Abdominal Actinomycosis: Case Report and Literature Review

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ABSTRACT

Objective actinomycosis is a rare cause of acute abdomen. There was a case that began as appendicitis and subsequently developed into ileocecal and rectosigmoid actinomycosis. Case Report: Eight months after being diagnosed with appendicular actinomycosis but receiving no treatment and being discharged without complications from another institution, our patient, a 39-year-old woman, arrived at our emergency room with fever and intestinal obstruction. She began treatment with penicillin and underwent an exploratory laparotomy that revealed an ileocecal and rectosigmoid mass of malignant appearance; the pathology results, however, discarded any malignancy. A right hemicolectomy with ileotransverse anastomosis and sigmoid colostomy was performed in order to solve the problem of occlusion. The lamellae showed the typical sulfur granules of actinomycosis. Abdominal actinomycosis is a differential diagnosis in an unusual mass or abscess revealed in an abdominal CT scan. Penicillin remains the treatment of choice for a period of 6 to 12 months. Prognosis is favorable with prolonged penicillin therapy combined with surgical debridement (if needed). This review of the literature offers us an update of this disease in epidemiology, pathophysiology and its clinical features.

Key words: Actinomycosis, abdominal, abscess, malignant, neoplasms, appendicitis, abdominal mass, penicillin.

INTRODUCTION

In 1877, Bolinger isolated micelles with arm-shaped branches from lesions in the jaws of livestock. They were called actinomycetes (from Greek “aktin”, beam and hence, filament, and “myket”, fungi) because of its similarity to fungi rye, a misconception that persisted for more than 70 years. Human actinomycosis was first described in 1878 by Israel, who along with Wolfe (1891), first isolated the causative agent in culture and defined it as an organism of anaerobic nature. The first report of abdominal actinomycosis was by Sir Zachary Cope in 1949. Erickson made the distinction between cultures that developed from humans and animals and proposed the name Actinomyces israelii for the one observed in humans and Actinomyces bovis for the cattle variant (Lerner, 1974).

Actinomycosis is a rare and insidious disease. Its most common agent is the Gram-positive anaerobic bacteria A. israelii. Highly invasive in nature, its presentation may include any organ. It is a chronic, supplicative disease with a great tendency to form multiple abscesses and abundant granulation tissue. It spreads by direct extension, crossing anatomical barriers and hematogenously. It may take from months to years before any clinical manifestation. It is, however, unable to cross mucosal barriers. Its tendency to involve neighboring tissues often causes it to simulate malignant tumors (Meyer, 2000; Uchiyama, 1997). Hence, it was called The Great Imitator. It has three main clinical forms: cervicofacial (55%), thoracic (15%) and abdominopelvic (20%); with other locations being less...
frequent (10%) (Deshmuck, 1986; Chanussot, 2011).

Despite the fact that the most common pathogen in humans is the A. israelii, other actinomycetes species pathogenic to humans was also reported. These are A. naeslundii, A. viscosus, A. odontolyticus and A. meyeri gerencseriae. Humans are its natural reservoir. However, there is no documentation of transmission of the disease from person to person (Kuri, 2011; Smego, 1998). It has a tendency to form granulomas and micro-abscesses containing characteristic granules of sulfur compounds in a matrix of calcium phosphate, polysaccharides secreted by Actinomyces, colonies of actinomycetes, cellular debris and other associated organisms. They are yellow, but can go from white to brown. These granules are considered diagnostic of infection by Actinomyces, though, are only present in 50% of cases (Garner, 2007; Weese, 1975).

A. israelii is a strictly anaerobic, microaerophilic bacterium once considered a fungus. It is present as a normal commensal of the organism, mainly in the mouth, lower gastrointestinal tract and female genital tract that can become pathogenic after trauma, local infection or surgery that alters the body's natural mucous barrier, invading the surrounding tissues. It is associated with the use of intrauterine devices (IUDs) in women (Antonielli, 1999; Olvera, 2005; Perez et al, 2002; Yeguez, 2000).

