Case Study

Shifting Paradigm of Adult Cancers at Young Age –A Case Series

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Abstract

Cancer is considered to be an age related disease because the incidence of most types of cancers increases with age rising more rapidly beginning in midlife. Adolescents and young adults are a distinct population, which is not a usual age for diagnosis of tumors that are usually found in older adults. Tumors in this group of patients tend to be different from tumors found in children or older adults. The treatment of such patients is challenging as they are at a higher risk of developing long-term side effects. In this case series, we report 3 cases of adult cancers that presented at an unusually younger age highlighting the fact that there is a recent shift in paradigm in terms of age of presentation of cancer. We present 3 cases namely, supraglottic larynx squamous cell carcinoma in a 21-year-old female, adenocarcinoma of the rectum in a 22-year-old male, and adenocarcinoma of the stomach and gastro-esophageal junction in a 25-year-old male. With this case series we want to highlight this recent change in the age presentation of adult cancers and this could foreshadow the future trend of the disease.

Keywords: *Epidemiology, Cancer, Trends, Young adults, India*

Introduction

The presentation of cancers in adolescents and young adults (AYA) is unique and differs from those found in children and older adults. The incidence of cancer in AYA is lesser than in older adults. However, the population of developing countries is predominantly younger which makes the treatment of this subgroup of cancers very challenging.

These cancers are more probably related to genetic predisposition or family history or specific health behavior or lifestyle pattern among young people exposing themselves to causative agents.[1] The most common cancers that develop in this age group are breast cancer, melanomas, lymphoma, sarcomas, germ cell tumors, bone cancer, thyroid cancer, and occasionally brain tumors as well.[2] These cancers are different in terms of distribution of types, risk factors, biology, prognosis, and survival rates.[3] In addition, as compared with older patients, AYAs have a greater risk of long-term and late effects including fertility issues, cardiovascular morbidities, sexual dysfunction, and second malignancies.[4]

There has been a recent trend that a proportion of cancers in older adults are being diagnosed at a young age. Tumors like cancers of the head and neck, lung, and gastro-intestinal tumors are generally diagnosed at an older age group with known established etiological factors.[5, 6] These types of cancers (usually occur in the 5th to 6th decade of life) occur rarely in young adults without any specific risk factors. It becomes challenging not only to manage the disease but also to explain the cancer incidence in such individuals.

In this case series, we consider three young adults who presented to our hospital with a type of cancer that is associated with elderly adults.

Case 1: Carcinoma supraglottic larynx in a 21-year-old female introduction

In India, laryngeal cancer is the eleventh most common cause of cancer and mortality.[7] In India, the incidence of laryngeal cancer is 1.26-8.18 per 100,000 population combined for different regions in the country.[8] The prevalence of laryngeal cancer is approximately 3-6% of all cancers in males while it is only about 0.2-1% of all cancers in females highlighting a male predominance.[8] The mean age of presentation is 65 years.[9] Squamous cell carcinoma (SCC) of the larynx is rare in adolescents and has an aggressive nature

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Access this article online

Website: www.ccij-online.org

DOI: 10.51847/wXhwcY0KXx

Quick Response Code:

How to cite this article: Pruthi DS, Nagpal P, Yadav A, Bansal B, Pandey M, Agarwal N. Shifting Paradigm of Adult Cancers at Young Age –A Case Series. Clin Cancer Investig J. 2022;11(2):1-6. https://doi.org/10.51847/wXhwcY0KXx

Risk factors of carcinoma larynx include tobacco use (both chewed and smoked), passive smoking, and long duration of exposure to indoor air pollution by coal usage.[9]

Only 10% of patients with laryngeal cancer are less than 40 years of age. The presence of the classic risk factors for carcinoma larynx in young patients is less evident as compared to older patients.[10] Other factors like the human papillomavirus and laryngopharyngeal reflux, are under investigation and their link is not well recognized yet.[11] Herein we introduce a case of a young female with HPV-positive laryngeal cancer.

