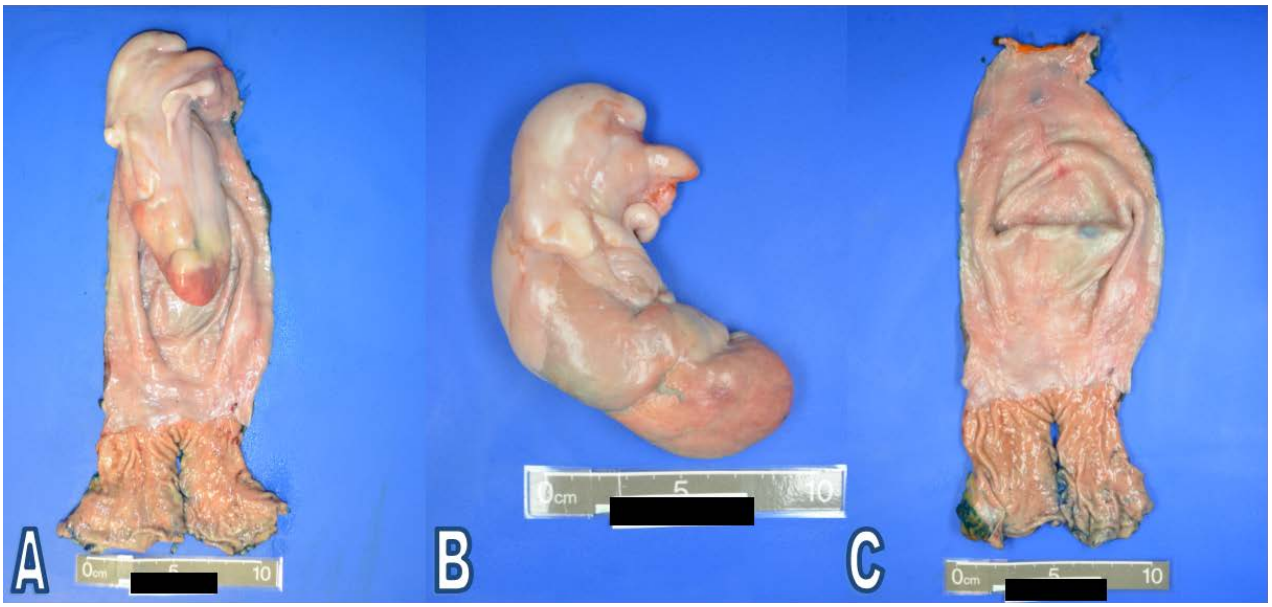
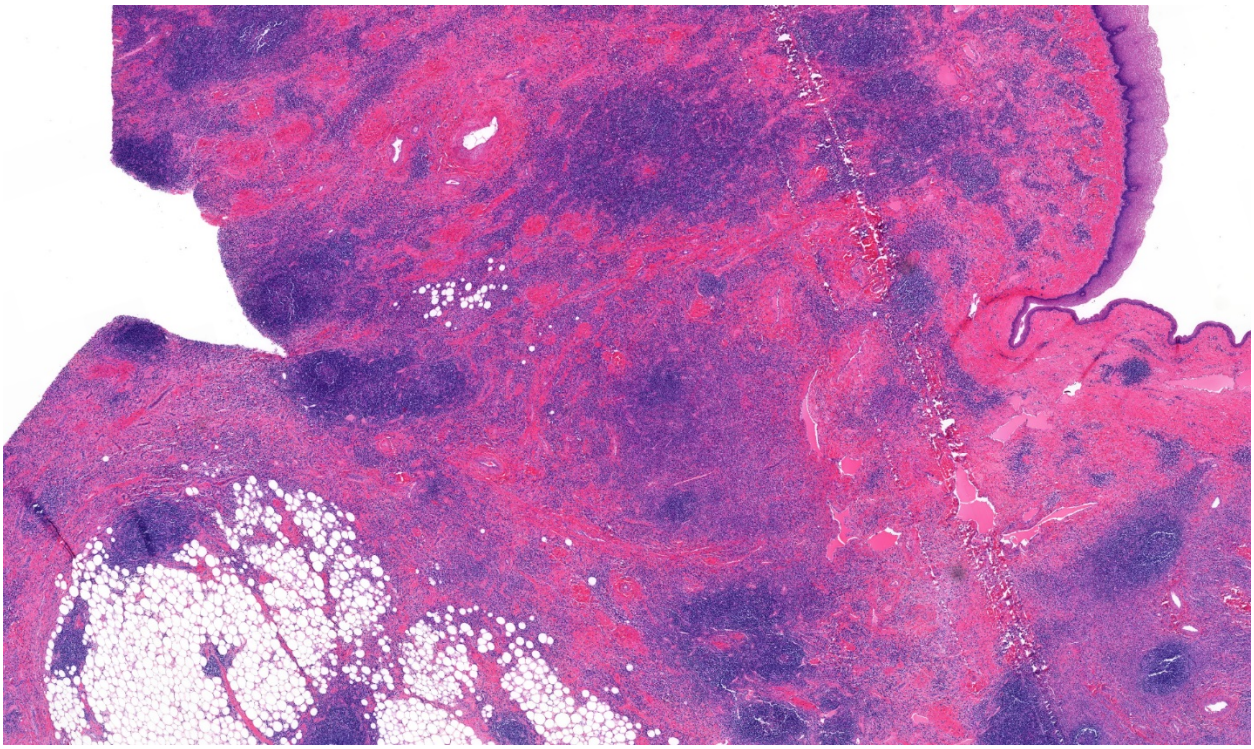
Case presentation