An idea of the importance of the disease is some of its main manifestations as reported: brain abscesses, abscesses of soft tissues in the neck, thyroid abscesses, in the skin, anywhere on the body, empyema, pneumonia, osteomyelitis, thoracic masses, esophageal ulcers, abdominal masses, pancreatitis, liver abscesses, mesenteric abscesses, spondylodiscitis, pericarditis, endocarditis, splenic abscesses, perineal abscesses, endophthalmitis and bladder masses (Fazili, 2012; Henrikus, 1987; Iwasaki, 2003; Kleonatas, 2011; Russo, 2010). Despite its frequency and large number of locations affected, it is not accounted in the initial differential diagnosis. For this reason, a clinical case representative of this type of pathology in the abdomen was presented.

Clinical case

The patient is a 39-year-old female who underwent an open appendectomy on another institution eight months prior to admission to our hospital. One and a half years before the appendectomy, she had a tooth extraction. There is no history of use of IUDs. Despite a histopathologic diagnosis of actinomycosis, she did not receive specific treatment at the time. She arrived at the emergency room of our hospital on an admission diagnosis of probable endometriosis and partial bowel obstruction due to post-operative adhesions. At the time of admission, she had tachycardia (100 bpm), fever of 38°C, with leukocytosis of 23,000 and 5 bands. A pelvic ultrasound revealed uterine myomas of small elements and free fluid in the pelvic cavity. The diagnosis at this time was updated to endometriosis versus pelvic inflammatory disease. General surgery service was interconsulted and after analyzing the background, the decision to initiate treatment for abdominal actinomycosis (crystalline sodium penicillin) was done. An abdominal CT scan reported a dilated small bowel of 4 cm, dilatation of ascending and descending colon, abundant free fluid in the cavity and right paravesical recess. It evolved successfully for fourteen days, with an almost total decrease of free liquid (controlled by USG), remission of fever and symptoms. On the fifteenth day of intrahospitality stance, however, she presented data showing intestinal occlusion characterized by nausea, vomiting, and intermittent colic pain in the right lower quadrant, abdominal distention and fever of 38°C.

After a colonoscopy failed to progress beyond 25 cm from the anal margin, a new CT scan was performed, which showed thickening of the distal ileum wall. On the right flank, a lobulation on the front wall of the intestine, similar to a subserosal tumor, which does not bind the mucosa with central lucency suggesting necrosis was observed. Its dimensions were 32 × 31 × 42 mm (Figure 1).

At this point, an exploratory laparotomy was performed, finding an inflammatory mass dependent of the terminal ileum at 5 cm of the ileocecal valve; multiple nodes in the mesentery of 1 to 2 cm in diameter and a friable hard mass behind the uterus rectosigmoid junction level was palpated (Figures 2 and 3). A right hemicolectomy with ileotransverse Anastomosis and a loop sigmoid colostomy was performed (Figure 4). Post-operative evolution was slow but with stable improvement. The patient continued with nocturnal fever for some days. The histopathology reported probable chronic active ulcerative colitis and transmural lymphoid hyperplasia, predominantly histosinusal. Antibiotic treatment continued with 20 million units of penicillin G q24 h and a levofloxacin 500 mg PO regimen q12 h for 4 weeks. The family managed to rescue the gills of the first surgery reviewed by our pathologist confirming an appendiceal actinomycosis. Consequently, the patient continued treatment with penicillin VK for a year. Later, a colostomy closure was performed and evolution went on without further complications (Figures 5 and 6).

Epidemiology

Actinomycosis occurs worldwide and can be found as often in rural as in urban populations (Lee, 2010). In a review of the medical literature, an incidence of actinomycosis was estimated at 1 in 119,000 and 1 of each 400,000 cases per year (Cintron et al, year). The incidence peak was reported in middle-aged individuals, occurring less frequently in
Figure 1. Subserosal tumor with central necrosis in the front wall of the right flank intestine with inflammation in peritoneal fat.

subjects younger than 10 years and older than 60. In children, abdominal Actinomyces infection is rare. In a review of the English literature, only 12 cases of children with abdominal actinomycosis were identified (Yiğiter, 2007).

Abdominal actinomycosis is more common in men than in women (3:1), despite an increase in the number of cases in women using IUDs; actinomycosis is endemic, appearing around the world. There is no correlation between the disease and the place of residence, social class or race. No predilection for season or occupation has been identified, although in the first reports it was considered a rural disease. While not considered an opportunistic infection, it was reported in patients with HIV, leukemia and other immuno-deficiencies. However, in most patients it was not found as a hidden disease or immunosuppression. All forms of actinomycosis could occur in patients positive for HIV. In the presence of severe immunosuppression more invasive and necrotizing forms develop.

