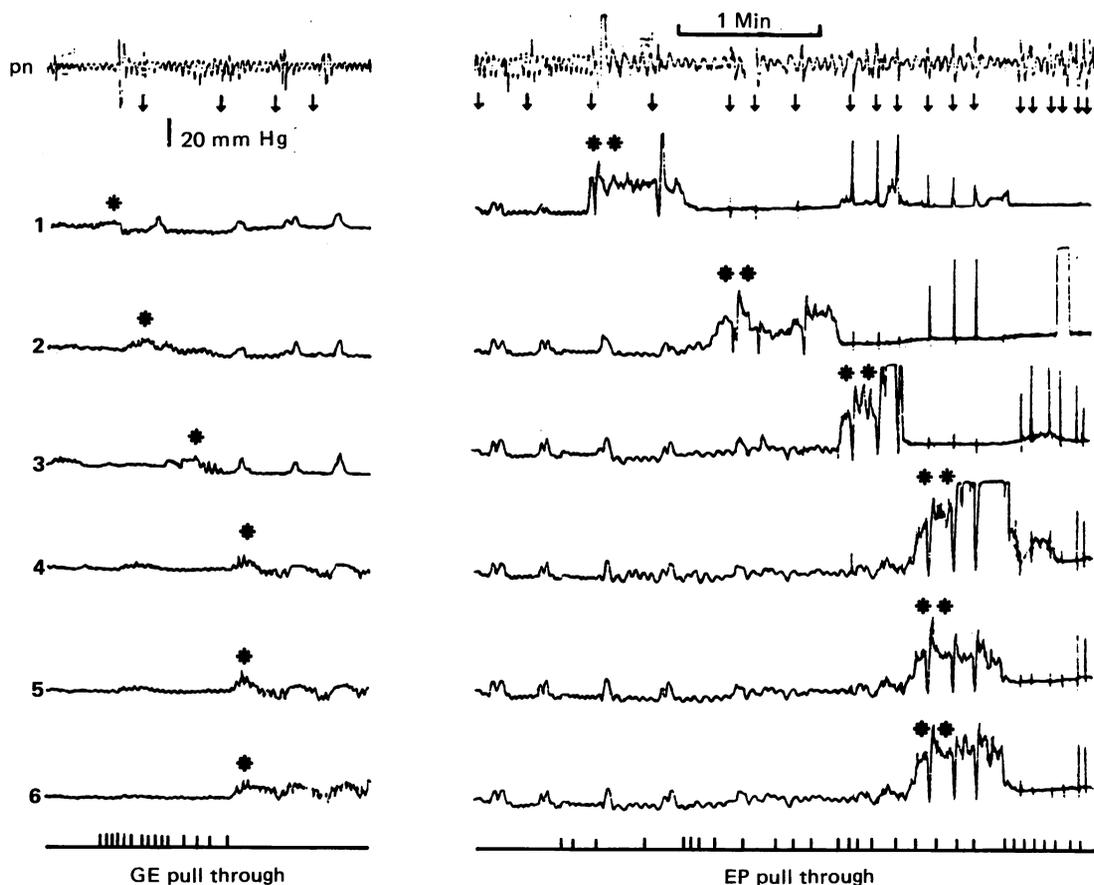


Fig. 3 Gastro-oesophageal (GO) and oesophagopharyngeal (EP), manometric pull through in the patient 2 with choking attacks caused by inspiration and an early stage of a motor neurone disease. Recording points 1, 2, and 3 are 5 cm apart, whereas 4, 5, and 6 are at the same level and 5 cm apart from No 3. Arrows indicate swallows, and 1 cm intervals of the stepwise pull-through are indicated at the bottom. Note the very low pressure of the lower oesophageal sphincter (\*) and the low and synchronous pressure waves of the oesophageal body. In addition, 2-3 cm below and 4-5 cm above the upper oesophageal sphincter (\*\*) the postdeglutitive pressure waves are absent indicating loss of function of the striated muscle.