Case presentation

A 21-year-old female presented with hoarseness of voice complaints for 6 months with no known comorbidities. There is no known history of smoking or tobacco use. The patient does give a history of passive smoking at home. The patient has no history of cancer in the family. She is non-vegetarian by diet. There was no history of reflux gastritis. She was evaluated and laryngeal Endoscopy showed a mass lesion-involving epiglottis and left the aryepiglottic fold.

MRI neck with contrast showed hyperintense, heterogeneous enhancing mass of size 3.1 x 3.2 x 2.0 cm involving, centered on the left aryepiglottic fold with obliteration of left pyriform fossa. The lesion is extending to the contralateral side, abutting the right aryepiglottic fold, and bulging into the right pyriform sinus. Superiorly it extends up to the tip of epiglottis, anteriorly extending into overlying para-epiglottic fat on the left side and abutting strap muscles and posteriorly abutting the posterior wall of the hypopharynx. There is the presence of mild edema on the vocal cords along with bilateral subcentimetric lymphadenopathy.

Biopsy revealed keratinizing well-differentiated squamous cell carcinoma. On immunohistochemistry, p16 was positive **(Figures 1a and 1b)**.

PET CT was done **(Figure 2)** which showed a soft tissue mass lesion that was FDG avid in the left part of the larynx involving the left aryepiglottic fold, involving the margin of epiglottis causing luminal narrowing measuring 2.1 x 1.4cm with SUVmax of 29.2. There was no evidence of any distant metastases.

The patient was then treated with concurrent chemoradiation with a dose of 70Gy in 35 fractions over 7 weeks along with concurrent weekly cisplatin.

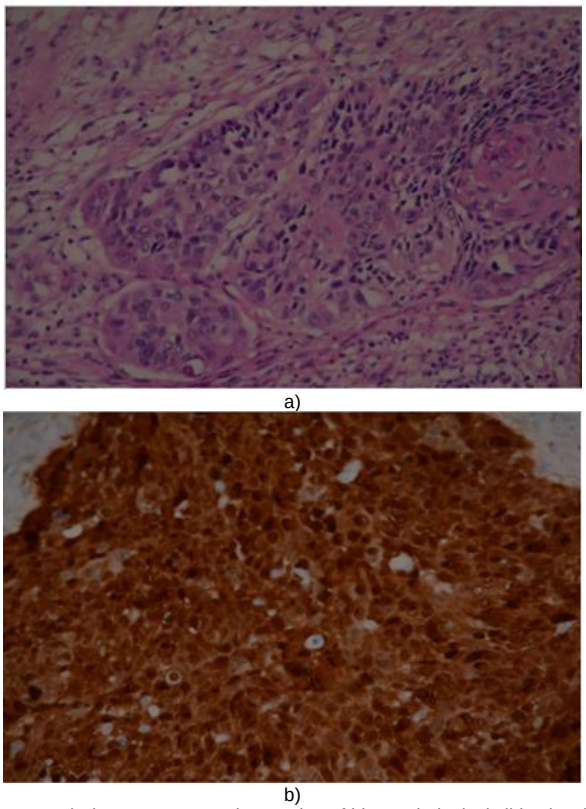

Figure 1. a) shows representative section of histopathological slide showing squamous cell carcinoma and b) shows immunohistochemistry positivity with p16

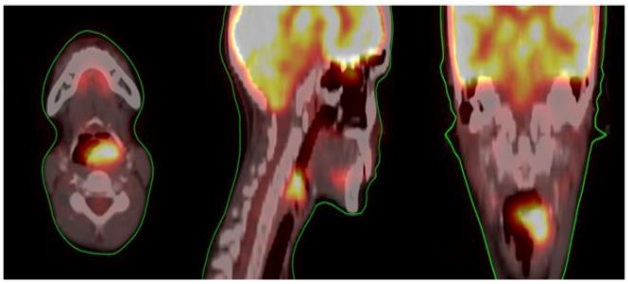

Figure 2. shows the PET CT scan of 21 year old female with squamous cell carcinoma of larynx in axial, sagittal and coronal views

