Oral Carcinoma Cuniculatum in a Young Child.

Hutton A*/ McKaig S**/ Bardsley P ***/ Monaghan A ****/ Parmar S ******

From the Department of Dental Specialties, Birmingham Children's Hospital. This case study describes a rare case of oral carcinoma cuniculatum in a 7 year old female. She presented with an enlarged mass of the anterior maxilla arising from the gingiva. An anterior maxillectomy with immediate prosthetic replacement and obturation of the residual defect were carried out. The management of this case was challenging given the rare nature of the disease, unclear etiology, the patient's young age and the mutilating effects of surgery. The treatment involved a large multidisciplinary team. The provision of obturators was particularly difficult due to poor patient compliance and the extent of surgery carried out in a growing child. Oral cancer in children under 15 years old is extremely rare and this is the youngest case of oral carcinoma cuniculatum reported in the literature.

***Keywords**: Carcinoma cuniculatum, children, mouth*
J Clin Pediatr Dent 35(1): 89–94, 2010

INTRODUCTION

Cancer can arise at any age, with 1 in 3 people developing a cancer at some point during their lifetime.[1] However only 26% of all new cancer cases registered in the UK in 2004 were in people under 60 and 0.5% were in children under 15 years of age.[2]

The incidence of oral cancer varies around the world. In the western world oral cancer is thought to account for 1-4% of all cancers, whereas in parts of India it accounts for 30-40% of all cancers.[3,4] In South East Asia it is thought to be the most common or second most common site for malignancy.[4] Over 80% of malignant neoplasms in the orofacial region are squamous cell carcinomas of the oral mucosa, tongue and lip. In England in 2004, malignant neoplasm of the lip, mouth and pharynx accounted for 2.4% of new cases diagnosed in males and 1.3% of total cases in females. Of the cases of malignant oral disease 0.6% of males and 0.7% of females were under 20 years old.[2] Unfortunately oral cancer in all age groups is thought to be rising worldwide. Some studies state an alarming increase in the incidence, particularly in young people. Martin-Granizo's Madrid report describes only six patients under forty with squamous cell cancer (SCC) of the head and neck area from 1979-1990, but from 1990-1994 there was a three fold increase, with eighteen patients under the age of forty being diagnosed with SCC.[4] While the Llewellyn *et al* literature search of English published journals from 1957-2000 reports evidence from epidemiological studies of an increased incidence in cancer of the tongue in the young adult USA and UK populations.[5]

Oral cancer in younger patients is thought to have different etiology and pattern of disease progression from older patients.[4] The traditional risk factors of smoking and tobacco usage are unlikely to be of relevance. Other possible etiological risk factors are thought to include: viral infections (such as Epstein Barr virus and human papilloma virus), diets low in fresh fruit and vegetables, genetic and familial factors. There is disagreement in the literature as to the significance of many potentially contributory factors being due to the short exposure time. However, genetic studies have indicated patients diagnosed with a squamous cell carcinoma at a young age may be predisposed to genetic instability.[4]

Carcinoma cuniculatum (CC) is a rare form of carcinoma most commonly affecting elderly smokers.[6] It was first described in 1954 as epithelioma cuniculatum.[7] Confusingly, Verrucous carcinomas (VC) and carcinoma cuniculatum are often conflated in the literature, because they both have a papillomatous keratinized surface. Odell and Morgan reviewed a series of patients aged thirty to eighty and felt that, despite a similar clinical appearance, it is important to distinguish between the two lesions, as CC can undergo local invasion (especially into bone), whereas VC is much less likely to invade local tissues[6] The literature describes CC occurring predominantly on the foot [8,9] but it has also

* A Hutton. Specialist Registrar in Paediatric Dentistry. BChD MFDS RCS Edin.
** S McKaig. Consultant in Paediatric Dentistry. BChD FDS RCS Edin, MPaed Dent Glasg FDS (Paed Dent) RCSEd
*** P Bardsley. Consultant in Restorative Dentistry. BDS FDS(Rest Dent) RCS EdMPhil
**** A Monaghan. Consultant in Oral and Maxillofacial Surgery. BDS FDSRCS MB ChB FRCS
*****S Parmar. Consultant in Oral and Maxillofacial Surgery. BMedSci, FDS, FRCS

