


Signet ring cell cancer of Ampulla of Vater—first ever case reported in a teenager and a review of literature

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Asad Ali Kerawala , Abid Jamal
and Lubna Saleem

Abstract

Ampullary cancers are rare accounting for 0.2% of all gastrointestinal cancers. Signet ring is a rare variant of adenocarcinoma, characterized by having more than 50% of mucin secreting cells and clinically having a worse prognosis. We present the case of a teenage girl with this tumor, the youngest ever reported in medical literature. An 18 years old girl with no significant past medical history presented to our clinic with symptoms of upper abdominal pain and jaundice. Her upper GI endoscopy showed an ampullary lesion which was biopsied—diagnosing it as adenocarcinoma. She underwent a pancreato-duodenectomy (Whipple's procedure) with Child's reconstruction and a feeding jejunostomy. Her final histopathology report was documented as infiltrating adenocarcinoma of Signet Ring variety arising from the Ampulla of Vater. Being such a rare entity, there is a lack of randomized trials advising the optimum treatment for such cases. Till then anecdotal experiences will drive the optimum management of this rare disease.

Keywords

Cancer, signet ring cancer, adenocarcinoma, whipple, Ampulla of Vater, ampullary

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Introduction

Ampullary cancers are rare accounting for 0.2% of all gastrointestinal cancers. Majority being adenocarcinomas, other varieties include papillary, Adenosquamous, and Mucinous. Histologically they are defined as being intestinal or Pancreatobiliary in origin. Signet ring is a rare variant of adenocarcinoma, characterized by having more than 50% of mucin secreting cells and clinically having a worse prognosis. We present the case of a teenage girl with this tumor, the youngest ever reported in medical literature.

Case

An 18 years old girl with no significant past medical history presented to our clinic with symptoms of upper abdominal pain and jaundice. Her ultrasound showed significant

intrahepatic biliary dilatation. Her upper GI endoscopy showed an ampullary lesion which was biopsied—diagnosing it as adenocarcinoma. On further probing it was found that her mother had also developed duodenal cancer few years ago, however she couldn't get any treatment and succumbed to the disease. On abdominal CAT scan the lesion was resectable and the decision was taken to operate her after discussion in the Institutional Tumor Board. She underwent a pancreato-duodenectomy (Whipple's procedure) with Child's reconstruction and a feeding jejunostomy. Her

Cancer Foundation Hospital, Karachi, Pakistan

Corresponding author:

Asad Ali Kerawala, Cancer Foundation Hospital, C – 130, Gulshan-e-Iqbal Block 09, Karachi 75000, Pakistan.
Email: asadali4@yahoo.com



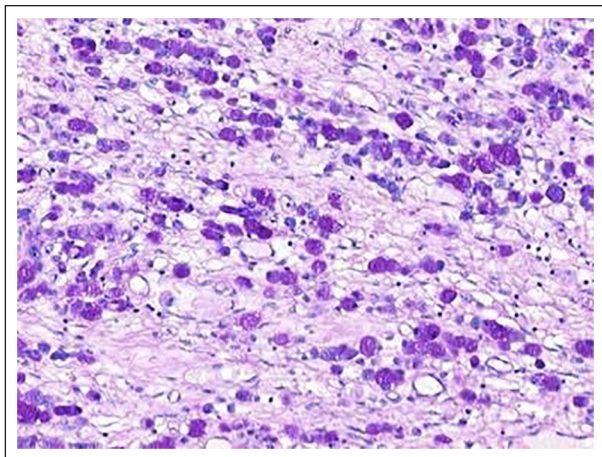


Figure 1. Biopsy of Surgical specimen. Signet ring cells on high magnification (poorly cohesive cells with central vacuoles containing intracytoplasmic mucin).

postoperative course was uneventful and she was discharged home on sixth POD. Her final histopathology report was documented as infiltrating adenocarcinoma of Signet Ring variety arising from the Ampulla of Vater (Figure 1). Size of lesion was 2.5 cm by 0.9 cm, margins clear and 0 out of 17 nodes were involved. The patient was advised Adjuvant Chemotherapy but not complied upon. She was lost to follow up and returned 8 months later with a large abdominal mass—biopsy proved it as metastatic adenocarcinoma of signet ring variety, confirming it to be recurrence of the Ampullary Carcinoma. She was put on Chemotherapy with palliative intent as the recurrent mass was surgically irresectable (Figure 2). After three cycles of Gemcitabine and 5 FU, she did not respond to the therapy.