Actinomycosis has also been reported in patients with systemic lupus erythematosus and vasculitis. Hereditary disease of the phagocyte NADPH oxidase system has been described as a risk factor, suggesting a possible role of phagocytes in the development of disease (Laish, 2012). The overall incidence is virtually impossible to know because of the failure to consider it in the differential diagnosis. That makes the disease underreported (Kolough, 1946; Putnam, 1950). There are no reports on its prevalence, but has been historically reported in 30 to 40 cases in the UK, in 122 cases in 35 years reported by the Mayo Clinic and even a Russian report found 2,000 cases in 11 years. The estimated prevalence in the population is one case for every 40,000 to 120,000 people and it is expected to decline (Acevedo, 2008; Garner, 2007; Minsker, 1974).

Abdominal involvement is produced in only 20% of all cases, and is in most cases confused with malignant processes, tuberculosis or inflammatory bowel disease (Filippou, 2005).

Diagnosis

The gold standard in diagnosis is the culture. It is however, reported positive in only 30% of cases (Hayashi, 2010). The reason for this is that a temperature of 37°C and an environment with a concentration of 6 to 10% of CO₂ for
Figure 2. Granulomatous mass on ileum, 5 cm from ileocecal valve.

the culture are the recommended conditions. Colonies can occur after 3 to 7 days of incubation but observations show cultures can take up to 21 days (Carkman, 2010; Finegold, 1997; Funke, 1995).

Other limitations for cultures include the necessity to use fresh material like pus or tissue, which must be transported in anaerobic containers or processed immediately. Even so, the test can be capricious and returns a negative result in 76% of cases (Katz, 1985; Spagnuolo, 1981). Recently, 16S ribosomal RNA gene sequence analysis has proven a powerful tool in identifying Actinomyces. This method allows for a more rapid and accurate identification of possible actinomycosis and thus, may be useful when actinomycotic chronic inflammation is clinically suspected but no microorganisms are identified in conventional cultures (Ha, 2015).
Histopathology

*Actinomyces* are closely related to the bacteria of the *Nocardia* genus, both of which were considered fungi because of their filaments’ stick shape. Nevertheless, they are classified as bacteria. Recently, Rothschild histopathologically reevaluated bones of individuals diagnosed with actinomycosis and the results of his work showed that *Actinomyces* has some unique presentations that distinguish it from other microorganisms. Surprisingly, it has striking similarities with fungal infections, leading to questions on their classification as bacteria (Acevedo, 2008).

The diagnosis is confirmed with the sulfur granules present in the exudate in 35 to 55% of cases. The histopathological literature revealed a chronic granuloma (neutrophils, lymphocytes, plasma cells and multinucleated foreign body giant cells). Staining with hematoxylin and eosin found multi-lobulated sulfur granules or grains, with basophils or ambophils coves of 30 to 400 microns, and

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**Figure 3.** Dissected granulomatous mass.
eosinophilic material surrounding the grain can be observed (Splendore-phenomenon Hoepli). The actinomycotic granules regularly show a positive reaction to periodic acid Schiff and Grocott’s staining, but Kossa reaction is negative (Arenas, 2008; Lancella, 2008; Sung, 2011).
Clinical presentations

Abdominal actinomycosis usually appears as a slow growing mass and may be associated with changes in bowel habits, nausea, vomiting, cramping pain, anorexia, weight loss, fever, tachycardia and night sweats. Mild to moderate leukocytosis is also present. The disease can lie dormant for years before manifesting as a mass, multiple abscesses, fistula, intestinal obstruction or hydronephrosis (Demir, 2009).

Pre-operative diagnosis is rare (in less than 10% of cases). Actinomycosis is generally identified with the resected surgical specimen, abscesses culture or autopsy. Radiographic evidence is usually not specific; barium studies may show signs of external compression with stenosis of the intestinal lumen. Colonoscopy is often not useful in the diagnosis because of the disease's extramucosal origin. However, it is important to exclude colitis or neoplastic disease. It can also show stenosis.

