

Emerging Trends in Early-Onset Adult Cancers: A Case Series

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Abstract

Cancer is generally associated with aging, with the risk of developing most cancer types rising significantly in midlife and continuing to increase with age. However, adolescents and young adults represent a unique demographic where cancers typically seen in older adults are increasingly being diagnosed. Tumors in this age group exhibit distinct characteristics when compared to those found in younger children or older adults, and management of these patients presents unique challenges due to the potential for long-term side effects. This case series examines three instances of adult cancers diagnosed at unusually young ages and sheds light on the recent shift in cancer presentation trends. These cases include a 21-year-old female diagnosed with supraglottic laryngeal squamous cell carcinoma, a 22-year-old male with rectal adenocarcinoma, and a 25-year-old male with adenocarcinoma of the stomach and gastroesophageal junction. This series aims to highlight the emerging trend of cancer diagnoses at younger ages, which could signal a change in the future landscape of cancer epidemiology.

Keywords: Cancer Trends, Young Adults, Age-Related Cancer, Epidemiology, India

Introduction

The occurrence of cancer in adolescents and young adults (AYAs) is notably different from that in children or older adults. While cancer rates are generally lower in the AYA group compared to older adults, the higher percentage of younger individuals in developing nations adds complexity to the management of these cancers. AYAs are often more vulnerable to cancers that are influenced by genetic factors, family history, and specific lifestyle choices, which increase their exposure to environmental and health risks [1-4].

The types of cancer commonly diagnosed in this demographic include breast cancer, melanomas,

lymphomas, sarcomas, germ cell tumors, bone cancer, thyroid cancer, and occasionally brain tumors. These cancers have distinct features in terms of type, distribution, biological behavior, and survival rates when compared to cancers in older populations. Furthermore, AYAs face an increased risk of long-term health issues such as fertility challenges, heart disease, sexual dysfunction, and secondary cancers [5-7].

Recently, there has been a shift in the age at which certain cancers are being diagnosed, with diseases usually seen in older adults now presenting in younger individuals. Cancers like those of the head, neck, lung, and gastrointestinal system, typically found in people aged 50-60 years, are now being detected in young adults who lack traditional risk factors. This trend presents difficulties not only in treatment but also in understanding the reasons behind the incidence of these cancers in younger individuals [8-11].

In this case series, we report on three young adults diagnosed with cancers typically associated with older age groups.

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Results and Discussion

Case 1: Supraglottic Laryngeal Carcinoma in a 21-Year-Old Female

Laryngeal cancer is the 11th leading cause of cancer-related deaths in India, with an incidence of 1.26 to 8.18 per 100,000 people, and more common in men than women. The prevalence of laryngeal cancer in men is approximately 3-6% of all cancers, whereas it is much lower in women at 0.2-1%. The typical age of onset is 65 years, with squamous cell carcinoma (SCC) being rare among adolescents, though when it occurs, it is often aggressive.

Risk factors for laryngeal cancer include smoking, passive smoke exposure, and prolonged exposure to indoor air pollution, especially from coal. Only a small percentage (10%) of laryngeal cancer cases are diagnosed in people under the age of 40 years, and these young patients typically have fewer of the classic risk factors seen in older individuals. Some studies are investigating the roles of human papillomavirus (HPV) and laryngopharyngeal reflux, though a definitive connection has not yet been established. In this case, we present a young female diagnosed with HPV-positive laryngeal carcinoma.

Case presentation

A 21-year-old female was referred to the hospital with complaints of hoarseness of voice persisting for 6 months, without any significant medical history. She had no history of smoking or tobacco use but mentioned passive smoking at home. There was no known family history of cancer. Her diet was non-vegetarian, and she reported no history of reflux issues. Upon examination, a mass was found on the epiglottis and left aryepiglottic fold during laryngeal endoscopy.

MRI imaging of the neck revealed a mass measuring 3.1 x 3.2 x 2.0 cm, located in the left aryepiglottic fold, extending across to the contralateral side, and involving the right aryepiglottic fold. The lesion also affected the pyriform sinuses, extended to the epiglottis, and invaded the para-epiglottic fat. The patient exhibited mild edema on her vocal cords along with small bilateral lymph nodes.

The biopsy confirmed the presence of keratinizing well-differentiated squamous cell carcinoma.

Immunohistochemical staining showed a positive result for p16 (**Figures 1a** and **1b**).

A PET-CT scan (**Figure 2**) revealed a soft tissue mass in the left larynx, specifically affecting the left aryepiglottic fold and extending to the margin of the epiglottis, leading to luminal narrowing. The mass measured 2.1 x 1.4 cm with a SUV_{max} of 29.2 and demonstrated FDG avidity. No distant metastases were observed.