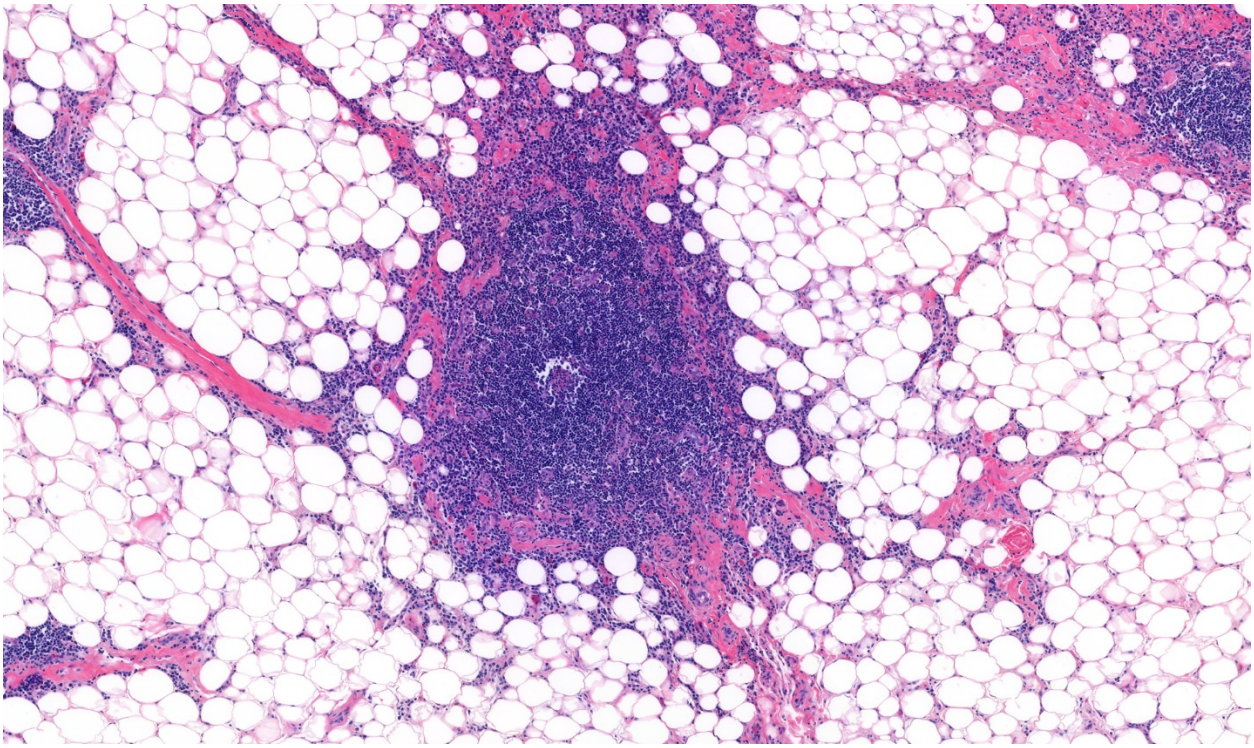
A 68-year-old man presented to the gastroenterology clinic with cough and dysphagia of 3-years duration. He stated that the dysphagia started initially to solid food, progressing to both solid food and liquids. He had lost 60 pounds over the last year and was severely fatigued. Laboratory evaluation revealed profound hypochromic microcytic anemia. Esophagogastroduodenoscopy (EGD) revealed a giant polypoid lesion arising in the proximal esophagus. The patient subsequently underwent open esophagectomy with the gross and histologic findings in the figures below.