Occasionally, umbilicated nodules in the center may be seen related to the intestinal wall fibrosis and chronic inflammatory changes. A CT scan is useful in identifying the inflammatory mass and the organs involved (Huang, 2004; Kim, 2000; Privitera, 2009). In the experience of Sung (2011), in a report of 23 cases of abdominal actinomycosis over a period of 15 years, 5 cases were in the appendix, 5 of ovarian and pelvic mass, 4 in the abdominal wall and omentum, 4 in the colon, 2 in the small intestine and uterus and 2 liver abscesses. Of all patients, only in four was it diagnosed preoperatively (Sung, 2011).

Ileocecal and appendicular

Even though the pathogenesis is not fully understood, the ileocecal region including the appendix is the most commonly involved area. However, actinomycosis after acute appendicitis declined due to early diagnosis, a low incidence of perforations and better antibiotic therapy (Lee, 2001). Still, prolonged use of IUDs is a risk factor in young women. Diagnosis is further complicated due to its similarity to diseases like diverticulitis, colon cancer, Crohn’s disease, ulcerative colitis and tubo-ovarian abscesses.

The direct extension of adjacent tissue is the primary route of spread after infection in the pelvic organs. This
may explain the characteristic radiologic findings, as seen on our patient (DiLauro, 2010; Karagülle, 2008; Lee, 2001; Maxová, 2012). On occasion, an infiltrative mass with unusual aggressiveness can be one of the most important radiological findings.

In some reports of appendiceal actinomycosis, CT scan findings have shown wall thickening and periappendiceal inflammation (Brook, 2008; Gil, 2011; Heidt, 2011; Maternini, 2008). One report of appendiceal actinomycosis mentioned that the histological findings should consider the diagnosis of chronic appendicitis in patients with pain in the right lower quadrant for more than 7 days of evolution even if there are no significant findings of inflammation in laboratory data or cabinet examinations. 75% of patients with these characteristics present histologic criteria for chronic appendicitis was reported.

In 1886, Fitz described the term chronic appendicitis. There are many reports in the literature about this pathology. Some doubt its existence and others corroborate it in findings based on pathologies related to chronic inflammation (eosinophilic or lymphocytic infiltrate in the wall of the appendix and/or fibrosis) (Joy, 2003; Kuri, 2011; Mattei, 1994; Mussack, 2002).

**Colonic**

Colon actinomycosis accounts for 15% of all abdominal cases (Cowgill, 1979). Since 1986, it has been reported in at least 50 cases, mostly in the sigmoid and descending colon, and usually related to widespread pelvic actinomycosis (with or without the use of IUDs). The most common clinical presentation is obstruction of the left colon with indistinguishable clinical and radiological signs of adenocarcinoma, as stenosis, wall thickening and mucosal folds, with presence or absence of anorectal fistula, all of which can be found in Crohn's disease and intestinal tuberculosis.

The dense fibrous reaction leads to the formation of stenosis with an associated mass and changes in bowel habits, bloating and possibly anorexia and weight loss. At laparotomy, there is a desmoplastic reaction involving the pelvis and internal genitalia strongly adhered to the colon and rectum. This clinical picture is the same as the one associated with our patient, whom also has an ileocolonic presentation (Garner, 2007). The most consistent finding in the CT scan is the presence of free liquid and wall thickening in average of 1.2 cm and in some segments an average of 8 cm. However, the most important finding is the presence of a mass adjacent to the intestinal segment involved, as observed in 17 of 18 patients in the series of (Lee, 2001).

**Hepatic**

Hepatic actinomycosis ranges from 5 to 15% of cases of abdominal actinomycosis and usually manifests as multiple
small abscesses (Hayashi, 2010). In a review of Fazili (2012), liver actinomycosis due to A. meyeri was the second most common cause of abdominal presentation, in contrast to A. israelii, which rarely causes liver abscesses. If actinomycosis is suspected, a puncture and cultivation of the liver abscess can be performed and antibiotic treatment started which would decrease the volume of the abscess and reduce peripheral inflammatory reaction. Thus, Hayashi (2010) suggested two cases that could be resected laparoscopically. There is a male predominance for hepatic actinomycotic abscesses (70 to 97%) with 30 to 50 years being the most common age group (Petračhe, 2013).

