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Case Report

A case of rectal cancers in teenager: A conundrum of genetics and clinical medicine

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ABSTRACT

Introduction: Signet cell carcinoma (SRCC)of the rectum is a rare subtype of the rectum cancer which accounts for only 0.8% of colorectal cancer in adolescents and young adults (AYAs) which spread aggressively to other organs and peritoneum.

Case presentation: We present a case of 15-year-old boy from rural area, presented with chronic diarrhea and per rectal bleeding for 3 months. The diagnosis was determined by colonoscope which revealed a fungating mass identified at 10cm from anal verge. Histological examination confirmed diagnosis of signet ring cell adenocarcinoma. CT scan of the abdomen showed thickening involving the recto-sigmoid colon and rectal mass, without evidence of distant metastatic disease. The patient's carcinoembryonic antigen level was within the normal range. He underwent a colostomy and was subjected to neoadjuvant CCRT and surgery.

Discussion: This CASE highlights the importance and challenges in achieving early diagnosis and surgical intervention of signet-ring cell carcinoma in adolescents, as most cases are detected at an advanced stage coupled with the scarcity of information on these rarer subtypes which leads to a poor prognosis.

Conclusion: In managing Signet cell carcinoma of the colorectal, physician have to know that it has a poor prognosis in patients of any age. However, in young teenagers delayed diagnosis and treatment option are narrowed to palliative management. Genetic profiling of family members and similar environment population may be a key to early detection.

1. Introduction

Signet cell carcinoma is a rare subtype of the rectum which accounts for only 0.8% of colorectal cancer in adolescents and young adults (AYAs) which spread aggressively to other organs and peritoneum. Proportions of cases with mucinous adenocarcinoma and signet ring cell carcinoma histopathologic subtypes significantly increased with younger age at onset [1]. Signet ring cell carcinoma is characterized by the abundant intracytoplasmic mucin that pushes the nucleus to the periphery giving a signet ring cell appearance. In order to meet the WHO classifications, signet cell should account for at least 50% of the cells [1]. We report a Case of signet cell carcinoma (SRCC) in a 15 year old boy. He presented with chronic diarrhea and rectal bleeding for three months. All literature points to the delay in diagnosis as the reason for worse clinical outcome in younger patients. The scarcity of information on these rarer subtypes merits further study and investigation. This case report has been reported in line with the SCARE 2020 criteria [2].

2. Case presentation

A 15 year old boy presented with history of chronic diarrhea for 3 months aggravated with passing fresh blood and progressive suprapubic pain. He is a non-smoker. He has paternal and maternal family history of colorectal cancer. Previously an active boy, he had to stop schooling due to uncontrolled bowel output and rectal bleeding.

Laboratory examination revealed liver function, random blood glucose and renal function tests were all within normal parameters. However, mean corpuscular volume was significant at 63.3 fl. Electrolytes were normal except for sodium of 131 meq/liter, albumin 28 and urea 12.5. His tumor markers such as carcinoembryonic antigen level, Alpha feto protein and CA 125 were within the normal range.

CT scan of the abdomen showed thickening at the recto-sigmoid area

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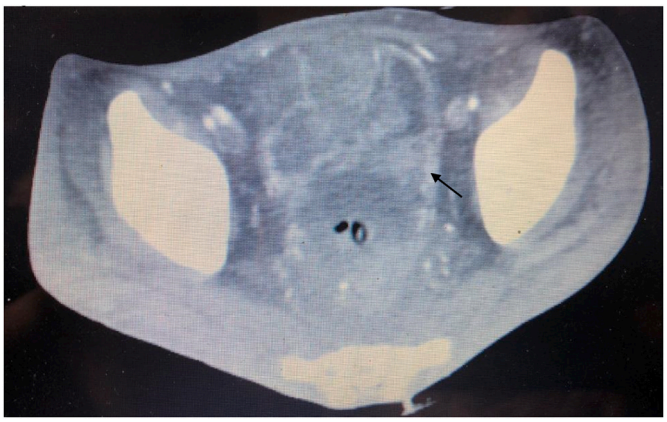

Fig. 1. CT- Scan showed upper rectal lesion (black arrow).