Discussion

Carcinoma larynx is very rare in young adults. Glottis (vocal folds) are the most common sub-site of involvement by SCC in adolescents and young adults, followed by supraglottis and subglottic.[12] In our patient, it was supraglottic primary in a young female. The classical risk factors, which include smoking and alcohol, are not prevalent among younger patients as compared to older ones, which was the case in our patient as well. Viral etiology with Human Papilloma Virus (HPV) has been most commonly associated with oropharyngeal cancer and is related to the clinical profile and prognosis of the patient.[13] However, the incidence of HPV positivity rate in the laryngeal primary is variable.[14, 15] This dissimilarity in the HPV occurrence in laryngeal cancer may be due to the diagnostic technique sensitivity, ethnicity and geographical variations among patients, small study size, poor quality of specimens, and differences in sample storage methods.[16] In our patient HPV was positive as evident by p16

positivity with immunohistochemistry. In a systematic review of 55 studies, out of a large sample of 2559 eligible patients with laryngeal cancer, the overall HPV positivity was 28%. 26.6% of laryngeal cancer patients were infected with high-risk HPV variants only with HPV 16 being the most common.[17] In a study done by Davidson *et al*., HPV-positive laryngeal cancer had a statistically substantial dissimilarity in overall survival as equated to HPV-negative laryngeal cancer.[18] In another study in the US, the authors showed that HPV may be involved in the development of a particular subset of laryngeal cancers and its role may be more predominant in women which were seen in our patient.[19] It is also termed the "new" head and neck cancer patient by Deschler *et al*.[20] In a case report described by Swain *et al*., an eleven year old was found to have squamous cell carcinoma of the larynx (glottis) who was treated with radiotherapy.[21] This highlights the fact that even in paediatric age group carcinoma larynx can occur. However HPV status of that patient was not known. Pugi *et al*., reported a case of HPV positive squamous cell carcinoma of supraglottic larynx in a 33 year old pregnant lady[22].

In our case, HPV infection might have caused the development of this adult malignancy at such a young age.

Case 2: Adenocarcinoma rectum in a 22-year-old male

Introduction

Cancer rectum is the 7th most common cancer in the world and is also the 10th leading cause of cancer-related mortality. In India, it is not that common ranking 16th and ranking 15 among causes of cancer-related death.[7] It is generally considered a disease in the adult age group with nearly 90% of patients diagnosed in the middle age group of 50-60 years.[23] However, it has been reported that there has been a recent rise in colorectal cancer incidence. Studies have suggested that almost 7% of patients who developed colorectal cancers are under 40 years of age.[24] The most common etiological factors involved in the adult age group are smoking and diet. However, in younger patients, the etiological factors are quite different. Inflammatory bowel disease, hereditary non-polyposis colon cancer, and polyposis syndromes of the gastrointestinal tract are known to be risk factors. Herein we report a case of a 23-year-old young male who was diagnosed with cancer rectum with no evident established etiological factor.

Case presentation

A 22-year-old male with a previous history of paraplegia due to spinal injury presented with bleeding per rectum for 1 month. The patient had no history of smoking. There was no family history of malignancy. Colonoscopy revealed large nodulo-proliferative growth seen extending from the anal canal up to 18 cm from the verge. Proximally, the mucosa appeared normal. Biopsy from the rectal growth showed poorly differentiated adenocarcinoma with mucinous differentiation.

PET CT showed FDG avid (SUV max 8.5) circumferential wall thickening (maximum thickness 21mm) with transmural involvement of length 10.8cms of the rectum and anal canal reaching almost up to anal verge. There is the presence of significant perilesional fat strandings and nodularities with few mildly FDG avid centimeter-sized perirectal and external iliac lymphadenopathy. There is no evidence of distant metastases.

The patient was then treated with neoadjuvant long-course chemoradiation with a dose of 50.4Gy in 28 fractions over 5.5 weeks along with concurrent chemotherapy.