episode was the last of a series that began about two years before, taking place once or twice a year, increasing in severity and frequency to twice a month. Treatment with antibiotics and steroids by aerosol prescribed in the last month by an ORL specialist, who observed corditis with indirect laryngoscopy, was ineffective, and the patient continued to have nocturnal crisis of choking that compelled him to remain awake for the major portion of the night, sitting on the bed. Laryngeal and chest x-ray examination, ECG, and EEG were normal, as well as serum calcium and magnesium. Ultrasonography of the upper abdomen was normal. Neurological examination showed hyperactivity of the muscle-stretch reflexes in the upper limbs and some rare fasciculations in the tongue. On the basis of the results of electromyography an early stage motor neurone disease, probably amyotrophic lateral sclerosis, was suspected. The only symptoms complained of by the patient, however, was a mild weakness in the upper limbs and some degree of dysphagia. Because of the latter symptom the patient was sent to us for further examination. Past gastroenterological history included duodenal ulcer 15 years before, the symptoms of which disappeared almost completely three years before, along with the healing of the ulcer, and were replaced by retrosternal pain. This pain was similar to that of angina pectoris, but ECG, treadmill test, and dynamic ECG were repeatedly normal. The patient also recently began to notice regurgitation of liquid with a 'bitter' taste in the mouth when bending over, and had noticed small yellow spots on the pillow. X-ray and endoscopy showed an apparently normal upper gut. The mucosal biopsy, however, from the superior third of the oesophagus revealed a deep chronic oesophagitis with achantosis and paracheratosis. The 24 hour oesophageal pH metric monitoring, carried out in a way similar to that used for the patient 1, showed a markedly higher than normal 'total reflux time' at the two recording levels (19.8% and 9.2%, respectively) with frequent and long standing acid refluxes reaching the upper oesophagus. Some long lasting increases of the oesophageal pH >7 were also observed in the upper oesophagus during the night. It was concluded that the patient had acid and bile refluxes. A relationship between some of the reflux episodes and the attacks of choking was established from the event marker of the pH-recorder and the diary kept by the patient. Manometric examination of the oesophagus showed: a very low basal pressure of the lower oesophageal sphincter (5.9 mmHg), low synchronous oesophageal body pressure waves, and absence of postdeglutitive pressure waves 2-3 cm below and 4-5 cm above the upper oesophageal sphincter (Fig. 3). This motor pattern fitted well with

the diagnosis of amyotrophic lateral sclerosis. The gastric emptying measured with a scintigraphic method showed a moderate delay in gastric emptying and spontaneous gastro-oesophageal refluxes of the radiolabelled meal. An antireflux treatment similar to that prescribed in the other patient was undertaken. As the therapy was followed by the disappearance of respiratory attacks, the patient was discharged from the Hospital with this treatment, followed by programmed follow ups. At the two months follow up, respiratory crisis had almost completely disappeared together with the laryngeal flogosis as the indirect laryngoscopy. Some degree of dysphagia persisted, however, probably as a result of the abnormal oesophageal motility for the underlying motor neurone disease, the diagnosis of which was confirmed by further examination. At six months follow up the patient showed a further worsening of the symptoms because of lateral amyotrophic sclerosis, particularly muscular weakness and dysphagia, but he did not have the choking crisis any more. It was not possible, however, to perform a 24 hour oesophageal pH metric follow up.

#### Discussion

Aspiration of gastric content which refluxes from the stomach into the pharyngo-oesophageal tract, mainly affects infants and the elderly,<sup>13</sup> as the mechanisms that prevent the reflux of the acid content from the stomach into the laryngotracheal tube may not then be fully operative. Aspiration is a not rare event in non-elderly adults, however, in whom it usually induces bronchopulmonary recurrent infections, chronic bronchitis, intermittent hoarseness and bronchial asthma.<sup>1-5</sup> Respiratory arrest caused by aspiration of gastric content in the larynx is a feature almost exclusively seen in infants where it may be characterised by laryngospasm and/or reflex central apnoea, and is believed to be the major cause of 'cot deaths'.<sup>6-9</sup> The aspiration of gastric contents in adults may lead to an intractable posterior laryngitis ('acid laryngitis')<sup>14</sup> or to a subglottic stenosis,<sup>15</sup> the aetiology of which is frequently not recognised. Respiratory arrest as a result of the aspiration of gastric contents is quite a rare event in adults. We collected two cases which presented choking attacks as a result of gastro-oesophageal reflux and aspiration. The cause of their respiratory attacks was at first unrecognised and their severity and intractability necessitated tracheostomy in one case. In the other case laryngospasm, induced by aspiration of refluxed gastric content, was the first clinical manifestation of the amyotrophic lateral sclerosis. The clinical interest of these cases lie not only in their rarity, but also in the fact that both patients did not present evident symptoms of gastro-