Discussion

Also known as poorly cohesive type—Signet ring cell cancer demonstrates characteristic signet-ring cells with intracytoplasmic mucin and typical eccentrically located, crescent shaped nuclei (Figure 3). Most commonly found in the stomach, signet ring variety of the ampulla is an unusual and aggressive variant with only a handful of cases being reported in the literature (Table 1). Gardner et al.¹ was the first one to report SRCC as a variant of adenocarcinoma in 1990. Since then only 38 cases have been reported in the medical literature most of them being ages 40 and above.² Twenty-one of them were males and 19 females. The youngest reported was 32 years old female by Purohit et al. in 2005³ and the oldest being 82 years old female by Ushida et al.⁴ in 2017. The average age at presentation was 59 years. Our case is strange because this is the only case of such a tumor in a teenager. The largest case series has been published by Wen et al.⁵ who reported eight cases from a single institution in Hangzhou, China. Adenocarcinoma arising

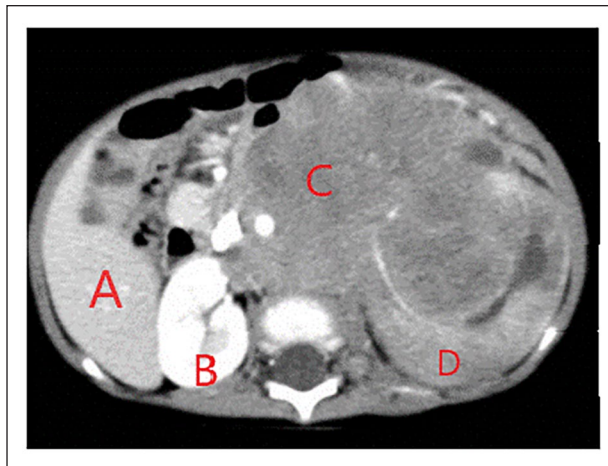


Figure 2. Large abdominal mass.
A-Liver, B-Right Kidney, C-Tumor Recurrence, D-Spleen.

from the Ampulla of Vater is unusual owing to the presence of three different types of epithelial cell linings there—intestinal, pancreatic, and Biliary. There is no consensus on the origin of Signet ring cell cancers. Blundell et al.⁶ hypothesized that these originate from neuroendocrine cells in the gastric mucosa causing metaplasia. However, Wen et al.⁵ from his study has proposed classification into four different types I, PB, gastric, and mixed. They also observed that presence of gastric mucosa or neuroendocrine cells was not mandatory for SRCC thus negating Blundell. Expression of CK7, along with negativity for CK20, CDX-2, and MUC2 signifies pancreatobiliary type SRCC, and vice-versa.

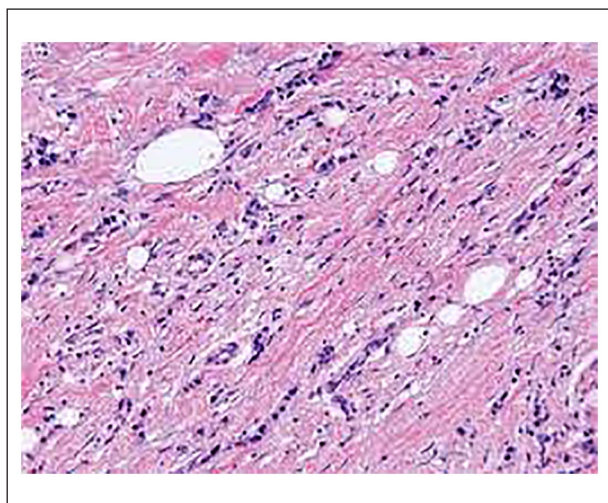
Most of the ampullary cancers present early² as they cause obstruction to the biliary tract and the patient presents with obstructive jaundice. Not all ampullary cancers are obvious on the CAT scan. Those that are visible, have subtle findings of thickening and mass in some cases. Hence, Endoscopic Ultrasound is considered the gold standard to visualize and biopsy any ampullary lesion. Once the lesion has been confirmed and the biopsy shows dysplasia or invasive cancer, the cornerstone of treatment is surgery—Pancreaticoduodenectomy with reconstruction. Most of the cases reported in the literature did not have lymph node involvement,² just like the girl in our case. Only seven cases out of all the reported ones had Lymph node metastasis or N1 disease.² Patients like these have been offered adjuvant chemotherapy in some cases while some have just been observed. Being such a rare entity, there is a paucity of data on adjuvant treatment and no randomized trials to show any benefit.