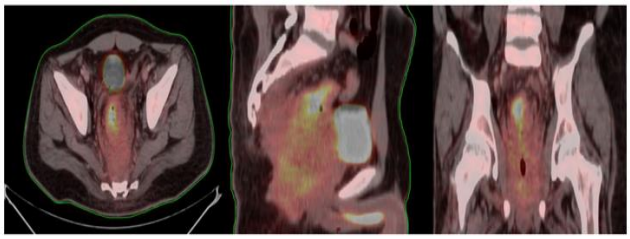

Figure 3. shows the PET CT scan of 23 year old male with adenocarcinoma in axial, sagittal and coronal views

Discussion

The incidence of CRC in the younger population has increased by 2% to 8% annually over the past two decades.[25] Younger patients have more clinically advanced stages and biologically more belligerent diseases. The most common histology is mucinous adenocarcinoma with poorly differentiated signet ring cells.[26] Although most cases are sporadic, in young adults, there is a complex mutation incidence, and a genetic assessment is commended for Lynch syndrome by looking for microsatellite instability or immunohistochemistry to find the DNA repair proteins presence (MSH1, MSH2, MSH6, and PMS2). In a recent retrospective study in which colorectal cancers in young adults was studied, it was found that nearly 25% of the patients had a family history of colorectal cancer and a similar proportion of patients were obese. Nearly 50% of the patients had locally advanced or metastatic disease.[27] In a case series, two patients of colorectal cancers in young adults were reported. A 24 year old female and a 33 year old man with no significant risk factor or family history were reported.[28]

The diagnosis in younger people is often late. A couple of reasons attributed for the same are that cancer is rarer in this age group and that the symptoms are usually attributed to benign pathologies. This is why it becomes necessary to pay close attention to symptoms in the younger population and conduct studies to evaluate the benefits of performing screening in the high-risk group. Overall, CRC occurring in the Adolescent and Young Adults (AYA) population also termed young-onset CRC, shows a predilection for the distal colon and rectum which was seen in our case as well. Large tumor size (> 5 cm), high rates of perineural or lymphovascular invasion, and signet cell or mucinous histology have been suggested found to be present in young onset CRC.[29] A multidisciplinary team decision is crucial because the majority of patients with early-onset CRC have locally advanced or metastatic disease.[30] In the absence of any biological traits,

the treatment strategies do not extricate early-onset CRC from late-onset disease.[31]

Case 3: Adenocarcinoma of the stomach in 25-year-old male

Introduction

Cancer stomach and GE junction is the 5th most common cause of cancer and is also the 3rd prominent cause of cancer-associated death in the world.[7] In India, it is the 6th most common cause and cause of cancer-interrelated death.[7] Gastric Cancer (GC) tends to be frequently diagnosed in elderly patients with the average age being 68 years. More than 95% of new cases are diagnosed in patients above 40 years of age.[32] However lately a stable or slightly increasing trend has been observed in young adults.[33] Various information has recommended that roughly 5% of gastric cancer patients are diagnosed below the age of 40.[32] The important risk factors include smoking, alcohol, family history, and dietary and environmental factors. Herein, we discuss a case of a 25-year-old young male with cancer stomach without any evident risk factors.

Case presentation

A 25-year-old male, with no comorbidities presented with dysphagia to solids for 2 months. The patient had no known history of smoking or alcohol. There was no family history of cancer as well. Upper GI endoscopy showed circumferential growth of around 3 cm with an overlying ulcer seen at the fundus and GE junction region. PET CT showed irregular circumferential wall thickening with increased FDG uptake seen involving gastric cardia and fundus (maximum wall thickness 1.2cm, SUVmax 9.4). Proximally, it is involving GE junction. The mass has ill-defined planes with splenic parenchyma. There is the presence of small lymph nodes in the gastrohepatic space adjoining the mass.

Histopathology showed adenocarcinoma. On immunohistochemistry CK 20, MUC1 and MUC2 were positive, and CK7 and Her2 were negative suggestive of the origin of the tumor from intestinal metaplasia of gastric origin.

The patient had received 4 cycles of chemotherapy however with no significant change on the interim PET CT scan.

Thereafter the patient underwent Laparoscopic distal esophagectomy with proximal gastrectomy and esophago-gastric anastomosis. On Histopathology, the tumor is 5.5 x 3.5 x 3.5 cm at the gastric cardia, fundus, and GE Junction., poorly differentiated adenocarcinoma, diffuse type, with the presence of perineural and lymphovascular invasion, margins free, 5 nodes out of 12 were positive with final staging ypT3 N2 M0.