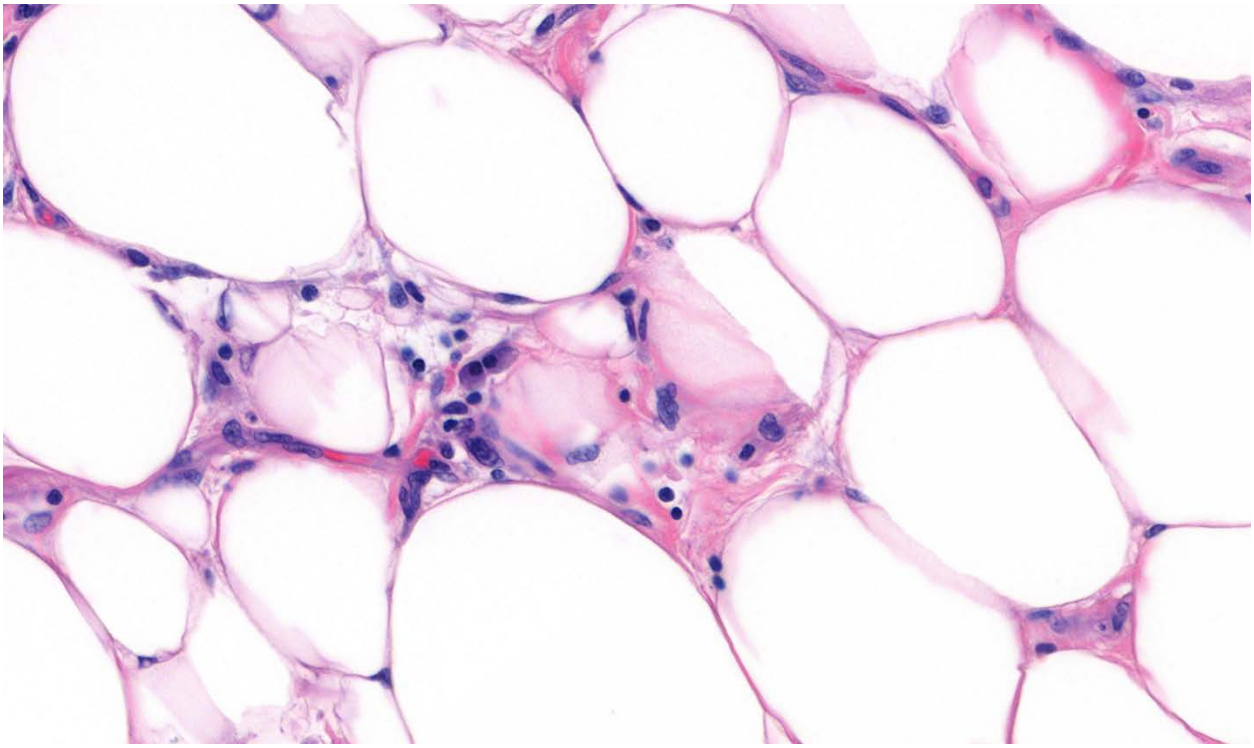
Gross photograph of the esophagectomy specimen (A–C). A shows a large (14 cm) pedunculated mass arising from the proximal esophagus. B shows the lesion after amputation from the esophagus. C shows the esophagus and the stomach with grossly unremarkable mucosa; note the marked esophageal dilatation.