Garner (2007) reported that the literature documents 68 cases of liver actinomycosis, most of them being unilobar, though might be bilobar with multiple lesions. On the other hand, Yang (2014) reported 32 cases found in the literature from 1996 to 2012 in a Medline search, and one more. According to Yang (2014), 92.6% of the patients reported fever; 60% reported weight loss and 70.8% had anemia. 93.1% of the patients showed increased number of peripheral blood leukocytes and/or neutrophils in accordance with other reports; 75% (24/32) of patients had a secondary HA infection in the lungs, chest, pelvic and abdominal organs, etc., while the original HA infection was confined to the liver. The laboratory frequently showed leukocytosis (75%) with left shift and elevated alkaline phosphatase (83.3%) (Cristodoulou, 2004; Sharma, 2002; Yu, 2010).

The imaging characteristic in hepatic actinomycosis in this series showed: Only low density in the liver (68.8%), abscess-like (18.7%), cystic (6.3%) and mass-like and nodular (6.3%). The lesion numbers in 72.4% were single and in 27.6%, multiple. The distribution showed a preference for the right lobe (65.5%) followed by both lobes in 27.6% and only 6.9% in the left lobe (Yanmayog, 2014).

Several studies have also shown an association with elevated levels of antigen CA19-9. This antigen is an epitope ciliated carbohydrate on the surface of some tumors. It is not an organ specific marker and is used clinically as a marker of pancreatic, hepatobiliary and gastric malignancy. This marker is often elevated in benign diseases of the hepatobiliary system, kidney failure, pleural effusion, pneumonitis intestinalis and systemic lupus erythematosus. Regardless, in these benign conditions, the CA19-9 elevation is lower than in malignant conditions. With levels of 1000 U/ml, the marker has a positive predictive value of 100% (Lall, 2010; Soardo, 2005). 7.6% of mortality rate was reported to be associated with hepatic actinomycosis (Hansen, 2009).

**Biliary system**

There have been 18 reported cases of biliary actinomycosis up to 2007, and Lee (2010) found one more manifesting as a gallbladder cancer, likely because it was a mass infiltration to adjacent tissues. It was very difficult to establish a diagnosis with a CT scan but through the aid of pathology study was established. We have found three more reports to date. The disease can manifest itself as cholecystitis, biliary colic, and pancreatitis and as a neoplastic mass with abdominal pain, fever, weight loss, a palpable mass and laboratory abnormalities such as leukocytosis with increased erythrocyte sedimentation rate and elevated alkaline phosphatase, bilirubin and/or amylase (Freeland, 1997; Merle, 1995; Ormsby, 1998).

**Actinomycosis** in the presence of bile salts cannot grow as reported by Marrie (1977). It can spread to the liver but its presence in the cystic duct and the common hepatic duct or common bile duct is very rare. In fact, this condition has only been described twice (Acevedo, 2008). The presentations are slightly different from the typical cholecystitis, with lots of fibrous tissue and adhesions. It was reported involving the bile duct with only one case of coexistence of cholecystitis and gallbladder adenocarcinoma. In both cases, the agent was A. naeslundii, reported in three other cases of actinomycotic cholecystitis (Garner, 2007).

**Pancreas, esophagus, stomach and small intestine**

The involvement of these organs is rare, despite the reports of cases from Parsons (1929). There are reports of pancreatic actinomycosis by A. meyeri, secondary to the use of stents, and others, developing a pseudocyst in the pancreatic head diagnosed by histopathological analysis of fluid obtained by a CT-guided puncture. After two months of medical treatment, they had complete resolution (Garner, 2007; Sahay, 2010).

It was observed that several of the pancreatic ducts distended in these patients while others are obliterated by fibrosis. About 50% of patients with chronic pancreatitis have cysts and calcifications with sizes ranging from a few millimeters to 5 cm.

Peripancreatic fibrosis is usually a late finding involving the portal vein and/or splenic veins (Clain, 1999), which causes stenosis or occlusion of the retroperitoneal lymph channels and develops ascites with portal hypertension, which complicates the clinical course of pancreatitis in 1 to 2% of cases respectively (Cintron, 1996; Milam, 2004).

