

A Case of Kindler Syndrome presenting with Dysphagia

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ABSTRACT

Kindler syndrome is a rare hereditary disorder that predominantly involves the skin and mucous membrane. Acral skin blistering, progressive photosensitivity, skin atrophy and poikiloderma that begin from infancy and childhood are considered to be characteristic manifestations. Urethral, anal, esophageal, mouth and laryngeal mucosa may be involved in this syndrome, thus periodontitis and gingival involvement, anal, esophageal or urethral strictures may be present in this disease.

Although gastrointestinal tract involvement in patients with Kindler syndrome is possible, it is rare in the literature. We report the case of a 34-year-old male with Kindler syndrome who had referred with dysphagia. Upper gastrointestinal endoscopy revealed an esophageal web in the upper third of the esophagus. Endoscopic dilatation of the esophageal web was performed by using a mechanical dilating bougie. Two months after esophageal dilatation we found significant improvement in the patient's dysphagia according to the validated Mayo Dysphagia Questionnaire (MDQ).

Keywords: Kindler Syndrome; Dysphagia; Gastrointestinal endoscopy; Dilatation; Esophageal stenosis

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INTRODUCTION

Kindler syndrome was originally described in 1954 by Theresa Kindler (1). It is a rare autosomal recessive disorder that mostly affects the skin and mucous membranes. A defect in the KinD1 gene localized on chromosome 20P 12.3 is considered to have a main role in Kindler syndrome. This gene

encodes Kindlin, a 677 amino acid protein, which is a membrane-associated structural protein. A defect in this protein leads to dissociation of cellular actin cytoskeletal and extracellular matrix.

This syndrome usually presents with skin manifestations in infancy and childhood that include blister formation, progressive poikiloderma, photosensitivity and diffuse cutaneous atrophy (particularly on the dorsal hands or feet)(2). Both blister formation and photosensitivity may decline with age. Additionally mucosal membranes can be involved in this disease, leading to esophageal, vaginal and urethral strictures. Other features include dental problems, nail dystrophy, webbing of the fingers and ophthalmic abnormalities, which may or may not be present. Occurrence of squamous cell carcinoma and bladder transitional cell carcinoma has been reported.

Morbidity and mortality from this disease are

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mostly related to secondary infectious that arise from blisters and bullas. Disease occurrence is equal among males and females, with no different in race (3).

Gene sequencing of the FERMT1 gene (KIND1 gene), is the current gold standard for diagnosis, but up to 30% of patients who present with features suggestive of this disease do not have a mutation in this gene(4).

Treatment is mainly limited to management of symptoms and disease complications by consultations with dermatologists, geneticists, dentists, ophthalmologists and gastroenterologists.

We report a case of a 34-year-old male with progressive dysphagia due to an esophageal stricture who was treated by endoscopic dilatation.

CASE REPORT

A 34-year-old male referred to our clinic with complaints of progressive dysphagia for sixteen years, since the age of 18. He could swallow liquids easily, but had difficulty with swallowing solid foods. He mentioned that dysphagia persisted through these years with variable severity. There was no problem with defecation or bowel movements. The patient had a history of skin lesions from infancy that included blister formation, progressive poikiloderma, reticular pigmentation, photosensitivity, webbing of his fingers and cutaneous atrophy which limited his hand movements. Additionally he suffered from nail dystrophy, unilateral hearing loss in the right ear, reduced tear secretion, xerophthalmia and periodontitis.

He was under the observational care of a dermatologist since childhood. Histopathological survey of his skin biopsy demonstrated nonspecific changes that included epidermal atrophy, capillary dilatation and upper dermal edema. No genetic analyses were performed due to the patient's reluctance. He was treated conservatively with emollients, protective sun creams and oral retinoids (neotigasonone 10 mg, 25mg) from age 11.