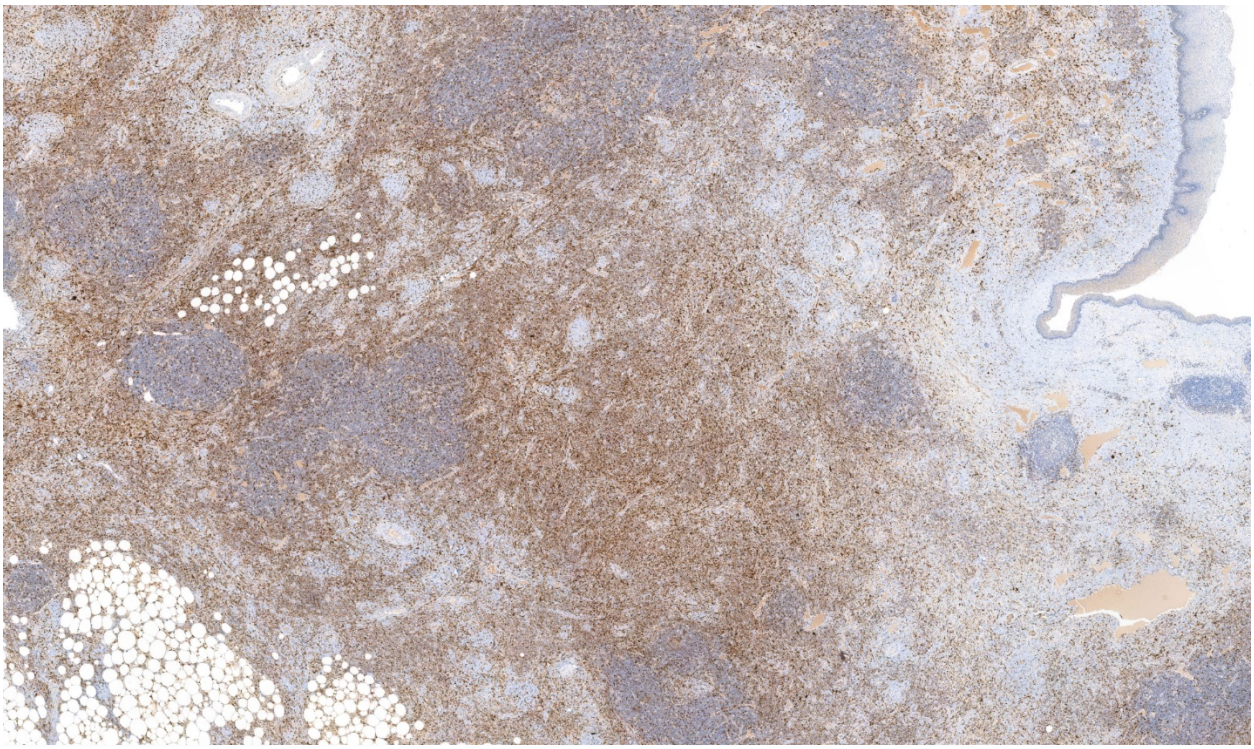
H&E (digital scan 2× magnification)