Send all correspondence to: A Hutton, Dental Specialities Department, Birmingham Children's Hospital, Steel House Lane, Birmingham, B4 6NH

E mail. alison.hutton2@nhs.net

been observed in the genitals,[10] esophagus,[11] nose,[12] skin,[13] nail bed[14] and oral cavity.[7] It usually presents as an exophytic ulcerated mass exuding material from numerous sinuses, and is described as deeply invading the tissues, destroying any bone and soft tissues as it progresses. Metastasis has been reported in cases involving the skin but this is very uncommon.[6] In the oral cavity the lesion usually involves the mucoperiosteum of the attached gingiva, hard palate or endentulous alveolus. From the few published reports, the metastatic behavior of the lesion is thought to be due to transformation of the lesion into a conventional squamous cell carcinoma. It is currently unknown how many CC lesions do transform into conventional squamous cell carcinomas.

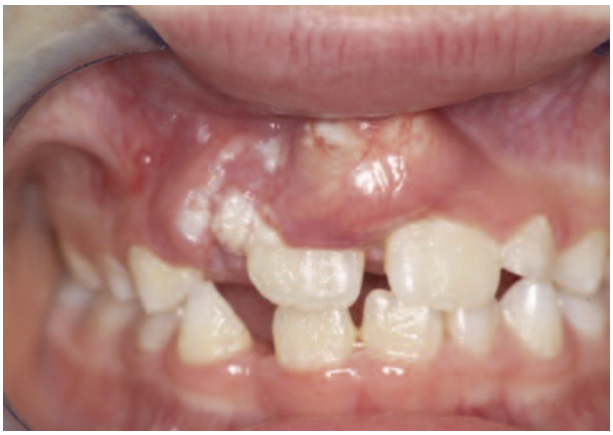

Figure 1- Clinical Presentation at Birmingham Children's Hospital.

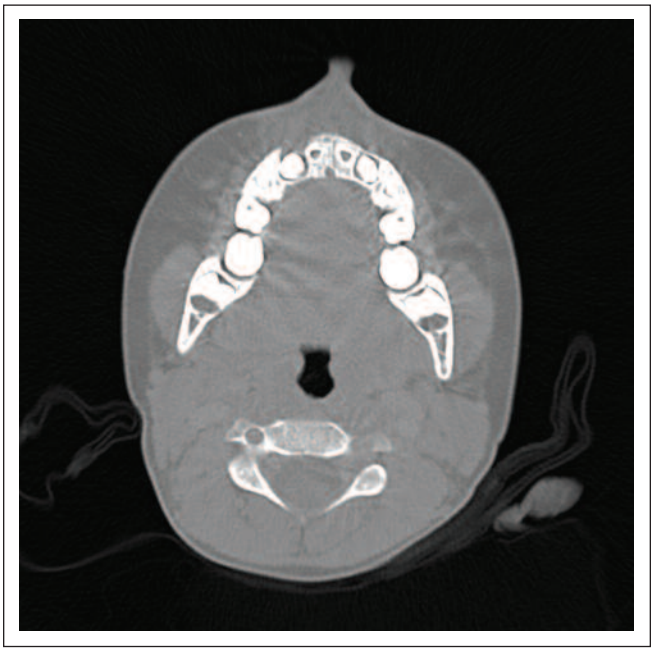

Figure 2- CT scan showing destruction of the anterior wall of the maxillary sinus.

Case Study

History

A young girl (GC) aged 7 years presented to her general dentist (GDP) with a swelling between the upper right central incisor and upper right primary lateral incisor. The GDP initially thought this was a dental abscess, attempted drainage of the lesion and prescribed antibiotics. At the two week review the lesion had not resolved and had increased in size. The GDP promptly referred the patient to their local maxillofacial unit where a biopsy was carried out under general anesthesia. The biopsy report described evidence of a well differentiated squamous cell carcinoma. GC was subsequently referred for further investigations and treatment at the Birmingham Children's Hospital (BCH) maxillofacial department.