Physical examination revealed poikiloderma and skin atrophy of the hands and feet which limited his movements. Additionally sclerodactyly of the fingers and toes was present; most of his nails were dystrophic (Figure 1). The only disease manifestation on his face was the presence of reticular erythema that predominantly affected his cheeks. The trunk and abdomen were unremarkable. No problems were



Fig. 1: A, B) Severe skin atrophy, webbed fingers and palmar keratosis. C) Nail dystrophy.

detected in his oral cavity and pharynx to explain the swallowing difficulty. Thus the history of progressive dysphagia was strongly suggestive of esophageal problems. As a result an upper gastrointestinal endoscopy was performed, which demonstrated an

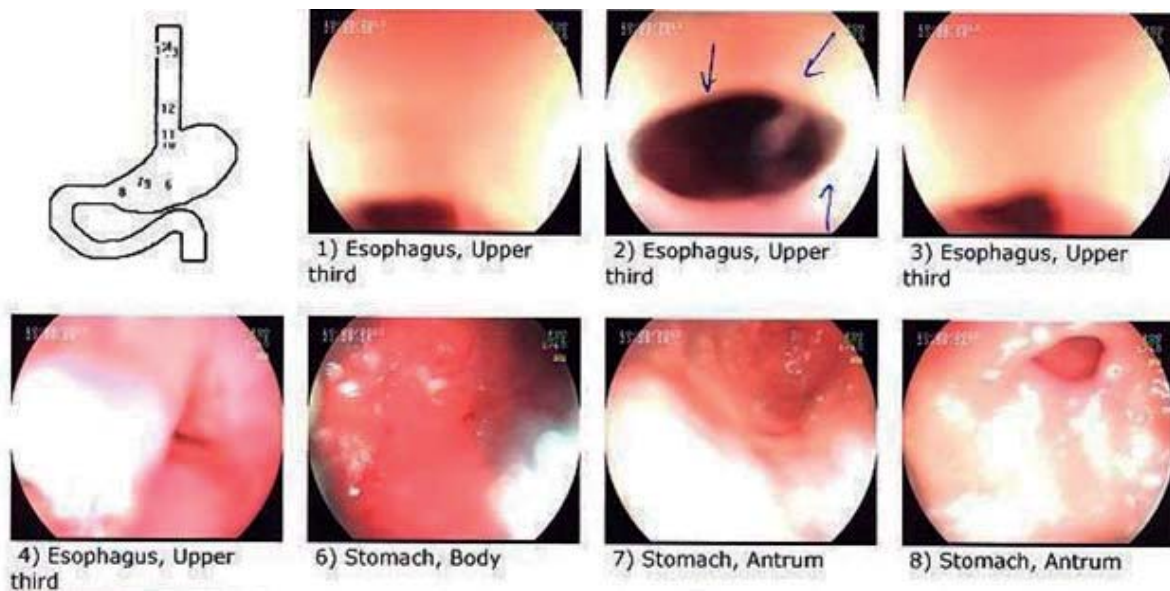


Fig. 2: Upper gastrointestinal endoscopy findings: an esophageal web in upper third of esophagus.

esophageal web in the upper third of the esophagus (Figure 2). Esophageal dilatation was performed by using a mechanical dilating bougie (Savary). Dilatation was started by using a 9 mm Savary and subsequently extended as follows: 9 mm, 11 mm, 12.8 mm, and 14 mm.

In a follow up visit that occurred two months later, there was significant improvement in the patient's dysphagia according to the validated Mayo Dysphagia Questionnaire (MDQ). The patient was able to easily swallow his tablet and capsule medications.

DISCUSSION

More than 100 cases of kindler syndrome have been reported worldwide since the first description of THIS disease in 1954(3). one of the leading studies performed on 26 Kindler patients in the year 2004 established that all shared four major clinical manifestations of acral blisters, progressive poikiloderma, severe skin atrophy and increased photosensitivity(3).

In an article in 2005, a set of clinical diagnostic criteria was proposed by Angelova-Fischer. He divided disease's clinical manifestations into three groups: major, minor and associated findings. The presence of four major criteria makes the diagnosis certain. The presence of three major and two minor

criteria makes the diagnosis probable. Major criteria consisted of acral blistering, progressive poikiloderma, skin atrophy, increased photosensitivity and gingival involvement. The minor criteria included syndactyly and urethral, anal, esophageal or laryngeal mucosal involvement. Associated findings included nail dystrophy, ectropion of the lower lid, keratoderma, pseudoainhum, leukokeratosis of the lips, squamous cell carcinoma, anhidrosis, skeletal abnormalities, dental caries and periodontitis(5).

