

## Early-onset aggressive oesophageal carcinoma in Down's syndrome — a coincidence or a game of extra genes?

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### Abstract

Patients with Down's syndrome exhibit a unique pattern for a number of malignant conditions but there is inconsistent data for the risk of oesophageal cancer. We present a case of early-onset aggressive oesophageal carcinoma in a young male patient diagnosed with Trisomy 21, who presented with complaints of progressive dysphagia, vomiting, voice change and weight loss. Barium swallow showed shouldering sign at distal oesophagus. GI Endoscopy revealed an irregular growth at 20cm from incisors obstructing the lumen. Histopathology confirmed well-differentiated adenocarcinoma. CT scan unmasked a circumferential mass involving the dorsal oesophagus with multiple enlarged nodes along with infiltration of basal segments of left lung staging the tumour as T3N1M0. A metallic stent was placed endoscopically through the stenotic tumour and the patient was referred for chemoradiotherapy. Contrary to the literature proposing a decreased incidence of solid tumours, this is a case reporting early-onset aggressive oesophageal carcinoma in a patient with Down's syndrome.

**Keywords:** Esophageal Carcinoma, Early onset esophageal adenocarcinoma, Down's syndrome.

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### Introduction

A distinctive pattern for occurrence of malignancies has been demonstrated in individuals with Down's syndrome (DS). These patients have a higher risk of developing leukaemia at early ages as compared to people who do not have trisomy 21.<sup>1</sup> Better survival rates have been demonstrated in myeloid leukaemia in DS patients on intensive medical treatment which are found associated with higher chemosensitivity due to over expression of genes on chromosome 21.<sup>2</sup>

With regards to solid tumours, less clear data is available. Whereas some studies have suggested a decreased

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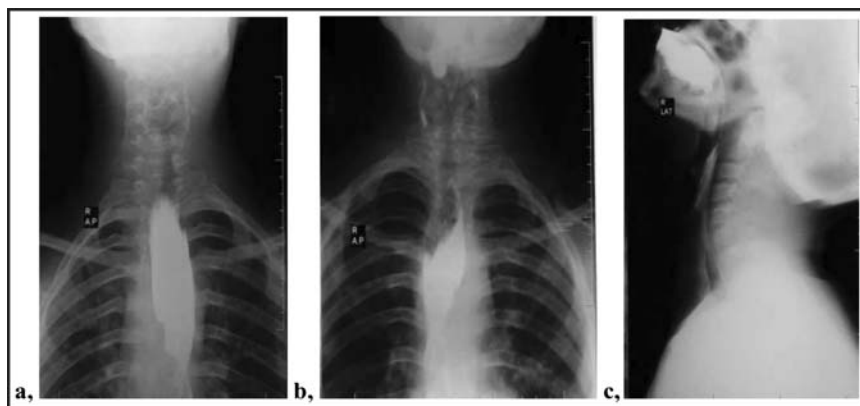
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incidence of solid tumours,<sup>3</sup> others suggest a higher likelihood of germ-cell tumour, lymphomas and retinoblastoma.<sup>4</sup> Breast cancer is rare, and the possibility of a subsequent neoplastic disease after being treated for leukaemia also seems to be on the lower side.<sup>2</sup> The possibility of exhibiting a lower risk of solid tumours and secondary carcinomas in patients with DS may be explained by the increased susceptibility of a cell to undergo apoptosis after cell injury or nuclear derangements leading to cell death rather than transformation into malignancy.<sup>2</sup> A gene (DSCR-1) found on chromosome 21 is over expressed in patients with DS. This gene encodes a protein responsible for inhibiting formation and growth of new blood vessels. This decreases angiogenesis associated with neoplasia and subsequently reduces tumour growth.<sup>5</sup> All this can explain the reduced risk of primary solid and secondary carcinomas. Similarly, a decreased risk for most digestive cancers has been reported in the literature with an exception for liver and pancreatic cancers.<sup>6</sup> However, cases have been reported pointing towards an increased risk for oesophageal cancers in DS.<sup>7,8</sup> Here we present a case of early-onset aggressive oesophageal cancer in a patient with Down's syndrome.

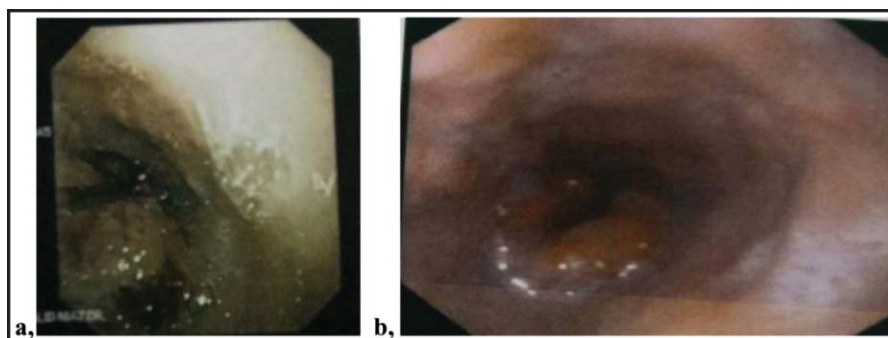
### Case Presentation

We present the case of a 14-year-old male with Trisomy 21 who attended outpatient department of Surgical Unit 4 at Dr. Ruth K. M. Pfau Civil Hospital Karachi on 13th of April 2017 with the chief complaints of progressive dysphagia for solids and vomiting of recently ingested meals for 2 months. These complaints were associated with change in voice and weight loss. On examination, he was mildly anaemic with crepitations on chest auscultation. There was no history of addiction to alcohol or tobacco, ingestion of caustic agent or exposure to radiation. The family history for any malignant disease was negative. Routine blood analyses for electrolytes, peripheral blood count and liver function tests were normal.