The patient's past medical and family history were unremarkable. She was fully immunized and on no regular medication. There were no known allergies. General and systematic examinations were normal. She lived with her mother and non-identical twin sisters, all of whom were fit and well. Her parents were separated but she had regular contact with her father. She attended a regular main stream school.

Examination

On examination she had no lymphadenopathy. The upper right primary lateral incisor had been removed during the previous surgery and she had a firm, non mobile swelling buccal to the upper right and left permanent central incisor area. There was some ulceration palatal to the lesion. The upper lip appeared to be unaffected. The lesion at presentation to BCH is shown in figure 1. The lesion is covered with pink mucosa and shows a creamy appearance beneath this. Verrucous white areas are visible next to the swelling.

Blood tests and imaging including a computerized tomography (CT) scan were performed. The CT scan (figure 2) showed some destruction of the anterior wall of the maxillary sinus and lymphadenopathy around the left carotid artery and jugular vein. The largest inflammatory lymph node measured 1.3 x 0.5cm. There were smaller inflammatory lymph nodes extending down the vessels on the right hand side of the neck. No large lymph node mass was seen and there was no obvious sign of metastatic spread. Her chest X-ray was clear. Her full blood count, clotting and routine biochemistry were all normal. GC also had DNA fragility tests to investigate for possible Fanconi anemia, but these were also found to be negative.

Initial Treatment

GC was initially seen in a multidisciplinary clinic with an oncologist, maxillofacial surgeon, paediatric dentist, speech therapist and psychologist. Upper and lower alginate impressions were taken for initial records and the later construction of a healing plate. GC went on to have radical resection of the anterior maxilla. The anterior maxilla from the upper right first primary molar to the upper left primary canine (including the nasal floor) was resected with a 1cm

margin. The nasal floor was closed, and the bone was covered with bilateral buccal fat pads. A healing plate was inserted and lined with a soft liner. It was secured using two x 2mm screws (figure 3). A further operation was carried out 2 weeks later to remove the healing plate, take further impressions for a post surgical obturator and replace the plate again. The healing plate was completely removed 3 weeks later under general anesthesia and a post surgical obturator fitted with a soft lining.

Histopathology

The lesion was sent for histological reporting. The

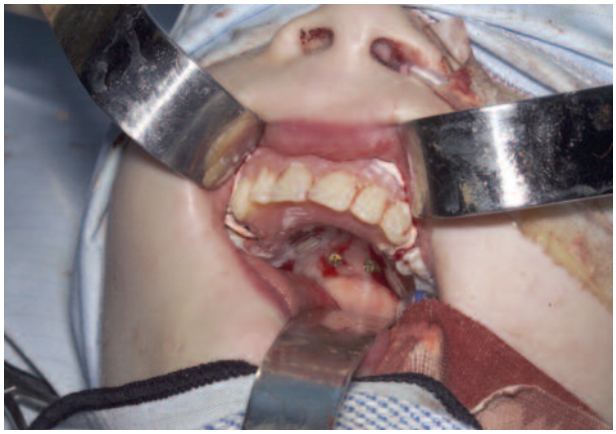

Figure 3 –Healing Plate.

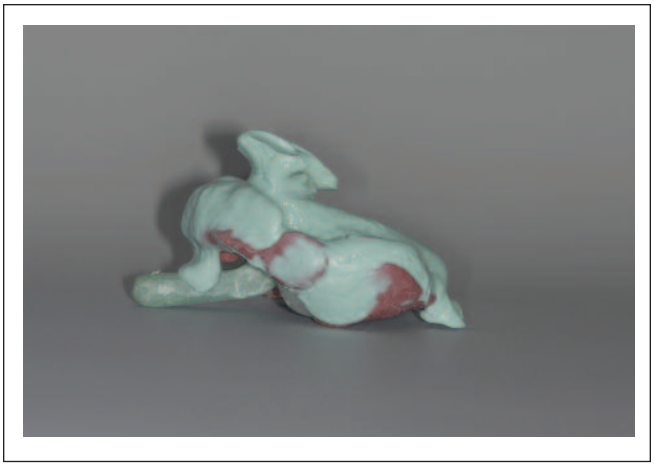

Figure 4. Impression taken for the obturator.

