

Case Report

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# Extensive Lower Lip Squamous Cell Carcinoma in a Fanconi Anaemia Patient and Treatment Delays during COVID-19 Pandemic

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## Keywords

Fanconi anaemia · Head and neck cancer · Oral squamous cell carcinoma · COVID-19

## Abstract

Fanconi anaemia (FA) is an autosomal recessive inherited disease that renders patients susceptible to congenital anomalies, bone marrow failures, leukaemia, and solid malignancies. FA is caused by the loss of function of at least one gene in the FA/BRCA biological pathway, which is involved in DNA repair. Patients with FA have an increased risk of developing head and neck cancer, particularly oral squamous cell carcinoma (SCC). Due to susceptibility of head and neck cancer at a very young age, relatively poor survival rate, low tolerance to oncologic interventions, and complexity of treatments, strict follow-up is mandatory to detect any changes or recurrence of SCC in the head and neck region in FA patients. Surgery is the mainstay of treatment, but adjuvant therapy should be instituted when needed. This short report describes a rare case of lower lip SCC in FA and its management. It also highlights the impact of the COVID-19 pandemic on healthcare practices.

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## Introduction

Fanconi anaemia (FA) is an atypical autosomal recessive disorder that is clinically associated with congenital abnormalities, pancytopenia with progressive bone marrow failure, and a predisposition to malignancies [1]. It is caused by the loss of function of at least one gene in the FA/BRCA biological pathway, which is involved in DNA repair. Haematopoietic stem cell transplantation (HSCT) is currently the standard treatment of choice to cure bone marrow failure, but it increases the likelihood for solid tumours [2]. In addition, patients with FA have an increased risk of developing head and neck cancer, particularly oral squamous cell carcinoma (SCC) [3]. Although the mainstay of treatment is surgery, adjuvant therapy should be administered as needed [4]. However, FA patients have a low tolerance to oncologic treatment due to their defective DNA repair [5]. It is conceivable that the number oral SCC cases will rise over time as HSCT improves overall life expectancies. Thus, preventive and early screening measures are critically required.

Many diseases, particularly head and neck malignancies, have seen delays in diagnosis and treatment phases as a result of the COVID-19 pandemic. Such delays lead to significant tumour growth, placing patients at an increased risk for more complex treatment and adverse outcomes [6]. We report a rare case of extensive lower lip SCC in an FA patient and treatment dilemma in the COVID-19 pandemic era.

## Case Presentation

In February 2021, a 29-year-old gentleman first noticed the appearance of a pea-sized swelling at the midline of his lower lip. He visited a nearby hospital in April 2021, and an excisional biopsy under general anaesthesia was planned. However, the procedure was postponed due to the rise in number of COVID-19 cases and reduced elective operating time. As the lower lip ulceration began to grow exponentially, an incisional biopsy was performed under local anaesthesia in July 2021, revealing well-differentiated SCC. In August 2021, he was referred to our centre owing to inability to proceed with surgery at the first hospital due to another COVID-19 outbreak.

The patient was diagnosed with FA at the age of six and underwent pre-treatment irradiation regimen followed by HSCT at the age of thirteen. Upon presentation at our centre, the tumour had encompassed his entire lower lip, was friable, and easily bled upon touch with bilateral palpable neck nodes (shown in Fig. 1). He was treated by wide local excision of tumour, bilateral functional neck dissection, and reconstruction with bilateral nasolabial flap (shown in Fig. 2). Final staging was confirmed as pT4aN2c cM0 with bilateral nodal micrometastasis at right level I to II lymph nodes and left level I to IV lymph nodes. He was referred to the oncology team, and they decided that concurrent post-operative chemotherapy and radiotherapy. One month after surgery, aesthetic and functional outcomes were satisfactory (shown in Fig. 3). However, adjuvant therapy was discontinued after 11 fractions of daily intensity-modulated radiation therapy at 70 Gy and two doses of weekly cisplatin therapy as he developed systemic toxicities. Following that, he received best supportive and palliative care. Repeated computerized tomography scan revealed multiple lung nodules suggestive of metastasis. There were no other sites of distant metastasis. The patient died from disease progression 4 months after surgery.