The patient was subsequently treated with concurrent chemoradiotherapy, receiving a dose of 70 Gy in 35 fractions over 7 weeks, along with weekly cisplatin.

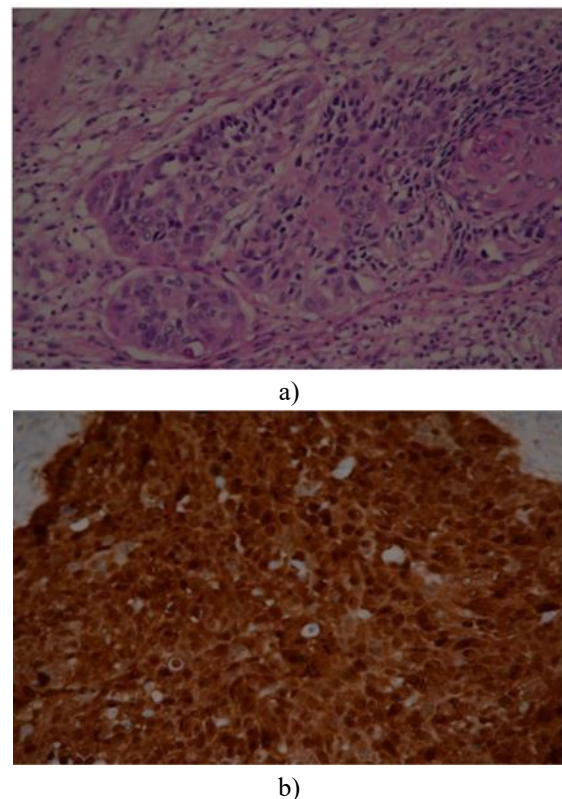


Figure 1. a) representative section of histopathological slide showing squamous cell carcinoma, and b) immunohistochemistry positivity with p16



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

Discussion

Laryngeal carcinoma is an uncommon condition in young adults. Typically, squamous cell carcinoma (SCC) affects the vocal cords (glottis) in adolescents and young adults, followed by the supraglottic and subglottic areas [12]. In this instance, the tumor was supraglottic in a young female. Traditional risk factors like smoking and alcohol use are less common in younger patients, as observed in our case. HPV infection, often associated with oropharyngeal cancers, has been linked to the clinical profile and prognosis of affected individuals [13]. However, the connection between HPV and laryngeal cancers remains debated, with varying rates of HPV positivity depending on factors like diagnostic methods, ethnicity, geography, and sample quality [14, 15]. In our patient, HPV positivity was confirmed through p16 immunohistochemistry. A review of 55 studies with 2,559 laryngeal cancer patients showed that 28% tested positive for HPV, with HPV 16 being the most common high-risk variant [11, 16]. Studies have shown that HPV-positive laryngeal cancer generally leads to better survival outcomes compared to HPV-negative cases [17]. In the U.S., researchers have suggested that HPV may play a larger role in female laryngeal cancer cases, a pattern observed in our patient's case [18]. This growing recognition of HPV's involvement has led to the classification of HPV-positive laryngeal cancer as a "new" type of head and neck cancer by some researchers [19]. Although Swain and Sahu [20] documented a case of squamous cell carcinoma of the larynx in an eleven-year-old, HPV status was not confirmed for that patient. Similarly, Pugi *et al.* [21] reported a case of HPV-positive supraglottic laryngeal carcinoma in a 33-year-old pregnant woman.

The HPV infection in our case could have been a factor in the early development of this malignancy in a young patient.

Case 2: Rectal Adenocarcinoma in a 22-Year-Old Male

Colorectal cancer ranks as the 7th most prevalent cancer worldwide and the 10th leading cause of cancer-related deaths. However, in India, it is less common, ranking 16th in incidence and 15th in cancer-related mortality [7]. Rectal cancer is typically diagnosed in older adults, with 90% of cases occurring between the ages of 50 and 60 years [22]. Recently, studies have shown a rise in

colorectal cancer cases among younger individuals, with nearly 7% of patients diagnosed under the age of 40 years [23]. While smoking and diet are known risk factors for colorectal cancer in older adults, younger patients are often affected by different factors, such as inflammatory bowel disease, hereditary non-polyposis colorectal cancer, and gastrointestinal tract polyposis syndromes. In this case, a 22-year-old male developed rectal cancer without any known risk factors.

Case presentation

A 22-year-old male with a history of paraplegia from a spinal injury presented with rectal bleeding for the past month. He had no history of smoking or any family history of cancer. A colonoscopy revealed a large nodular growth extending from the anal canal up to 18 cm from the anal verge. The mucosa proximal to the lesion appeared normal. Biopsy results confirmed poorly differentiated adenocarcinoma with mucinous differentiation.