(Fig. 1), with no distant metastatic disease. Colonoscopy findings was a constricting ulcerative mass at 10 cm from anal verge which the scope was unable to pass beyond the tumor. Biopsy results confirmed signet ring cell adenocarcinoma (Fig. 2). Sigmoid colostomy was done due to impending obstruction. He was then treated with the 6 cycles of FOLFOX regimen (folinic acid, fluorouracil, oxaliplatin) with concurrent radiotherapy. A restaging evaluation with chest and abdominal CT after completion of the treatment showed no response to treatment. The treatment was then changed to the FOLFIRI regimen (folinic acid, fluorouracil, irinotecan).

However, the patient subsequently defaulted treatment due to logistic and financial issues which prevented him from travelling from his home which was situated deep in the rural area of Borneo.

He then came back 1 year later with intestinal obstruction symptoms. Due to tumor and disease progression with metastatic features on restaging CT patient was manage as palliative. The patient's performance status declined afterward, and he was transferred to supportive care unit. The patient was placed on patient controlled analgesia (PCA) hydromorphone and TPN. Patient subsequently succumbed to the disease and passed away.

3. Discussion

Signet cell cancer of the colon is a rare subtype of colorectal cancer,

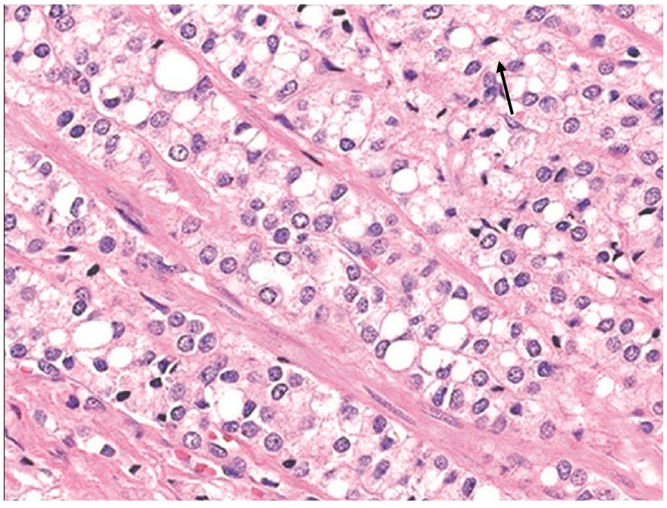

Fig. 2. Signet-ring features such as abundant intracytoplasmic mucins, ample and clear cytoplasm, and eccentrically located nuclei compressed by intracytoplasmic mucins are seen (black arrow). (H&E, original magnification x400).

where abundant intracytoplasmic mucin pushes the nucleus to the periphery giving a signet ring appearance. In order to meet the WHO classification, signet cells should account for at least 50% of the cells [3,4].

There are reports that signet ring cell carcinoma has been increasing in incidence and currently Signet cell carcinoma accounts for 0.8% of the colorectal cancer [5].Patients are often noted to be younger compared to the non-signet cell tumors of the colon. Median age is about 59 years when compared to the non-signet cell cancer, where the median age is about 61 years [5] Our CASE is very significant because of very young age of presentation of this cancer, whereby the incidence rate below 19 years is 0.2 in 100,000 population.

The most common presenting symptom is abdominal pain. Other symptoms include rectal bleeding, change on bowel habits and weight loss [6].Most often about half of the of signet cell ring cell carcinomas were found in the rectum and colon, most predominant site being the right hemi colon in about 29%. Left colon comprises about 15% and approximately 9% of the tumors are noted in the transverse colon [5]. A majority of the signet cell carcinomas initially present with the distant metastasis in about half of the patients. Presentation in children does not differ significantly from the adults. However, the symptoms can mimic inflammatory bowel disease and a high suspicion index should be maintained and not be confused with common childhood problems such as intussusception, appendicitis, gastroenteritis and simple constipation [6].

Family history and inherited syndrome increase the risk of colon cancer . Genetic syndromes can be passed through generations of the family. These syndromes include familial adenomatous polyposis and hereditary nonpolyposis colorectal cancer, which is also known as Lynch syndrome. If more than one family member has colon cancer or rectal cancer, the risk is even greater [7].

In general, surgery is the mainstay of treatment for patients with early rectal cancer stages (T1-T2N0M0). In this CASE whereby the patient was diagnosed as T3N1M0 the preferred option is neoadjuvant concurrent chemoradiotherapy (CCRT) followed by surgery. However, due to default in treatment leading to progression of disease and metastasis, the appropriate modality involves best supportive care and in bulky tumors-surgery, chemotherapy and radiation for palliation. The median survival period is about 9 months. One of the reasons for poor survival period is that most of the signet cell colon cancers are diagnosed at more advanced stages [8,9].