## Discussion

FA is attributed to a genetic deficiency in a group of proteins involved in DNA repair, with 16 different FANC genes recognized [7]. The outcome for HSCT has improved over the last few decades, resulting in a higher percentage of patients surviving into adulthood. This led to an



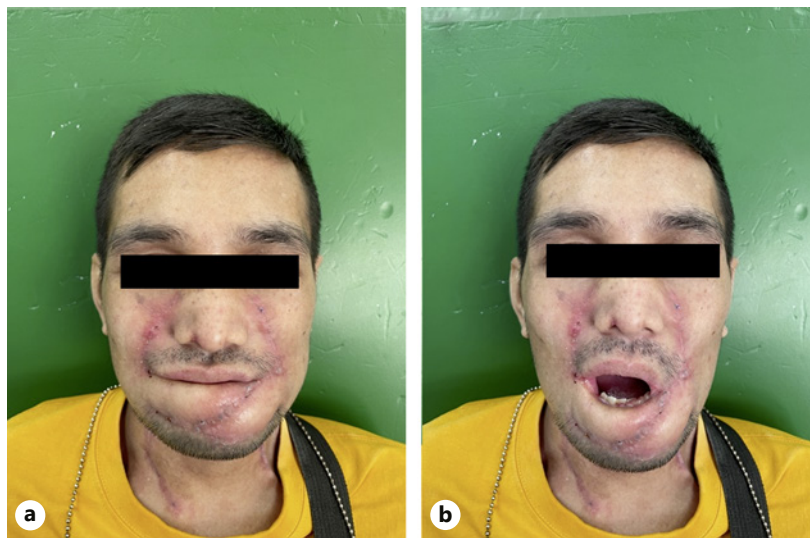
**Fig. 1.** Initial presentation of cauliflower-like exophytic lesion on lower lip.



**Fig. 2.** Post-wide excision of tumour and reconstruction with bilateral nasolabial flap.

increase in development of malignancies such as head and neck SCC among FA patients [8]. Oral malignant transformation following HSCT has been linked to chronic graft versus host disease, prolonged immunosuppressive therapy, chromosomal instability, and DNA repair defects [8–10].

Surgery is the primary therapeutic option for head and neck SCC in FA patients. Large reconstructions and lymph node removals are tolerated with similar morbidity as non-FA patients. However, chemotherapy and radiotherapy are hampered by their high toxicity, due to defective DNA process in FA patients [5]. In view of the advanced stage of cancer upon presentation and



**Fig. 3.** Post-operative view of the patient after 1 month, showing (a) good lip seal and (b) good mouth opening.

lymph node metastasis, concurrent post-operative chemotherapy and radiotherapy was still decided for this patient. Despite experimentally decreased radiation dose, FA patients often have symptoms such as severe mucositis, dysphagia, and haematological abnormalities. Small patient cohorts have shown positive therapeutic tolerance [11]. Radiotherapy can be administered with acceptable toxicity in FA patients including those who underwent HSCT [12]. Cetuximab has emerged as a substitute treatment for head and neck SCC in recent years, owing to its decreased toxicity when compared to standard chemotherapy [13, 14]. It was concluded that most FA patients with head and neck SCC did not tolerate cytotoxic chemotherapy (often with a platinum-based regimen) well, either with or without radiation therapy. Hence, EGFR inhibitors may be a safe and effective alternative to platinum-based drugs in this group of patients [12]. A thorough risk assessment by oncologists is mandatory prior to the commencement of adjuvant therapy to prevent systemic complications.

In the wake of the COVID-19 pandemic, physicians and surgeons are reconsidering standard cancer therapy paradigms. Surgery for malignant tumours must be done without delay with proper biosecurity measures in place [15]. The diagnosis and treatment of many diseases, including head and neck malignancies, have experienced delays as a result of the pandemic. Admissions with advanced disease and need for more difficult reconstructive procedures were observed to be on the rise. This could be due to the disruption brought about by the pandemic's distribution of essential resources. This was evident in immediate effects, such as bigger resection and more complex reconstruction cases, but the broader ramifications, such as survival and long-term care, are still unknown [6]. In our case, the proposed treatments could not be carried out in view of reduced elective operating schedule due to multiple COVID-19 outbreaks in the first centre. This in turn led to a more complex treatment as a result of the aggressive nature of the tumour and local neck metastasis.

### Conclusion

FA patients with history of HSCT should be informed of oral malignant transformation risks and placed under periodic surveillance from a young age. Management of FA patients with locally advanced disease is more challenging due to significant morbidity and treatment-related

toxicities. We believe that during a pandemic, diseases that cause morbidity and mortality should be prioritized and not overlooked due to limited resources.

## Statement of Ethics

Written informed consent was obtained from the patient's next of kin for publication of this case report and any accompanying images. Ethical approval is not required for this case report in accordance with local and national guidelines.

## Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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## Author Contributions

Dr. Mohd Faizal Abdullah drafted the initial manuscript and revised the manuscript. Dr. Shobina Sivanganam reviewed and revised the final manuscript. Professor Dr. Shaifulizan Abdul Rahman critically reviewed the manuscript for important intellectual content.

## Data Availability Statement

All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

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