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Case report

Squamous Cell Carcinoma Companionship With Fanconi Anemia: Rare Situation or Increasing Hazard?

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ABSTRACT

The increased susceptibility of malignancies in Fanconi Anemia (FA), an autosomal recessive disease, is a major concern of this syndrome. According to previous reports, Head and neck squamous cell carcinoma (HNSCC) is one of the most frequently diagnosed solid tumors in these patients. Herein the authors report a unique case of HNSCC in the hard palate of a 31-year old female patient with FA syndrome, which was treated by surgical removal. Additionally, the literature about Squamous Cell Carcinoma companionship with Fanconi Anemia is reviewed.

1. Introduction

Fanconi anemia (FA) is a rare disease, with autosomal recessive hereditary pattern. A syndrome with predisposition of malignancy. The syndrome known by triad of congenital defects, bone marrow failure (BMF), and increased susceptibility to cancers [1].

As first described in 1927, Fanconi Anemia(FA) characterized as a progressive lethal anemia associated with brown pigmentation of skin [2]. Nowadays, the most serious early adverse event in patients with FA, aplastic anemia can often be managed with medical treatment (such as androgens and growth factors) or even cured with hematopoietic stem cell transplant using bone marrow, cord blood, or peripheral blood stem cells. Also, the new techniques such as use of genetically corrected autologous stem cells may be available in the future [3]. Then it must be considered that elimination of the early hazard of death such as hematopoietic failures increases the competing risks related to malignancy.

The clinical findings in FA patients mainly include hyperpigmentation, small reproductive organs in males, kidney problems, thumbs and arm abnormalities, skeletal anomalies of hip, spine or ribs, low birth weight, short stature, growth retardation, defects of the tissue separating the heart chambers and mental retardation or learning disability [4,5]. Although, FA can have a relatively mild phenotype and internists and medical oncologists are generally unfamiliar with this typically pediatric disorder [6]. Consequently, there are undoubtedly persons with FA in whom cancer developed without the diagnosis of FA being made.

Literatures show in FA patient, HNSCC is the most frequently diagnosed solid tumor [7,8]. The current medical treatment available for management of HNSCC is a multidisciplinary approach, including surgery, chemo- and radiotherapy options [9]. Unfortunately, The sensitivity of FA patients' cells to DNA cross-linking agents [10,11] makes the complete surgical resection, the most important therapeutic option in FA patients with HNSCC [12].

The authors report a unique case of squamous cell carcinoma in the hard palate of a young female FA patient. The clinical history and localization of the tumor make this case unique.

2. Case report

The patient was a 31 years old white and married woman. She was referred to department of Oral & Maxillofacial Surgery for evaluation of a hard palate lesion that had appeared 3 months ago. (Fig. 1) The patient was diagnosed with FA about 10 years ago after

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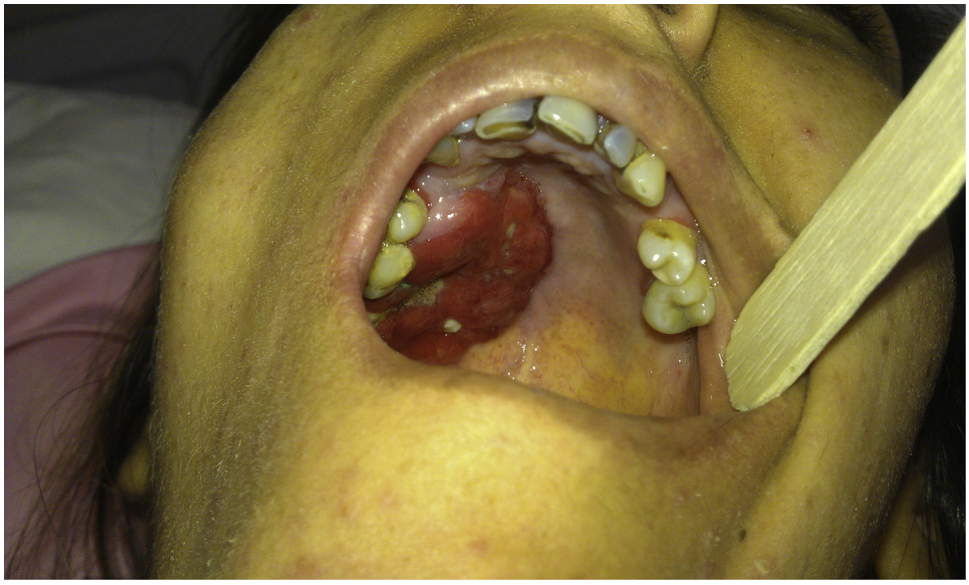

Fig. 1. Pre-operative clinical evaluation revealing a relatively well-defined, nearly circular, concave ulcer measuring 2 × 4 cm, which extended majorly in the hard palatal mucosa in the upper right molar region.

her brother had died due to complications of the same disease at the early age of 9; although she had some clinical finding of FA patients such as hyperpigmentation, short stature and abnormal hands.