Esophageal actinomycosis is infrequent, with only about 20 cases described in the literature. Patients with esophageal actinomycosis are usually immunosuppressed by malignancy, HIV, or a solid transplant. Most patients present ulceration, and a few had perforations, abscesses and sinus tracts (Abdalla, 2005). Gastric actinomycosis presents similarities to malignant neoplasm with symptoms like weight loss and epigastric mass, bloating, anorexia, fever and leukocytosis which may be related to peptic ulcer or bariatric surgery (Fernandez, 2004). CT scans usually
show a mass that is indistinguishable from a malignant tumor.  

The small intestine is usually involved in direct extension of actinomycosis anywhere in the abdomen. It is extremely uncommon to find the disease in this isolated organ. Very rarely does actinomycosis complicate inflammatory bowel disease (Garner, 2007).

Abdominal wall

Actinomycosis may affect the hepatobiliary ileocolic region, rectosigmoid, pancreas, stomach, small intestine, omentum, uterus, annexes, kidneys and retroperitoneum. There are many reports of primary affection of the abdominal wall. This may be the expression of a primary local infection or a secondary one to any of the aforementioned regions (Hefny, 2006).

Cutaneous fistulas involving the abdominal wall in the intraperitoneal actinomycosis are common, but the disease isolated on the wall is very rare, with only 16 cases reported until 2010 in English literature (Aquaro, 2010). It is typically present as a slow-growing mass mistaken for a muscle tumor. Moreover, abscesses are fast growing and can cause fever and leukocytosis. Sometimes it can manifest with several outlets abscess in a large area on the skin of the abdomen.

In several series and case reports of primary affection of the abdominal wall, there was a history of recent and prolonged use of IUDs, which can result from hematogenous spread (Aquaro, 2010). Injuries require complete resection of muscle and omentum tissue adhered completely (Abela, 2004). Defects in the abdominal wall can require the use of mesh (Carkman, 2010).

Treatment

Penicillin remains the antibiotic of choice for Actinomyces species. Other antibiotics that have good activity in vitro and extensively used with good results are erythromycin, tetracycline, doxycycline and clindamycin. For a localized disease, especially cervicofacial, the recommended drug is a relatively short course of oral penicillin (500 mg to 1 g q 6 h) for two months. For a more extensive and disseminated disease, the current expert opinion suggests intravenous penicillin (20 to 30 million units per day) for a period of 2 to 6 weeks followed by oral penicillin or amoxicillin (500 mg q6 h) 31. The recommended duration of treatment is 6 to 12 months but needs to be personalized based on clinical and radiological response. For patients who are allergic or intolerant to penicillin, options include erythromycin (500 mg q6 h), tetracycline (500 mg q6 h), doxycycline (100 mg q12 h) and clindamycin (300 to 450 mg q6 h). Erythromycin is a reasonable choice for a pregnant patient allergic to penicillin. In reviewing the study of Fazili (2012), the average duration of antibiotic treatment as observed is 6 months. Penicillin or β lactam antibiotics such as amoxicillin were the most commonly used, followed by doxycycline and clindamycin (Cenetec, 2010; Fazili, 2012).

Surgical treatment is used for drainage of abscesses, or mass resection. According to reports from early last century, before the advent of penicillin, management was based in resection of lesions and sometimes peroxide compounds, such as zinc, were used (Wangesteen, 1936). Recently, it was observed that removing granulomas, pus and necrotic tissue to drain placement enhances the effect of antibiotics and therefore, reduces the time of use. The prognosis was favorable, even in patients with a disseminated disease, including the brain (Groves, 1996).

Conclusions

Conclusions drawn from the study are:

1) Actinomycosis is a disease caused by a Gram-positive anaerobic bacterium, which tends to form granulomas and abscesses.

2) It can affect any organ in the body.

3) It must be included in the differential diagnosis of inflammatory, infectious and malignant diseases of the organs of the abdominal cavity, especially when there is a mass or abscess confirmed by a CT scan.

4) Needle aspiration and proper handling of samples is crucial because the culture can be problematic.

5) Surgery, accompanied by washing, drainage and debridement of necrotic tissue can be a significant component in controlling the disease.

6) The most difficult task in managing actinomycosis is reaching an accurate diagnosis before a surgical approach. Preoperative diagnosis is difficult because of the non-specific clinical picture and laboratory findings.

7) The treatment of choice is penicillin in large doses for the duration of 6 months to a year, this is important to avoid the risk of recurrence.

REFERENCES


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