PET-CT imaging showed FDG-avid circumferential wall thickening (SUV_{max} 8.5), measuring 21 mm in thickness, and involving 10.8 cm of the rectum and anal canal, nearly reaching the anal verge. The scan also revealed significant perilesional fat strandings and mildly FDG-avid, centimeter-sized lymphadenopathy in the perirectal and external iliac regions, without any evidence of distant metastases.

The patient received neoadjuvant chemoradiation, with a total dose of 50.4 Gy delivered in 28 fractions over 5.5 weeks, along with concurrent chemotherapy (**Figure 3**).

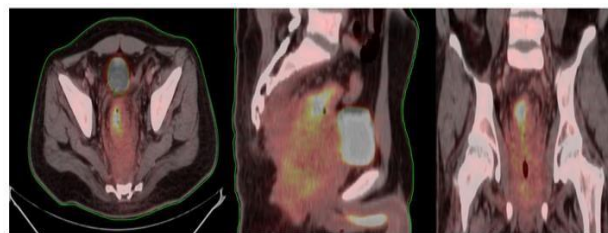


Figure 3. The PET CT scan of a 23-year-old male with adenocarcinoma in axial, sagittal, and coronal views.

Discussion

Over the last 20 years, the number of colorectal cancer (CRC) cases among younger individuals has seen a steady annual increase of 2% to 8% [24]. These patients are often diagnosed at more advanced clinical stages and tend to have more aggressive disease biologically.

Mucinous adenocarcinoma and poorly differentiated signet ring cell types are the most frequent histological patterns in this age group [25]. While the majority of CRC cases are sporadic, younger individuals tend to show more complex genetic alterations. Therefore, genetic testing—especially for Lynch syndrome—is advised, which involves checking for microsatellite instability or evaluating mismatch repair proteins (MSH1, MSH2, MSH6, PMS2) using immunohistochemistry.

A recent retrospective study analyzing CRC in young adults found that about a quarter of patients had a family history of the disease, and a similar proportion were classified as obese. Additionally, nearly half of the patients were diagnosed with either locally advanced or metastatic disease at the time of presentation [26]. Another case series described two young adults, aged 24 and 33 years, who developed colorectal cancer despite having no family history or clear risk factors [27].

Delayed diagnosis in younger patients is a common issue. This is often due to the rarity of CRC in this group and the tendency to misinterpret symptoms as benign conditions. These factors highlight the need for greater awareness and potentially early screening strategies for high-risk young populations. CRC in adolescents and young adults (referred to as “young-onset CRC”) often affects the distal colon and rectum, as was also observed in our patient. Features commonly found in young-onset CRC include tumors larger than 5 cm, high occurrences of perineural or lymphovascular invasion, and mucinous or signet ring cell histology [28].

Given that many early-onset CRC cases present with advanced disease, treatment planning should involve a multidisciplinary team [29]. However, in terms of treatment approach, current guidelines do not differentiate between early- and late-onset CRC unless specific biological markers are identified [30].

Case 3: Gastric Adenocarcinoma in a 25-Year-Old Male

Introduction

Gastric and gastroesophageal (GE) junction cancers rank as the fifth most frequently diagnosed cancers globally and the third leading cause of cancer-related deaths [7]. In India, stomach cancer is the sixth most prevalent cancer and similarly ranks high in cancer mortality [7]. Although gastric cancer typically occurs in older

individuals—most often after age 68 years—recent data suggest a gradual rise in incidence among younger adults [31, 32]. It is estimated that around 5% of gastric cancer cases occur in patients under 40 years of age [33]. Known risk factors include tobacco and alcohol use, family history, and certain dietary and environmental exposures. The case described here involves a 25-year-old man who developed gastric cancer despite lacking any identifiable risk factors.

Case presentation

A 25-year-old male with no underlying health conditions reported experiencing difficulty swallowing solid food for the past two months. He had no history of smoking, alcohol use, or a family history of cancer. An upper gastrointestinal endoscopy identified a 3 cm circumferential lesion with an overlying ulcer located at the gastric fundus and GE junction. PET-CT imaging revealed irregular thickening of the gastric cardia and fundus walls, with increased FDG uptake (SUV_{max} 9.4) and a maximum wall thickness of 1.2 cm. The tumor extended proximally to involve the GE junction and showed poorly defined borders with the spleen. A few small lymph nodes were noted in the gastrohepatic region adjacent to the tumor.

Histological examination confirmed the presence of adenocarcinoma. Immunohistochemical testing showed positivity for CK20, MUC1, and MUC2, while CK7 and Her2 were negative—indicating the tumor originated from intestinal metaplasia in the stomach.