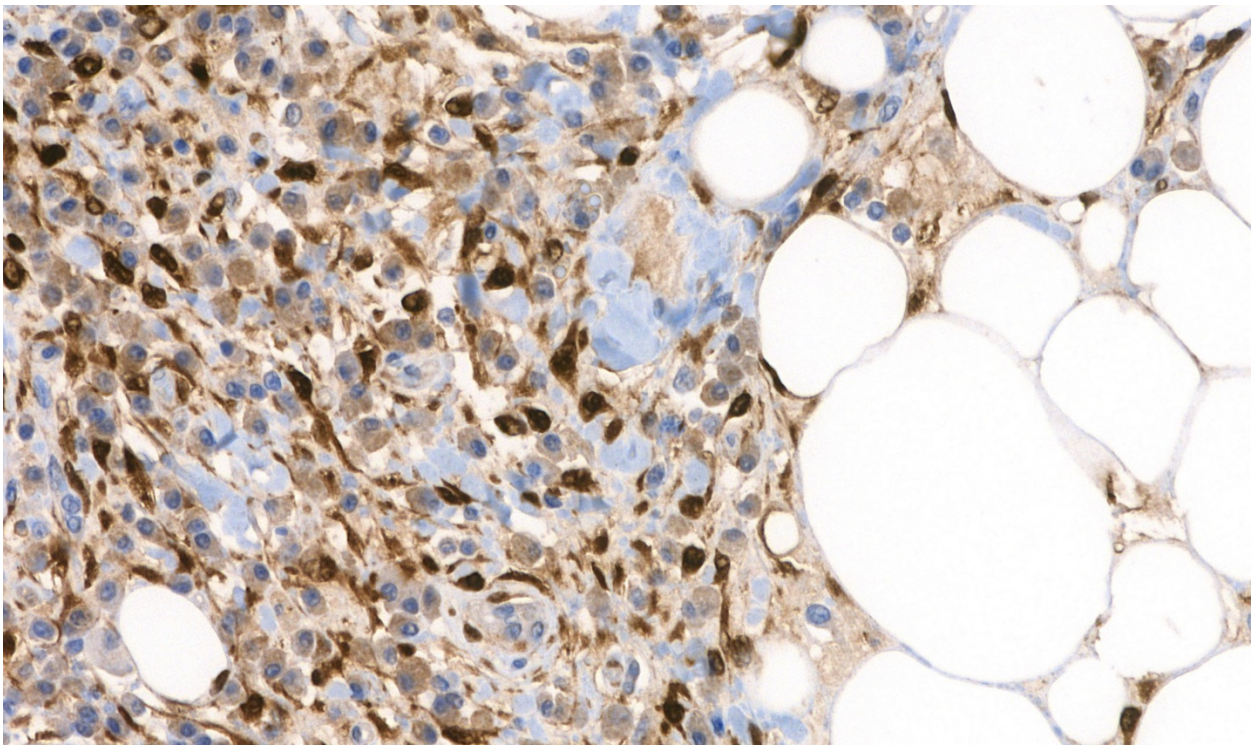
H&E (digital scan 10× magnification)



H&E (digital scan 40× magnification)



CDK4 immunostain (digital scan 2x magnification)



CDK4 immunostain (digital scan 40× magnification)

What is your diagnosis?

A- Carcinosarcoma

B- Lipoma

C- Well-differentiated liposarcoma

D- Inflammatory fibroid polyp

E- Inflammatory myofibroblastic tumor

Correct answer: C: Well-differentiated liposarcoma

The gross and histologic pictures depict the esophageal presentation of well-differentiated liposarcoma. In addition to MDM2 and CDK4 overexpression by immunohistochemistry, *MDM2* was amplified by fluorescence in situ hybridization (FISH). Almost all these lesions were historically diagnosed as esophageal giant fibrovascular polyp (EGFP). EGFP presents as a large (up to 23 cm in length), sausage-shaped, pedunculated lesion arising from the esophagus and extending into the lumen without invading the wall.[1,2] Since its initial description as a unique diagnostic entity by Stout and Lattes in the 1st edition AFIP Esophagus Fascicle, it has been considered a benign lesion with reactive etiology.[3,4] Several case reports over the last decade of atypical lipomatous tumor/well-differentiated liposarcoma "masquerading as" EGFP led to a reconsideration of that entity. Graham et al demonstrated *MDM2* amplification in 100% of 13 esophageal tumors originally diagnosed as EGFP (n=5), lipoma (1), well-differentiated liposarcoma (3), or dedifferentiated liposarcoma (3).[5] In their discussion of the histology of these lesions they emphasized limited atypia in the neoplastic stromal cells, usually less than is seen in well-differentiated liposarcoma of somatic soft tissue. We, thus, recommend ancillary testing (e.g., *MDM2* FISH) in any lesion presenting as "EGFP," as most (if not all) will be shown to represent giant pedunculated esophageal liposarcoma (GPEL). Of note, neither term is included in the most recent World Health Organization (WHO) classification of digestive system tumors.[6]

GPEL is extremely rare, representing ≤0.5% of all esophageal malignant neoplasms.[7] Most tumors occur in older male patients. However, cases occurring in infants and children have also been reported.[8] Most commonly reported presenting symptoms include dysphagia, cough,

postprandial retrosternal pain or discomfort, sensation of the mass, eructation, and profound weight loss due to dysphagia.[1,2,9,10] In rare extreme cases, the polyp can be regurgitated into the upper airway and even protrude from the mouth. This life-threatening complication might lead to laryngeal impaction and airway obstruction.[1,9,11-14] GPEL usually arises in the cervical esophagus near the region of the cricopharyngeus muscle, which accounts for its tendency to prolapse into the mouth and ability to impinge on the larynx.[8]