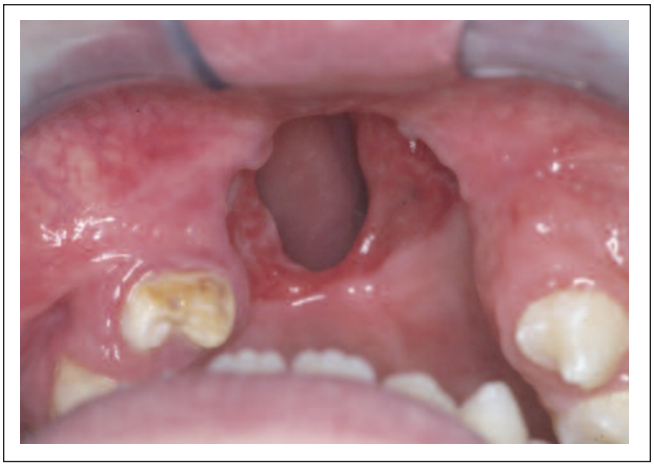

Figure 5- Intra oral appearance 22 months post operatively.

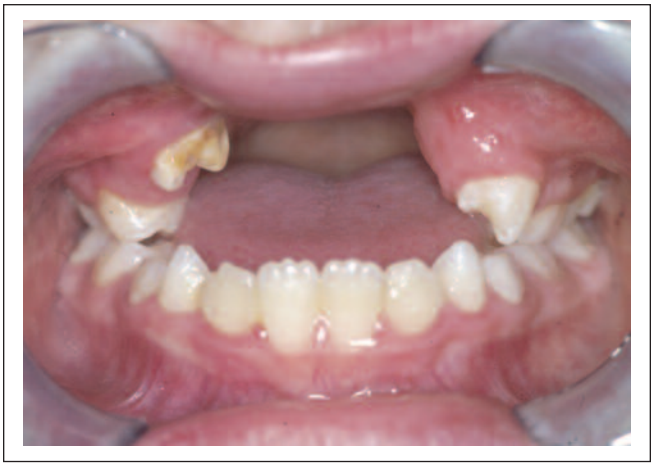

Figure 6- Anterior view at 22 months.

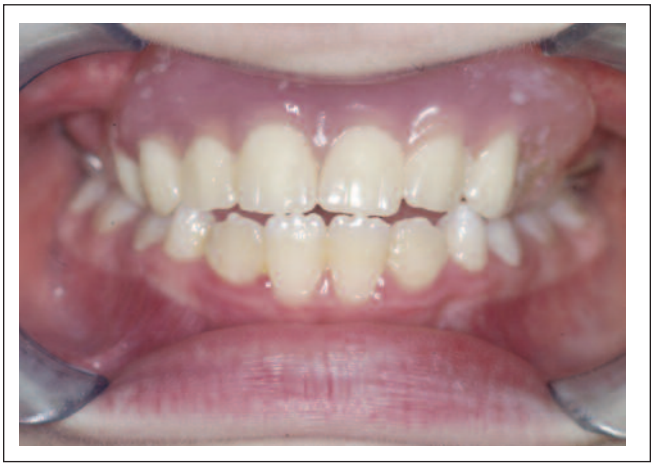

Figure 7- Obturator appearance at 22 months.

