Oesophageal changes in systemic sclerosis

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EDITORIAL COMMENT These studies provide evidence for the primary lesion in the oesophagus in cases of systemic sclerosis being in the smooth muscle fibres rather than in the neural plexus. The loss of oesophageal peristalsis could often be demonstrated by cine-radiography and manometry before symptoms appeared. By the same techniques it was shown that as the disease progresses the oesophageal wave becomes incoordinated and finally disappears and muscle is atrophied early.

Visceral involvement in systemic sclerosis is now recognized to be common and to occur in the absence of the skin changes of acrosclerosis (Rodnan and Fennell, 1962). Of the many visceral disturbances this disease may produce, those in the oesophagus were the first to be described (Ehrmann, 1903) and frequently dominate the clinical picture. Dilatation of the oesophagus was noted by Rake (1931) who suggested that this was the result of spasm of the cardiac sphincter brought about by an irritative lesion of the sympathetic nervous system. Goetz (1945) and Rafsky and Herzig (1946) subscribed to this view, believing this oesophageal disorder in systemic sclerosis to be a neuromuscular dysfunction allied to cardiospasm.

Oesophageal motor studies revealed that in systemic sclerosis, unlike cardiospasm, the predominant abnormality is impairment of motility with atrophy of the smooth muscle coat. A delay in oesophageal transit time when the subject is in the recumbent position, and inability to swallow against gravity, were observed radiologically in systemic sclerosis by Kuré, Yamagata, Tsukada, and Hiyoshi (1936), Lindsay, Templeton, and Rothman (1943), Hale and Schatzki (1944), Olsen, O'Leary, and Kirklin (1945), Mahrer, Evans, and Steinberg (1954), and Boyd, Patrick, and Reeves (1954). The manometric studies of Kramer and Ingelfinger (1949) and of Dornhorst, Pierce, and Whimster (1954) confirmed the impairment or complete absence of oesophageal peristalsis in many patients with systemic sclerosis. Creamer, Andersen, and Code (1956) found that the peristaltic wave disappeared a short distance below the pharyngo-oesophageal sphincter and showed that the oesophago-gastric sphincter had lost its tone and response to swallowing. Treacy, Baggenstoss, Slocumb, and Code (1963) were able to correlate the extent of the loss of peristaltic activity with that of atrophy of the muscular coat in patients

subsequently coming to necropsy and demonstrated atrophic smooth muscle fibres intermingled with unaffected striated fibres.

Although the early clinical descriptions of the oesophageal disturbance in systemic sclerosis mention dysphagia as the predominant symptom, Lindsay *et al.* (1943) pointed out that gastro-oesophageal reflux is a frequent occurrence. The reddening and thickening of the mucosa of the lower oesophagus found at oesophagoscopy in each of their four patients led them to the view that oesophagitis and stricture formation are the result of gastro-oesophageal reflux rather than of the sclerodermatous process itself. The belief that reflux accounts for many, if not all, of the mucosal changes in systemic sclerosis has been supported by Lushbaugh, Rubin, and Rothman (1948) and by Bourne (1949). However, Bevans' (1945) finding of a cellular fibrillar tissue in the oesophageal mucosa, and the frequency of leukoplakia in the oesophageal mucosa (Goetz, 1945; Leinwand, Duryee, and Richter, 1954) suggest that specific mucosal changes may be present in systemic sclerosis.

Of possible relevance to the gastro-oesophageal reflux which occurs in systemic sclerosis is the high incidence of hiatus hernia reported by Olsen *et al.* (1945), who noted this to be present in nine of 18 patients with the disease subjected to careful radiological examination. On the other hand, Somerville, Bargaen, and Pugh (1959) found hiatus hernia in only two of their 11 patients and Harper (1953) in two of his 14, while the reviews of radiological findings in systemic sclerosis by Hale and Schatzki (1944) and Leinwand *et al.* (1954) make no mention of hiatus hernia.

The objects of the present survey are twofold: first to study the frequency with which symptoms, radiological, and manometric changes of oesophageal involvement are present in systemic sclerosis,

and secondly to examine the light shed on the closing mechanisms at the normal cardia by the disturbance found in systemic sclerosis.

CLINICAL FEATURES

The clinical and other features recorded are summarized in the Table.

Twenty-two patients with systemic sclerosis were included in this series and each suffered from Raynaud's phenomenon, often of many years' duration. Twenty had acrosclerotic changes in the hands and the two remaining patients showed typical telangiectasia of the face.