Conclusions

Gardner et al.¹ was the first one to report SRCC as a variant of adenocarcinoma in 1990. The Dutch guidelines do not recommend any adjuvant therapy for completely resected ampullary

Table 1. Reported Cases of Signet Ring Cell Cancer of Ampulla of Vater in Medical Literature.

Author	Year	Age	Sex	Stage
Sekoguchi and Mizumoto ⁷	1979	47	Male	T3 N0
Gardner et al. ¹	1990	69	Female	T3 N0
Tseng et al. ⁸	2002	47	Male	T3 N0
Hara et al. ⁹	2002	68	Male	T2 N0
Eriguchi et al. ¹⁰	2003	83	Male	T3 N0
Nabeshima et al. ¹¹	2003	49	Male	T3 Nx
Fang et al. ¹²	2004	53	Male	T2 N0
Ramia et al. ¹³	2004	67	Female	T2 N0
Li et al. ¹⁴	2004	56	Female	T2 N1
Valeri et al. ¹⁵	2005	66	Male	N.A
Purohit et al. ³	2005	32	Female	N.A
Bloomston et al. ¹⁶	2006	58	Female	T2 N0
Akatsu et al. ¹⁷	2007	43	Female	T2 N0
Ishibashi et al. ¹⁸	2009	59	Male	T3 N0
Gao et al. ¹⁹	2009	38	Female	T3 N0
Kim et al. ²⁰	2010	47	Male	Tx N1
Maekawa et al. ²¹	2011	72	Male	T3 N0
Garcia et al. ²² (2 cases)	2011	74, 73	Males	T3 N0, T2 N1
Paplomata and Wilfong ²³	2011	45	Female	T4 N1
Tas et al. ²⁴	2011	40	Male	Tx N1
Gheza et al. ²⁵	2011	66	Male	NA
Daoudi et al. ²⁶	2012	55	Male	T3 N0
Lesquerex-Martínez et al. ²⁷	2012	78	Female	Tx N0
Terada ²⁸	2012	74	Female	NA
Acharya et al. ²⁹	2013	78	Female	T3 N0
Wen et al. ⁵ (8 cases)	2014	40 - 78	4 Males, 4 Females	T3 N0–T4 N1
Wakasugi et al. ³⁰	2015	59	Female	T3 N1
Rahul et al. ³¹	2016	53	Male	T4 N1
de Klein et al. ³²	2018	45	Female	T2 N0
Ushida et al. ⁴	2017	82	Female	T3 N0
Forneli et al. ³³	2019	49	Male	NA
Ikeda et al. ²	2019	74	Female	T2 N0
Our case	2020	18	Female	T2 N0

**Figure 3.** Signet ring cells—on Surgical specimen biopsy.

cancer.³⁴ However the SRCC variety being more aggressive may need adjuvant therapy. Being such a rare entity, there is a lack of randomized trials advising the optimum treatment for such cases. Till then anecdotal experiences will drive the optimum management of this rare disease.

Author contributions

AAK drafted the initial manuscript. AJ and LS reviewed the final draft and helped in critical analysis.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

Reporting of individual rare cases does not require Ethical Committee approval at our institute—cancer Foundation Hospital, Karachi.

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Informed consent

Written and informed consent was Taken from patient and family.

ORCID iD

Asad Ali Kerawala  <https://orcid.org/0000-0002-8732-5750>

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