The lesion had been diagnosed initialing as aphthous ulcer by the general dentist and treated with local topical medicines without any remission.

Oral examination revealed a relatively well-defined, nearly circular, concave ulcer measuring 2 × 4 cm, which extended majorly in the hard palatal mucosa in the upper right molar region. The surface was erythematous and smooth. Clinical examination showed just firm 1 × 0.5 cm lymph node in submandibular region. An incisional biopsy performed under local anesthesia revealed a well-differentiated squamous cell carcinoma. CT and MR imaging showed a hard and soft tissue mass extending from molar region mucosa to the soft palate mucosa. The nasopharynx appeared normal. No significant cervical lymphadenopathy was observed. Also, images revealed tumor primary location. (Fig. 2) With described diagnosis, tumor was classified according to TNM classification as $T_2N_0M_0$.

She had been treated with androgenic therapy and had not received a bone marrow transplant. The hematological test revealed pancytopenia. Complete examinations revealed blood Hb 11.4 g/dl, and platelets 21×10^9/l also other data revealed HCT 35.4%, MCV 9.8 fL, MCH 31.5 pg and MCHC 32.2 g/dl.

After hematologic consultation for the treatment of thrombocytopenia, the tumor was planned to be surgically removed with a right partial maxillectomy to achieve clear margins.

Due to Fanconi disease, bone marrow stem cells are unable to produce more cells as result of reduction in their number and on the other hand for their inherent incompetency. So, for surgery platelet level have to increase up to 80×10^9/l also hemoglobin levels should be maintained above 9 g/dl. So for this case, due to sub-standard level of platelets and hemoglobin pre-operative blood and platelet transfusions was performed and after surgery daily CBC, blood and platelets level were checked and required blood and platelet transfusion were performed. Fresh Frozen Plasma (FFP) was not needed, because in this case, coagulation disorders were not observed. Although hematopoietic stimulants are not effective in this disease, but fortunately after injection of subcutaneous Granulocyte colony-stimulating factor (GCSF) in amount of 300 um daily for five days before operation increase amount of white blood cells up to 3000 which prevent serious post-operative infections.

The patient received general anesthesia with nasal intubation. After injection of lidocaine + epinephrine 1:100000 (8cc) the exposure of the tumor area was done by the standard Weber-Ferguson incision. Based on imaging analysis, tumor had crossed midline, so osteotomy crossed midline by 5 mm and partial maxillectomy was performed. (Fig. 3) Hemostasis was achieved and since there was palpable lymph node in submandibular region, through a submandibular (Risdon) incision, submandibular glands and lymph nodes were completely removed. The post-operative pathological study confirmed tumoral invasion of the same lymph node though the rest was free. (Fig. 4) An inter-operative obturator was placed and fixed by opposite teeth and circumzygomatic suspension.

Post-operative complications included just a slight oozing of blood in 5 days which was locally well-controlled. The patient has been followed up for 12 months without any evidence of recurrence or metastasis and prosthodontic rehabilitation was performed for the patient.

3. Discussion

As mentioned, we presented a rare localization of squamous cell tumor in a young female FA patient; to our knowledge it is a third report of such rare HNSCC presentation [13,14]. We also have done a narrative review on published related literatures; MEDLINE, EMBASE, Scopus and PubMed databases were searched and result have been shown based on tumor location in Table 1.

Literature review shows that, the commonest localizations of squamous cell carcinoma in FA patients in descending order are: tongue, anogenital region, pharynx, larynx, oral mucosa, mandible and skin [15].

The pathogenesis of the malignancies that occur in persons affected with such a bone marrow failure syndrome remains unknown. However, progress is mainly achieved by identifying the genes responsible for this syndrome during the last decades. It has been proposed that several of the FA gene products form a complex that interacts with one or more other FA proteins, which ultimately may be involved in DNA damage response foci. These proposed genes include Diamond–Blackfan anemia (DBA) genes, were iden-

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