Symptoms of gastro-oesophageal reflux were present in 13 of the 22 patients. In the majority these developed some years after the skin changes had appeared, but in two chest pain from reflux oesophagitis preceded the sclerotic changes in the hands. In nine patients gastro-oesophageal reflux constituted a severe disability, causing chest pain on recumbency and acid reflux into the mouth. One of these nine suffered from recurrent bleeding from the inflamed oesophageal mucosa and two others underwent operation for oesophageal stricture. In the remaining four patients symptoms of gastro-oesophageal reflux were mild and usually only elicited by specific questioning.

Only five of the 22 patients would admit to dysphagia. In two difficulty in swallowing was an early symptom which occurred intermittently and was not severe. The chief difficulty encountered was

with solid matter which tended to stick in the lower oesophagus, and the patient had to swallow copious draughts of fluid to clear the oesophagus and so relieve his dysphagia. In contrast the other three patients developed a severe and progressive dysphagia late in the course of the disease and were found to have fibrous strictures resulting from reflux oesophagitis.

PATHOLOGY

Tissue from the oesophagus was obtained at operation (for resection of a stricture) in one patient and at necropsy in three others. In each the smooth musculature of the lower oesophagus was replaced by fibrous tissue and the oesophageal mucosa was inflamed. In three ulceration was present and in two extensive leukoplakia had developed (Fig. 1). No lesions specific for systemic sclerosis could be identified and no histological abnormality could be detected in the collagen of the submucosa. The ganglion cells in Auerbach's plexus were neither deficient nor histologically abnormal. The striated muscle of the upper oesophagus appeared normal.

RADIOLOGY

Barium studies of the upper gastrointestinal tract were done in each of the patients studied, and in 17 a record of the oesophageal motor disturbance was obtained by means of cine-fluoradiography using a Marconi image intensifier fitted with a 16 mm. Bolex

TABLE

Case No.	Clinical Features				Radiological Findings				Manometric Findings			
	Dysphagia		Symptoms of Gastro-oesophageal Reflux		Stricture	Oesophagus		Gastro-oesophageal Reflux	Hiatus Hernia	Oesophageal Peristaltic Wave		Tone of Oesophago-gastric Sphincter (mm.Hg)
	Presence	Duration (years)	Presence	Duration (years)		Dilatation	Peristalsis			Upper	Lower	
1	+	2	+	5	+	+	Not seen	+	+	—	—	0
2	+	2	+	6/12	—	+	Not seen	+	+	—	—	0
3	—	—	+	5/12	—	+	Not seen	+	+	—	—	0
4	—	—	+	5	—	+	Not seen	+	+	+	—	3
5	—	—	+	10	—	+	Not seen	+	—	—	—	0
6	—	—	+	10	—	+	Not seen	+	—	+	—	3
7	—	—	+	1	—	+	Not seen	+	—	+	—	0
8	—	—	+	5	—	+	Not seen	+	—	+	—	0
9	—	—	+	3	—	+	Not seen	+	—	+	—	0
10	+	3	+	5	+	+	Not seen	+	+	—	—	—
11	+	8	+	13	+	+	Not seen	+	+	—	—	—
12	—	—	+	27	—	+	Not seen	+	+	—	—	—
13	—	—	+	8	—	+	Not seen	+	—	—	—	—
14	+	2	—	—	—	+	Not seen	+	+	—	—	0
15	—	—	—	—	—	+	Not seen	—	—	+	+	12
16	—	—	—	—	—	—	Not seen	—	—	+	—	0
17	—	—	—	—	—	+	Present	—	—	—	+	9
18	—	—	—	—	—	—	Not seen	—	—	+	—	12
19	—	—	—	—	—	—	Present	—	—	+	+	15
20	—	—	—	—	—	—	Present	—	—	—	—	—
21	—	—	—	—	—	+	Present	—	—	+	—	2
22	—	—	—	—	—	+	Absent	—	—	+	—	4

FIG. 1.

FIG. 1. *Oesophagus and stomach showing intense oesophagitis and leukoplakia in the lower half of the gullet (case 18).*

FIG. 2.

FIG. 2. *Early dilatation of the oesophagus, which in the resting state contains air, in a patient with early systemic sclerosis (case 16).*

cine camera. Studies were made of swallowing in the upright and recumbent postures and a careful search was made for gastro-oesophageal reflux and hiatus hernia, using the technique described by Johnstone (1957).

The earliest changes were prolongation of transit time and failure of the peristaltic wave to clear barium from the oesophagus with the patient in the supine position. Cine-radiography was particularly valuable in showing loss of peristaltic activity and in the head-down, supine position barium was often retained for many minutes after swallowing. The oesophagus showed a progressive atonic dilatation (Fig. 2) often containing air in the fluid or much mucus in the resting state. Dilatation was radiologically demonstrable in 17 of the 22 patients in this series, and was not infrequently found in the absence of oesophageal symptoms.