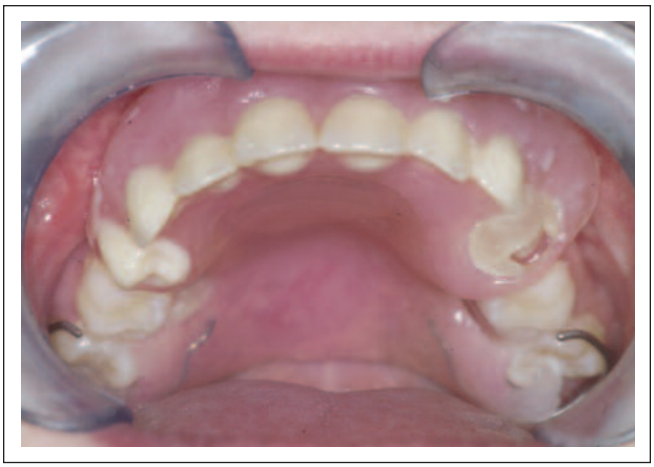

Figure 8- The obturator requiring alterations as the premolar erupts.

macroscopic report describes a segment of the anterior maxilla containing front teeth, adjacent teeth and the anterior part of the palate. An unerupted tooth was noted superiorly. The microscopic report portrays a squamous lesion present within the tissue. The lesion extended both anterior and posterior to the teeth, it consisted of broad expansile bands of squamous epithelium. The epithelium was well differentiated. At the margins of the lesion there was a more infiltrative pattern invading the underlying bone. Due to the rare nature of the tumor and age of the patient a second opinion was sought. It was agreed this was a well differentiated squamous cell carcinoma arising in the gingival mucosa and extending into cancellous bone and muscle. The carcinoma showed an extensive endophytic architecture with areas where there were islands of deeply penetrating carcinoma containing plugs of keratin. The lesion was completely excised with clear margins. The tumor was described as an example of a carcinoma cuniculatum. The clinical implication of this diagnosis is that there is a possibility of reoccurrence when the lesion extends into bone as it does in this case.

Follow up treatment

Regular follow up treatment was carried out with the multidisciplinary team. GC was coping reasonably well. Her post surgical obturator was replaced three months later with an interim obturator. GC was very reluctant to have impressions taken of the mouth and was therefore given the special tray to take home and practice with. On returning the following week an impression with alginate was successfully taken and the occlusion recorded. Her interim obturator was subsequently fitted. GC and her parents were very happy with the improved facial appearance. Regular reviews continued. Concern was raised a year later when GC presented with an ulcerated lesion on the palate. It was noted that the interim obturator had become ill fitting. Fortunately, this lesion resolved after a lab reline of the interim obturator. However, despite numerous relines, much to GC's distress, eighteen months post surgery the interim obturator required re-making. GC was then referred to a consultant restorative dentist for a more definitive prosthesis. During the initial stages the dental team had considerable difficulty gaining impressions, fitting and maintaining GC's obturators. However as GC built up her confidence and became accepting of both the prosthesis and her remaining intraoral defect, behavior management became considerably easier. Figure 4 shows the depth of impression required for a satisfactory obturator. GC had significant preventative advice throughout her treatment with oral hygiene instruction, tooth brushing instruction, instructions on cleaning her obturator, provision of a fluoride mouth rinse and constant reminders of the importance of maintaining a healthy dentition.

The prosthetic replacement of the removed tissues was complicated as GC was continually growing. There was no stable foundation because of the loss of the existing primary teeth, further eruption of the clasped teeth (first molar teeth), and the eruption of the remaining adult dentition. The initial definitive prosthesis became ill fitting within six months, mainly due to the eruption of the upper left first premolar in a slightly palatal position and the continued eruption of the first molars. At the multidisciplinary review clinic, the possibility of incorporating and orthodontic appliance to guide the eruption of the premolar with a future obturator was discussed. It was thought this would have little benefit at GC's current stage of development (nine years old) but would be considered in the future once the second premolars and second molar teeth had fully erupted. The orthodontic advice was to make a space in the acrylic base plate to allow the eruption of the premolar. Two years post surgery, GC remains well with no recurrence and manages extremely well with her obturator (figures 5-8). Both premolars have now erupted but are palatally displaced in the arch.