Histologically, GPEL is lined by benign squamous mucosa, which may be ulcerated, and contains variable admixtures of mature adipose tissue lobules and fibrous septa.[4,15] The fibrous component can have collagenous or myxoid morphology and usually contains cytologically atypical cells.[1] The demonstration of MDM2 and CDK4 overexpression by immunohistochemistry or MDM amplification by FISH is usually needed to confirm the diagnosis of liposarcoma.[4,5,7] A well-differentiated liposarcoma contains only mature adipose tissue and fibrous septa, while dedifferentiated liposarcoma shows solid areas of non-lipogenic spindle cell sarcoma.[5]

Standard of care for GPEL is surgical resection with clear margins. Surgical techniques that have been employed include radical esophagectomy, local endoscopic resection, or esophagostomy, as described recently.[16] Open surgery has classically been the standard treatment, but over the past decade endoscopic resection has become a viable option. The main indication for esophagectomy over endoscopic removal is the presence of bulky submucosal tumor needing clear resection margins, though obviously this is not the typical clinical presentation.[17] Following complete resection with clear margins, most authors advocate surveillance with EGD and/or imaging such as computed tomography scans, as well-differentiated tumors have a

propensity for local recurrence.[18,19] As with somatic soft tissue liposarcoma, dedifferentiated examples frequently metastasize.[5] The role of adjuvant radiotherapy is controversial and may be complicated by radiation pneumonitis, pulmonary fibrosis, and/or constrictive pericarditis.[20] In our case, the stalk of the polyp lacked neoplastic tissue, possibly suggesting the adequacy of surgery alone.

Choice A is incorrect

Carcinosarcoma can also present as a pedunculated mass mimicking GPEL/EGFP. Histologically, in contrast to liposarcoma, carcinosarcoma is a biphasic tumor in which both components (the carcinomatous and sarcomatous) are cytologically malignant.[21-26]

Choice B is incorrect

Esophageal lipoma, if it exists, would be expected to present as a pedunculated mass mimicking GPEL/EGFP clinically, endoscopically, and grossly. Histologically, lipoma would lack the fibrous septa and atypia of a well-differentiated liposarcoma. Of note, neither MDM2/CDK4 immunohistochemistry nor *MDM2* FISH were performed in two recently reported cases.[27,28] While the authors of the latter report noted “neither increased mitotic activity nor lipoblasts” in their lesion, neither of these are reliable diagnostic features of well-differentiated liposarcoma.

Choice D is incorrect

Inflammatory fibroid polyp (IFP) is a rare, benign tumor that can arise throughout the gastrointestinal tract, with a predominance in the stomach and ileum.[29,30] This tumor’s

epicenter is in the submucosa, though it often presents as a pedunculated lesion. Histologically, IFPs is composed of bland spindle cells set in a loose collagenous stroma. Perivascular edema, prominent concentric fibroblastic growth (onion skinning), and an eosinophilic infiltrate are typical features, as is CD34 immunohistochemical expression.[31] Many IFPs harbor *PDGFRA* mutations and PDGFRA is also overexpressed immunophenotypically, though this is not specific for a mutation.[32]

Choice E is incorrect

Inflammatory myofibroblastic tumor (IMT) is a mesenchymal neoplasm with a very low rate of metastasis (<2%) and hence falls into the "intermediate, rarely metastasizing" category of the WHO classification.[33] IMT predominantly occurs in children and young adults, and may be found throughout the body.[33] Histologically, IMT is composed of fascicles of myofibroblastic spindle cells in a background with a prominent inflammatory infiltrate.[34] The myofibroblastic component is typically positive for smooth muscle actin. IMT displays a wide morphologic spectrum, depending on the relative predominance of its two components.[35] Three main patterns have been described, including myxoid/vascular pattern, compact spindle cell, and fibromatosis-like, though these often occur in combination. About two-thirds of IMTs harbor gene rearrangement involving tyrosine kinase receptors such as ALK, ROS1, PDGFRB, and NTRK3.[34-36] ALK rearrangement is most common, found in up to 50% of all cases. ALK-rearranged IMTs are thought to have a lower rate of metastasis than ALK-negative ones.[33] Interestingly, 90% of fusion-negative IMTs are seen in adults, while more than 90% of pediatric IMTs show gene rearrangements.[35]

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