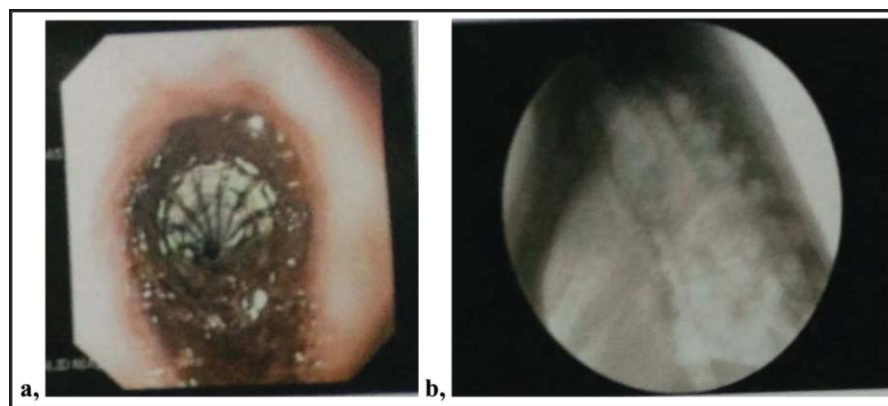
Barium swallow showed marked irregularity and hold up of barium with shouldering sign at dorsal oesophagus (Figure-1). Upper GI Endoscopy showed an irregular growth at 20cm from incisors obstructing the lumen beyond which the scope could not be negotiated. Histopathology of the growth confirmed well-



**Figure-1:** X-ray Barium Swallow (a,b = AP View , c = Lat. View).



**Figure-2:** Endoscopic views of esophagus (a,b).



**Figure-3:** Endoscopic placement of metallic stent (a = Endoscopic view, b = Fluoroscopic view).

differentiated adenocarcinoma (Figure-2). CT scan of chest and abdomen revealed a circumferential mass lesion 1.4 cm long involving the dorsal oesophagus, obliterated para-oesophageal fat planes and indentation of the trachea. Multiple enlarged nodes were identified along with infiltration of basal segments of left lung. The tumour was staged as T3N1M0.

Since the tumour was found irresectable, a 14-cm metallic stent was placed endoscopically from 18-30cms through the stenotic tumour (Figure-3). The patient was thereafter

referred for chemoradiotherapy and called for follow up. The patient however did not complete his chemoradiotherapy and was lost to follow up.

## Discussion

Literature has shown a higher incidence of leukaemia in patients with Down's syndrome (DS) who have a decreased risk of developing a solid tumour.<sup>1</sup> This unusual pattern has guided for the search of leukaemogenic genes and tumour suppressor genes on chromosome 21. This unique pattern has also helped in early diagnosis and management of these cancers in patients with DS. While studies suggest a decreased incidence of solid and digestive cancers,<sup>9</sup> we find cases of oesophageal carcinoma in patients with DS. In one report, a 31-year-old male (who was asymptomatic in childhood), was found to have congenital duodenal membrane, leading to hiatal hernia, stricture of the oesophagus, and finally carcinoma in oesophageal stricture. The membrane in this case was resected with Nissen fundoplication followed by resection of carcinoma and oesophagogastronomy.<sup>7</sup>

In another report, two cases of oesophageal carcinoma in young patients of Down syndrome were presented with the cancers being inoperable and palliative management was done like in our case.<sup>8</sup> Another review demonstrates a moderate excess in risk of gastrointestinal cancers.<sup>4</sup> All these cases may be attributed to medication in these individuals that

raise liver enzymes, obesity and gastroesophageal reflux which is a precursor to a premalignant condition of oesophageal carcinoma. Gastroesophageal reflux disease (GERD) has been linked to the development of adenocarcinoma of the oesophagus and is a proven risk factor.<sup>10</sup> A small series of case reports suggest a relationship of DS with GERD.<sup>11</sup> However, a large prevalence study carried out among institutionalised intellectually challenged individuals did not show Down syndrome to be a predisposing factor for GERD.<sup>12</sup>

Down syndrome is well known to be linked to multiple non-malignant abnormalities in the oesophagus, such as; motor dysfunctions, achalasia, tracheo-oesophageal fistula and oesophageal atresia. These abnormalities can be a predisposing factor for development of oesophageal carcinoma, however a clue linking DS directly to oesophageal cancer is lacking.

The main risk factors predisposing an individual to squamous cell carcinoma include a positive family history of pharyngeal, oesophageal or gastric carcinoma, caustic ingestion, use of alcohol or tobacco. Intellectually challenged patients tend to suffer more from accidental ingestion of a caustic substance that can lead to the development of squamous cell carcinoma, however once again we lack a direct link between oesophageal cancers and DS.

### Conclusion

The case of early-onset oesophageal carcinoma in a patient with Down's syndrome is presented. This is contrary to the literature showing decreased risk of solid tumours in these patients. The tumour at presentation was aggressive and irresectable this could be due to the fact that our patient suffered with intellectual disabilities and may have found it difficult to convey his pain and symptoms effectively that lead to delayed diagnosis. Thus, it is important to have a low threshold for early investigations with atypical symptoms of less common pathologies in this group of patients.

**Consent:** Written consent was obtained from the parents of the patient for publishing the case.

**Disclaimer:** None to declare.

**Conflicts of Interest:** None to declare.

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