According to the above mentioned criteria, our patient demonstrated four major criteria, thus the diagnosis was certain.

Gastrointestinal manifestations are not as common as dermatological symptoms in Kindler syndrome. Aside from esophageal or anal stenosis, gastrointestinal tract involvement seems to be rare in this syndrome. Here we review some gastrointestinal manifestations of the disease that have been reported in the literature.

Elk Sadler et al. reported two cases with severe gastrointestinal manifestations. One of the cases was an Australian infant with proven Kindler syndrome who presented bloody colic stool during the first postnatal week. Gastroduodenoscopy and colonoscopy were performed. Biopsy specimens

from the upper gastrointestinal tract showed normal histology. However histological assessment of mucosa of the descending and sigmoid colon and the rectum was remarkable for erosions and ulcers with pseudomembranous alterations of an overall highly vulnerable mucosa. The researchers stated that although bloody diarrhea could be considered a symptom of other common diseases, it was more likely due to Kindler syndrome. A 49-year-old male underwent partial resection of the small bowel because of stenosis. Initially, his stenosis was thought to be caused by Crohn's disease, however it was unclear whether his gastrointestinal tract involvement was caused by Crohn's disease or Kindler syndrome, which was diagnosed four years after the resection. In this report, the researchers stated that no cases with this severe gastrointestinal tract involvement had been described prior.

After describing these two cases, the researchers have mentioned the feasibility that gastrointestinal tract alterations in Kindler syndrome could be observed more frequently than described. Considering that the highest expression of the KIND1 gene can be found in keratinocytes, the colon and kidneys, it is proposed that gastrointestinal tract involvement should be looked at more frequently in Kindler syndrome(6).

According to Lai-Cheong, gastrointestinal manifestations of Kindler syndrome including anal and esophageal stenosis are more frequent than believed; additionally patients can develop other gastrointestinal symptoms such as severe colitis and bloody diarrhea. Furthermore, esophageal dilatation has been mentioned as an appropriate treatment for esophageal stenosis and it may be indicated in cases with severe esophageal dysfunction along with temporary parenteral nutrition(4).

In 2007, Tulin described the case of a 16-year-old female with Kindler syndrome who suffered from dysphagia, weight loss and anemia. Esophagoscopy and a barium esophagogram confirmed esophageal stenosis and web formation. She was scheduled to undergo a series of esophageal dilatation sessions, following temporary parenteral nutrition to improve her general condition(7).

The esophageal length in an adult is approximately 18-26 cm, which is anatomically divided into the cervical and thoracic sections. Its diameter is 2 cm

in the anteroposterior plane and 3 cm in the lateral plane. When the lumen is narrowed to less than 13 mm due to strictures, web, rings and other structural abnormalities, solid food dysphagia develops. However, poorly masticated food or motor dysfunction can result in dysphagia in larger diameters. Additionally, dysphagia is more likely in circumferential lesions than lesions that involve only a partial circumference of the esophageal wall(8).

Different endoscopic techniques are currently available for treatment of esophageal strictures or webs. Three general types of dilators are commonly in use, including: (1) mercury or tungsten-filled bougies (Maloney or Hurst)(2), wire-guided polyvinyl dilators (Savary Gilliard or American), and (3) TTS ("through-the-scope") balloon dilators(9). The Maloney type bougies have a tapered tip and can be passed either blindly (10) or under fluoroscopic control. This type of dilator is used for simple strictures that have diameters of 12 to 14 mm. The risk of esophageal perforation may be higher with blind passage of Maloney dilators than with Savary or TTS balloons, particularly in the patient with a large hiatal hernia, a tortuous esophagus, or a complex stricture(11). Savary and American dilators are passed over a guide wire that has been positioned with the tip in the gastric antrum, with or without fluoroscopic guidance(12). There are a variety of TTS balloon dilators available in either single or multiple diameters that may be passed with or without wire guidance.

We performed esophageal dilatation by using a 9 mm Savary that was extended to 14 mm. After two months the patient expressed satisfaction with his swallowing function according to the results of the validated Mayo Dysphagia Questionnaire (MDQ).

Kindler syndrome is a chronic, severe syndrome for which treatment is mainly symptomatic. Physicians should attempt to reduce patients' symptoms and disease complications, which would result in improvements in quality of life.

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