The patient underwent four cycles of chemotherapy, but follow-up PET-CT scans showed minimal response. As a result, he underwent laparoscopic distal esophagectomy combined with proximal gastrectomy and reconstruction via esophagogastric anastomosis.

Post-surgical pathology revealed a 5.5 x 3.5 x 3.5 cm tumor at the gastric cardia, fundus, and GE junction. It was classified as a poorly differentiated diffuse-type adenocarcinoma with evidence of both lymphovascular and perineural invasion. Surgical margins were clear, and 5 of 12 examined lymph nodes were positive. The final staging was ypT3 N2 M0.

The patient subsequently received adjuvant radiotherapy totaling 45 Gy in 25 fractions over five weeks, along with concurrent chemotherapy (**Figure 4**).

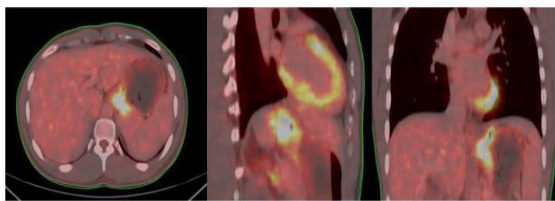


Figure 4. The PET CT scan of a 25-year-old male with adenocarcinoma of the stomach and GE junction in axial, sagittal, and coronal views

Discussion

Gastric cancer in young adults (GCYA) presents a unique clinical challenge due to its aggressive nature and often late diagnosis. Some researchers have proposed recognizing GCYA as a distinct clinical subset of gastric cancer [31]. Its development is influenced by multiple factors, including co-infection with *Helicobacter pylori*, genetic susceptibility, environmental exposure, and dietary habits [33]. Pisanu *et al.* [34] have highlighted the common presence of *H. pylori* infection in younger patients diagnosed with gastric cancer. Gastric intestinal metaplasia (IM), a known pre-cancerous lesion, often arises from chronic *H. pylori* infection and is considered a key step in gastric carcinogenesis [35]. Notably, studies show a higher rate of *H. pylori* infection and pre-neoplastic lesions among first-degree relatives of gastric cancer patients, suggesting a familial or hereditary link [36].

Approximately 10% of gastric cancer cases demonstrate familial clustering, with a significantly elevated risk observed among first-degree relatives [37]. Of these, 1–3% are linked to inherited syndromes such as hereditary diffuse gastric cancer (HDGC), Lynch syndrome, juvenile polyposis syndrome (JPS), and Peutz–Jeghers syndrome (PJS) [38].

Environmental and lifestyle factors also contribute to gastric cancer risk. Tobacco use, alcohol consumption, diets high in smoked foods, and low intake of fruits and vegetables have all been implicated. While obesity itself hasn't been directly tied to GC, it may indirectly increase risk by predisposing individuals to gastroesophageal reflux disease (GERD), which has been associated with proximal gastric cancers [39]. Witt *et al.* [40] reported a case of gastric adenocarcinoma in a 17-year-old male in Canada who had no known risk factors or family history; the tumor was inoperable, and the patient underwent palliative chemotherapy.

In our presented case, the patient lacked identifiable familial or dietary risk factors. However, the presence of intestinal metaplasia in the histopathology supports a potential role of *H. pylori* infection in the pathogenesis. From a clinical perspective, GCYA more commonly affects females, tends to be more biologically aggressive, and is frequently diagnosed at an advanced stage [41]. Despite this, current treatment guidelines for gastric cancer do not differentiate based on patient age, and GCYA is not yet recognized as requiring specialized treatment protocols [41].

Conclusion

These three case reports underscore an emerging pattern of cancer presenting in younger individuals, typically in diseases that historically occurred in older populations. The cases—laryngeal squamous cell carcinoma, rectal cancer, and gastric cancer—were all diagnosed in patients in their twenties, an age group in which such malignancies are generally uncommon.

Interestingly, traditional risk factors seen in adult-onset cases were largely absent in these patients. This suggests that a mix of genetic predisposition, lifestyle elements, and possibly viral infections may contribute to the pathogenesis in younger individuals. In some instances, however, cancer may develop even in the absence of identifiable risk factors.

Cancers in young adults tend to present as poorly differentiated, more aggressive, and at more advanced stages, as seen in this series. This highlights the importance of maintaining a high level of clinical suspicion for early, non-specific symptoms in this age group to enable earlier diagnosis and improved outcomes.

A crucial takeaway is the growing trend of cancer diagnoses in individuals under 40, reflecting changing exposure to carcinogenic factors within the general population. This shift may signify the beginning of a broader rise in cancer burden among younger generations—potentially the tip of the iceberg in terms of future public health impact.

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