The patient was then treated with post-operative adjuvant radiotherapy with a dose of 45Gy in 25 fractions over 5 weeks along with concurrent chemotherapy.

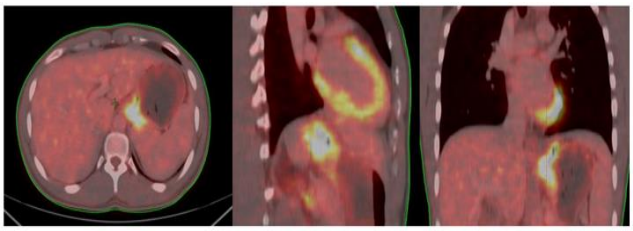

Figure 4. shows the PET CT scan of 25 year old male with adenocarcinoma of stomach and GE junction in axial, sagittal and coronal views

Discussion

Gastric Cancer in Young Adults (GCYA) presents a clinical challenge because of its aggressive growth and this present a further innovative step at the time of diagnosis. GCYA should be considered as a separate clinical entity as some authors have suggested.[32] It has multifactorial etiology with H. pylori co-infection, genetic predisposition, dietary constituents, and environmental factors being important factors.[34] Pisanu *et al*. described the frequent association of H. pylori infection as related to GCYA patients.[35] Gastric intestinal metaplasia (IM) is a pre-neoplastic gastric lesion, which is usually caused by chronic Helicobacter pylori infection.[36] Studies have revealed the H. pylori infection occurrence and the frequency of these precancerous lesions was high among the GC patient's first-degree relatives.[37]

Familial clustering and hereditary aspect were found in 10% of gastric cancer cases and it has been shown that the risk of GC in first-degree relatives is increased.[38] Between 1% and 3% are Hereditary Diffuse Gastric Cancer (HDGC), Lynch syndrome (also known as hereditary non-polyposis colorectal cancer), Juvenile Polyposis Syndrome (JPS), and Peutz-Jeghers syndrome (PJS) are manifestations of numerous inherited predisposition syndromes.[39]

Other etiological factors include dietary and lifestyle factors. Amongst these tobacco smoking, alcohol intake, smoked food, and a lack of fruits/ vegetables have been implicated. Although the association between obesity and GC has not been established, the increased incidence of gastroesophageal reflux disease (GERD) related to obesity might prejudice individuals to additional proximal gastric cancers.[40] Witt *et al*. described a case of gastric adenocarcinoma in a 17 year old boy in Canada. There was no apparent risk factor or family history. The tumour was un-resectable and the patient was treated with palliative chemotherapy.[41]

In this regard, our patient did not have a family history or any dietary factor, which could be implicated. The histology showed intestinal metaplasia so there is a role of H. Pylori.

In terms of clinical profile, GCYA usually occurs in the female gender, is more aggressive, and is present in the advanced stage.[42] Therapeutic options for GC are not yet stratified to date by age. According to the recommendations, GCYA has not considered a criterion for compliance with other treatment strategies.[42]

Conclusion

These 3 cases highlight the fact that lately there has been a trend of diagnosing cancer in young adults which generally would have presented in older individuals. All three cases namely squamous cell carcinoma larynx, cancer rectum, and cancer stomach generally present in the adult age group, and in this case series all of these are presented in their early to mid-twenties. The conventional etiological factors, which are found in adult patients, are not present in these patients. However, a combination of lifestyle, genetic factors, and viral etiologies do play a role in their etio-pathogenesis. Whereas in some cases they can rarely develop with no apparent risk factor as well. Cancer in young adults tends to be poorly differentiated, present in an advanced stage and is more aggressive as seen in our case series. There is a need to be vigilant for the pre-cancerous symptoms so that these aggressive tumors can be detected and treated at an early stage.

The important takeaway message is that these cancer trends in young adults, often under 40 years, reflect a recent change in carcinogenic exposure in the population, which could foreshadow the future overall disease burden. This could yet be the tip of the iceberg!!

Acknowledgments
None.

Conflict of interest
None.

Financial support
None.

Ethics statement
None.

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