Gastro-oesophageal reflux was demonstrable

radiologically in 15 of the 22 patients. When the disorder was in its early stages, several examinations were sometimes required to demonstrate reflux, but as the disease progressed the cardia became widely patent and the oesophagus and stomach became virtually a common chamber, shut off only at the height of inspiration by the right crus of the diaphragm (Fig. 3). If the patient remained supine, barium which had flowed back into the oesophagus would remain there for some time because of the impairment of peristalsis.

Hiatus hernia was noted in eight patients and in each reflux was demonstrated (Fig. 4). In a further patient hiatus hernia was suspected because silver clips placed at the oesophago-gastric mucosal junction at oesophagoscopy lay above the diaphragm, although no hernia could be shown radiologically. In each instance the hiatus hernia was small and of the sliding variety. Sometimes several

FIG. 3.

FIG. 3. *Gross dilatation of the oesophagus with wide patency of the cardia in a patient with advanced systemic sclerosis (case 8).*

FIG. 4.

FIG. 4. *Oesophageal dilatation and a small sliding hiatus hernia in systemic sclerosis (case 2).*

radiological examinations were necessary before the hernia could be found; loss of competence of the cardia caused much difficulty in this respect because pressure over the stomach simply resulted in barium flooding up into the oesophagus, instead of a hernia being pushed through the hiatus. In the remaining 13 patients, six of whom had radiologically demonstrable reflux, no evidence of hiatus hernia was obtained.

Because in several patients with reflux the oesophago-gastric angle appeared less acute than normal, special attention was paid to this region during the radiological examination to decide whether this was in any way related to loss of competence of the cardia. In spite of standardization of the position of the patient, the quantity of barium given, and the phase of respiration in which the films were taken, considerable variation was found in this angle, both in normal individuals, and in patients with systemic sclerosis. This precluded quantitative assessment of the angle, but the impression was gained that in

certain subjects with gastro-oesophageal reflux and no demonstrable hiatus hernia, the oesophago-gastric angle was abnormally wide.

MANOMETRY

Manometric records from the oesophagus and oesophago-gastric junction were obtained in 17 patients, using water-filled, open-ended tubes connected to capacitance manometers (Atkinson, 1959).

Peristaltic contractions were consistently absent from the lower oesophagus in 14 of the 17 patients (Fig. 5). In five of these patients no contractions could be recorded from any part of the oesophagus, whereas in the other nine peristaltic waves could be found in the upper oesophagus. The presence of dysphagia seemed to correlate with the extent of the muscular lesion, as the only two patients with this symptom both showed absence of peristalsis throughout the oesophagus. When present, peristaltic waves were usually of small amplitude compared

with those found in normal subjects; in one patient serial studies as the disease progressed showed a gradual loss of amplitude until the waves disappeared altogether, but at no time was incoordination of the peristaltic reflex seen.

The oesophago-gastric sphincter was detectable by manometric means, as a localized zone of increased pressure at the oesophago-gastric junction, in only eight of the 17 patients. The tone of the

FIG. 5. Intra-oesophageal pressure changes during swallowing in a patient with systemic sclerosis (case 6). A normal peristaltic wave is visible in the upper tracing, but no wave can be seen in the middle and lower oesophageal tracings. The lowermost tracing, which is at the level of the oesophago-gastric junction, shows little elevation of resting pressure, but a normal fall on swallowing, indicating that the sphincteric tone is reduced, but that it functions in a coordinated way during swallowing.

FIG. 6. Record of resting intraluminal pressure during withdrawal of recording device from the stomach (43 cm.) into the oesophagus (40 cm.). The zone of raised intraluminal pressure seen at the normal cardia is absent, indicating loss of sphincteric tone.

oesophago-gastric sphincter appeared good in four of these patients, in that the rise in intraluminal pressure at the oesophago-gastric junction was 9 mm. Hg, or more; none of these patients suffered from symptoms of gastro-oesophageal reflux and in none was this demonstrated radiologically, nor was hiatus hernia present. The tone of the sphincter was lower in the other four patients, two of whom suffered from gastro-oesophageal reflux, and one had a small, sliding, hiatus hernia.

In the nine remaining patients repeated attempts failed to demonstrate any zone of increased intraluminal pressure at the oesophago-gastric junction consistent with a normally functioning sphincter (Fig. 6). Eight of these patients suffered from symptoms of reflux, and in eight the presence of reflux was confirmed radiologically; four of the nine had a demonstrable hiatus hernia, but in the remaining five no hernia could be found.

These manometric observations indicate that gastro-oesophageal reflux and hiatus hernia occur in patients in whom the paralytic lesion of the intrinsic musculature of the oesophago-gastric junction is most severe. Although hiatus hernia was a very common finding, it did not appear to be essential for the development of gastro-oesophageal reflux.