Long term options

GC remains under close monitoring by the maxillofacial team, especially as CC is known to reoccur. In the future, with little or no maxillary growth, there is likely to be a class three tendency. Some maxillary expansion may be possible with orthodontic appliances but anteroposterior growth is not achievable this way and is unlikely to improve. As GC grows she will require new obturators to compensate for her growth and allow for changes in the appearance of the teeth as they begin to represent an adult dentition. Once GC has stopped growing she could undergo dental rehabilitation using implants. This will require bone grafting. These are likely to be free bone grafts but free tissue transfer for soft tissue or bone may be required.

DISCUSSION

Head and neck carcinoma in childhood is rare with very few reported cases of oral carcinoma cuniculatum. There is, however, thought to be a degree of under reporting and its frequency may be underestimated as a result of failure by oral pathologists to recognize the condition.[7].

In the literature the number of reported cases of head and neck squamous cell carcinoma in children is minimal, with few studies including the age 0-10 years. Most studies consider anyone under the age of 45 to be young for the onset of oral cancer.[5,15,16] The tongue is the most frequently mentioned primary site of oral cancer. [7] Amichetti identified 21 cases of SCC of the tongue in patients under 15 years old between 1894-1989.[17] Sarkaria and Harari identified 152 cases of oral SSC in patients under 40 years old.[18] Ohlms *et al* published a study in 1994 showing 56 reported cases of laryngeal carcinoma in children since 1868.[19]

Allon *et al* found 76 cases of carcinoma cuniculatum from 1976-2000, with 14 of these involving the oral cavity. The youngest of these cases was a 9 year old male and the lesion was situated in the hard palate. The remaining cases all involved patients between the ages of 30 and 69. Of these 14 reported patients, 10 were male, 9 cases involved the attached gingiva or palatal mucosa and 11 cases involved the underlying bone [7]. Since then, there have been few reported cases of carcinoma cuniculatum within the oral cavity and

none in children. Most of the identifiable cases are in the French and German literature.[20-22]

Given the low numbers of such cases it is difficult to draw conclusions about the etiology of the lesions and the best way to manage their treatment. Some cases of oral carcinoma in patients under 15 years are related to known risk factors such as Fanconi anemia.[23-24] Other suggested risk factors in young children include immunosuppression,[25] viral infections (particularly Epstein Barr virus (EBV) and human papilloma virus (HPV)),[26-27] poor diet and nutrition[28-30] and genetic factors .[30]

Fanconi anemia (FA) is a rare autosomal recessively inherited condition involving defects in DNA repair. This results in chromosome breakage and rearrangements. Subsequently patients suffer from congenital abnormalities, developmental abnormalities and progressive bone marrow failure. They also have a predisposition to cancer, particularly acute myeloid leukemia and solid tumors.[24,32,33] Many patients with FA are diagnosed in early childhood due to one or more of its medical complications or a known family history. Occasionally, however, it is not noted until the patient is in their 30s or older.[34] It is therefore important, when oral cancer is diagnosed in a young child, that possible causative factors such as FA are ruled out due to the known high incidence of oral squamous cell carcinoma in FA patients.[35,36]

At present GC has no known specific risk factors predisposing her to oral cancer. She was tested and was negative for FA, has a well balanced diet, has not been immunosuppressed in the past or found to have any family history of cancer. She has however not been tested for HPV or EBV at the present time.

CONCLUSIONS

Oral carcinoma cuniculatum is rare within the general population and even less frequent in children. It is important that tests for Fanconi anemia are carried out in cases of oral cancer in children, due to the known links with cancer. The aetiology is likely to be a mixture of factors on which few conclusions can be drawn due to the small number of cases. The management of this child involved a multidisciplinary team with a lot of sensitivity and understanding. The psychological affect of cancer alone is significant and was accentuated by the mutilating and obvious position of the tumour. Management of the patient and her family was particularly challenging for all concerned.

Long term maxillofacial monitoring is required due to the possibility of recurrence and subsequent rehabilitation. Dental follow up is required to maintain her with appropriate prostheses into adulthood, monitor the eruption of the remaining dentition and maintain the developing dentition in a healthy state.

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ACKNOWLEDGEMENTS.

The authors would like to thank Matt Burnell dental technician for his outstanding laboratory work and help during this case.