Genetic testing is now accepted as the pathway to streamline cancer diagnosis using state-of-the-art technologies to better characterize, grade, stage, prognosticate and predict response to treatment leading to best possible effective personalized treatment and outcome.

Molecular profiling of tumors is the next generation of genetic screening which has led to the identification of gene expression patterns that are associated with specific phenotypes and prognosis, allowing molecular characterization to become an essential part in the management of colorectal cancer. The ability to identify the location of this faults helps to target the treatment of choice. Another technology,Next-Generation Sequencing (NGS), has the ability to detect uncommon mutations and single nuclear polymorphism in DNA sequence which gives it the advantage over the traditional Quantitative Polymerase Chain Reaction (qPCR) [9,10].

Despite the diversity in the approaches used, three main steps are needed for genomic prognostication. First, data expression levels of several hundreds of thousands of genes are quantified and processed. Second, expression data are clustered and risk score is generated to produce a gene signature that correlates with a clinical outcome. Third, the signature is validated with datasets of independent cohorts. As each molecular profiling test are not created equal,a single or combination technique approach may be used [10].

Targeted therapies also becoming more available as a treatment for colorectal cancer. It is generally divided to anti angiogenic and anti EGFR antibodies. Most commonly bevacizumab (anti VEGF) and

cetuximab (anti EGFR) which is used in non mutated k-ras metastasis rectal cancer, potentiates the cytotoxic effect of chemotherapy. When combined with chemotherapy, it improves life, comfort and overall survival in 1st line metastatic treatment with accepted toxicity. However the treatment is not readily accessible and highly cost in our setting [6, 9].

The incidence of cancer is expected to rise globally with rapid progress of modernization and growing adaptation of unhealthy lifestyles. There are many challenges in early detection for colorectal cancer. In Malaysia, early detection and control activity for prevention are done independently by various agencies. There is strong evidence to support population screening compared to the current selective opportunistic screening practice. Poor awareness regarding signs and symptoms of colorectal cancer by the public and healthcare provider which leads to late detection and poor prognosis in management of patient can be improved by conveying the knowledge of cancer in general and the common risk factors to the public and making the knowledge gained by them being transferred into practice [11,12].

One of the major hurdles in rural areas such as Borneo is the lack of promotion and poor screening uptake among patients who face logistic and resource limitation. However it is essential to avoid "high technology" but poor cost-effective approaches, or methods which do not achieve the needed coverage of the targeted population. Screening programs should not be introduced unless there is adequate manpower to perform the tests and enough facilities for diagnosis, treatment and follow-up of individuals with abnormal test results. The WHO stepwise framework is a good solution consisting of a three steps which implements intervention based on feasibility and existing resources with a realistic projection of resources if and when available.[11–13].

4. Conclusion

In conclusion, Signet cell carcinoma of the colorectal, has a poor prognosis in patients of any age. However, in young teenagers the diagnosis seem to be delayed and treatment option are narrowed to palliative management. Genetic profiling of family members and similar environment population may be a key to early detection.

Ethical approval

No ethical approval required for the mentioned case report. However ,permission was obtained from local administrative and Director General of Health Ministry ,this included consent from patient family.

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Author contribution

Dr Moveendra Kumar took lead in writing the paper ,Dr Nik Amin Sahid arranged the framework of manuscript with supervised correction and Dr Mahadevan Deva Tata encouraged Dr Moveendra to investigate colorectal cancer in adolescence and supervised the writing. All authors discussed the final draft and contributed to final manuscript.

Research registration number

1.Name of the registry: Not applicable
2.Unique Identifying number or registration ID: Not Applicable
3.Hyperlink to your specific registration (must be publicly accessible and will be checked). Not Applicable

Guarantor

Dr Moveendra Kumar will be the guarantor and accepts full responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish at this given time of submission.

Consent

Patient consented for the write up and publication.

Consent

Written informed consent was obtained from the patient for publication of this CASE report and accompanying images. Permission was also obtained from local administrative. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Declaration of competing interest

Dr Moveendra Kumar,Dr Nik Amin Sahid and Dr Mahadevan Deva Tata declare that they have no conflict of interest.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.amsu.2021.102353.

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