THE MECHOLYL TEST

The response of the oesophageal musculature was studied manometrically in two patients after an injection of 10 mg. methacholine chloride. In contrast to the exaggerated response seen in achalasia, both showed diminished sensitivity and in one no contraction occurred.

DISCUSSION

Smooth muscle atrophy is the dominant lesion in the oesophagus in systemic sclerosis and the functional effects are twofold. First, the amplitude of peristalsis in the mid and lower oesophagus gradually dimin-

ishes until it disappears altogether and this may cause dysphagia. Secondly, the closing mechanisms at the cardia fail and reflux oesophagitis results. The failure of peristalsis is initially confined to that part of the oesophagus in which the wall contains mainly smooth muscle, and in the upper part, where striated muscle predominates, peristalsis is normally retained until much later in the course of the disease. The impairment of peristalsis correlates well with the extent of smooth muscle atrophy, and Treacy *et al.* (1963) found that striated muscle was unaffected, even when in close proximity to atrophied smooth muscle fibres. In our experience the peristaltic wave remains coordinate until it disappears completely as a consequence of smooth muscle atrophy. Dysphagia is rarely disabling and, except in recumbency, liquids can usually be taken without difficulty, since the unaffected pharyngeal musculature is able to propel liquid boluses into the lower oesophagus in the normal way. Solids are more difficult to swallow because peristalsis is normally necessary for their propulsion through the gullet, but these can usually be washed through by taking liquids and by swallowing in the upright posture, when gravity assists.

The site of the primary lesion in the oesophageal wall is uncertain, but the patho-physiological evidence available all points to this being either in the smooth muscle fibres themselves, or in the neural elements in the oesophageal wall. Our findings indicate that this is a primary affection of the smooth muscle fibres. Normal numbers of ganglion cells were present in the plexuses of the oesophageal wall in the four oesophagi examined histologically. The pattern of derangement of motility differs strikingly from that seen in achalasia and Chagas disease, where peristalsis becomes disorganized early in the course of the disease, and where the oesophageal wall may, indeed, be hypertrophied and capable of very powerful contractions. Furthermore, the response to methacholine chloride is subnormal or absent in systemic sclerosis in contradistinction to achalasia and Chagas disease, where parasympathetic denervation gives rise to hypersensitivity to acetylcholine and its derivatives (Kramer and Ingelfinger, 1951; Ferreira-Santos, 1961).

Gastro-oesophageal reflux occurs commonly in systemic sclerosis, often in the absence of hiatus hernia. The closing mechanism at the cardia fails presumably because the smooth muscle of the gut wall atrophies and the surrounding supportive structures, including the diaphragm, are unaffected. Involvement of the stomach in systemic sclerosis is much less obvious than that of the oesophagus (Hale and Schatzki, 1944; Harper, 1953) but, as the disease progresses, loss of peristalsis and gastric dilatation

with delay in emptying may occur (Meszaros, 1958; Gil, 1951). It seems probable that atony of the oblique muscle fibres of the gastric wall accounts for the loss of the oesophago-gastric angle and the opening out of the cardia into the shape of an inverted funnel. Patency of the abdominal segment of the oesophagus due to loss of tone of the oesophago-gastric sphincter is an important contributory factor.

The high incidence of hiatus hernia in systemic sclerosis has been attributed to reflux oesophagitis causing muscle spasm or fibrotic contracture of the oesophagus, so pulling the cardia through the hiatus. It is difficult to believe that the atrophic muscle of the gullet can retain sufficient contractile power to act in this way, and in the majority of our patients, including one coming to necropsy, the degree of oesophageal fibrosis appeared altogether insufficient to cause traction. Furthermore, the hiatus herniae noted in our patients were small and usually easily reducible. The most probable explanation appears to be loss of the anchoring function of the gastric musculature because of its loss of tone and atrophy.

SUMMARY

A clinical radiological and manometric study of the oesophageal lesion in 22 patients with systemic sclerosis is reported. Symptoms of gastro-oesophageal reflux were present in 13 and radiological evidence was found in 14. Five complained of dysphagia: in two this was the result of failure of oesophageal peristalsis, whilst in the other three it was caused by peptic stricture of the oesophagus.

Cine-radiography and manometry indicated that loss of oesophageal peristalsis could often be demonstrated before symptoms appeared. When the disorder was more advanced, manometry showed loss of tone of the oesophago-gastric sphincter and cine-radiography indicated that the oesophagus was atonic and dilated and the cardia widely patent.

In contrast to achalasia and Chagas disease, the oesophageal wave remains coordinated until it finally disappears as the disease progresses, muscle atrophy occurs early, and the mecholyl test is negative. It is, therefore, suggested that the primary lesion in the oesophagus in systemic sclerosis is in the smooth muscle fibres rather than in the neural elements.

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