oesophageal reflux. In fact they did not complain of heartburn, pyrosis, or acid regurgitation, at the beginning of the respiratory symptoms, with the exception of sporadic regurgitations of bile in one case. In addition, when the suspicion of gastric content aspiration arose, and we tried to prove it, neither upper gut x-ray nor endoscopy showed any apparent lesion of the oesophagus, with the exception of some rare barium refluxes at radioscopy in one case. Only hystobioptic examination done after pH metric testing showed a deep chronic oesophagitis in both cases. The respiratory attacks were almost the sole manifestation of gastro-oesophageal reflux in these patients. In any case, many of the patients who present with head and neck manifestations of gastro-oesophageal reflux such as hoarseness, loss of voice, pharyngeal tightness, sensation of a lump in the throat, are frequently misdiagnosed as neurotics, because their examinations are normal.<sup>15 16</sup> Consequently, the absence of an evident cause in patients with laryngeal disturbances should alert the ORL specialist to ask for a further examination of the oesophageal motor function. This examination consists mainly of the manometric study of the oesophageal motor activity and of the 24 hour pH metric monitoring of the lower and upper oesophagus. Moreover, in our patient who underwent tracheostomy, the definitive diagnosis was obtained by means of the 24-hour pH metric 'hypolaryngeal' monitoring which showed the arrival of acid in the hypolarynx at the same time the attack of choking occurred. To our knowledge this is the first report of the 'hypolaryngeal pH metric monitoring'. In most cases, however, the diagnosis is based on the results of upper oesophagus pH monitoring which shows a drop in pH just before the appearance of the respiratory symptoms. The scintigraphic evaluation of the oesophageal function may also be of some help, for it gives useful information on oesophageal propulsive activity and occurrence of refluxes.<sup>17</sup> Pulmonary scintigraphy to detect aspiration, performed with the technique described by Ducoloné<sup>5</sup> is also helpful, but its sensitivity is very low, as only one fifth of the pulmonary aspirations are detected. With regard to the mechanisms of these choking attacks caused by aspiration, either laryngospasm or reflex central apnoea may be taken into account. In fact, the quantity of material aspirated was not likely able to give a mechanical occlusion of the bronchial tree, as testified by the rapid and spontaneous improvement of the ventilation, and by the absence of inflammatory events in the pulmonary tissue. In infants, a small quantity of refluxed material is able to induce a local reflex laryngospasm or a reflex central apnoea or both.<sup>7 18 19</sup> Experimental respiratory arrest may be produced in

piglets by instillation of water or cow's milk into the trachea. This response may be abolished by cutting the superior laryngeal nerve and may be reproduced by its stimulation.<sup>18</sup> The reflex central apnoea is caused by the overriding of central and peripheral respiratory drive mechanisms by stimulation of laryngeal chemoreflex system. It is usually followed by a 'break through' with resumption of normal respiratory activity. This mechanism may explain the discrepancy between the patients' symptoms and the paucity of their laryngeal alterations. The mucosal laryngeal receptors responsible for this reflex<sup>20</sup> are stimulated by the refluxed acid/or bile which should sensitise or alter the sensory component of this reflex. In fact, both bile and acid have been shown experimentally to damage the respiratory mucosa when aspirated.<sup>21 22</sup> In infants, this mechanism of the central reflex apnoea is believed to take place for the incomplete maturation of central and peripheral respiratory drive mechanisms.<sup>18</sup> In adults the explanation of why one patient responds with reflex central apnoea to acid aspiration, whereas the great majority of patients present other kinds of laryngeal and broncopulmonary symptoms, is lacking. The epidemiological evidence, however, suggests either a mechanism for sensitisation of this receptors system or the presence of concomitant depression of the respiratory drive mechanisms, similar to that observed in central sleep apnoea.<sup>22</sup> The pathogenesis of laryngospasm in the patient with motor neurone disease involving the brainstem, may be also explained with the 'irritability'<sup>23</sup> of the damaged motor neurons of the laryngeal nerve which fire repetitively, when stimulated by the afferent sensorial fibres coming from the laryngeal mucosa injured by the acid material.

In conclusion, the occurrence of respiratory arrest in patients with gastro-oesophageal reflux is quite a rare event, easily misdiagnosed if the symptoms of gastro-oesophageal reflux are absent and the upper gut x-ray and endoscopy are negative. Accurate studies of oesophageal motor function should be made in cases where the respiratory symptoms are of unclear origin.

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