Case Report

102/10/29

Intern C組
林吟品, 廖之綺, 黃筠婷, 廖秀淳
指導醫師： 陳玉昆醫師
暨 口腔病理科全體醫師

General data

- Name 蔡O O
- Sex : Female
- Age : 26 y/o
- Native : 高雄市
- Marital status : 已婚
- Attending V.S. : O O O 醫師
- First visit :08/13/2013

Chief Complaint

- Swelling mass over R't maxilla palatal side

2013/08/13

Present Illness

- This 26 y/o female suffered from swelling mass over tooth 14-17 palatal side on 08/13/2013 at 全家 dental clinic routine follow up, and Dr. O O O suggested her to come to our OPD for further evaluation and examination.
- 08/13/2013 This day afternoon, she came to our OPD to examination, and Dr. O O O arranged CT scan on 08/29/2013.
- On 09/10/2013, she came back our OPD to check CT report, and report noted the lesion was retention cyst
- Dr. O O O arranged OP schedule on 09/27/2013 under GA to remove lesion

- 2003/11/24 incisional biopsy under LA in O O Hospital

  -0.7x0.4X0.2 retention cyst

- 2004/02/05 Excisional biopsy under LA in O O Hospital

  -0.8x0.6x0.3 retention cyst

Past Medical History

- Underlying disease: (+)

  1.Liver disease: hepatitis B

- Hospitalization experience: (+)

  1. Surgery for maxillar r't cyst

  2. Maternity

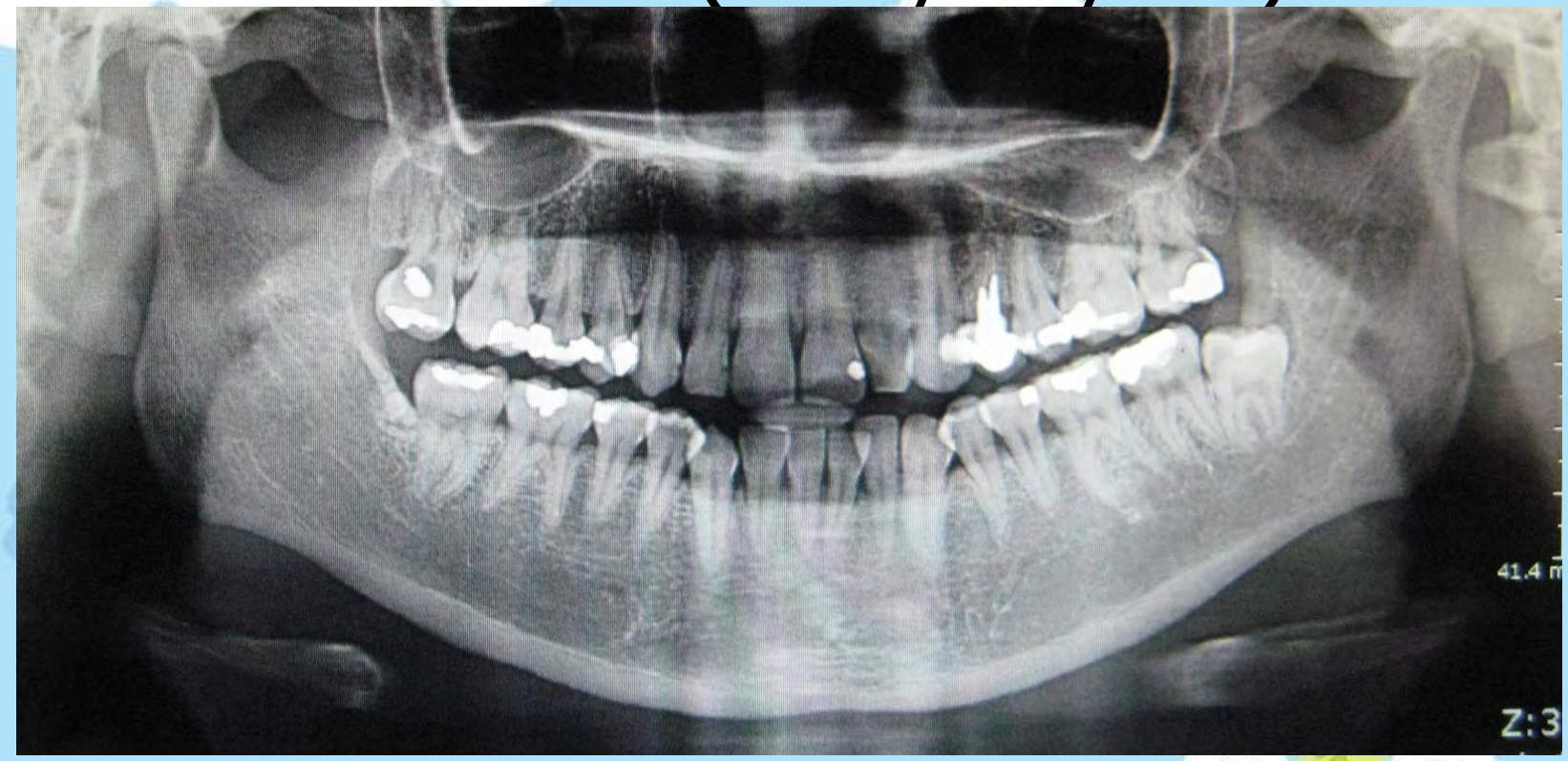
- Surgery under GA: (-)
- Denied any drug or food allergy

Intraoral Examination

- Dimension: 2 x 4 cm
- Swelling: Tooth 14-17, palatal side
- Surface: Smooth, non-ulcerated
- Consistency: Rubbery
- Fluctant (+)
- Pain (-)
- Tenderness (-)
- Induration (-)
- Right maxilla , LAP(-)

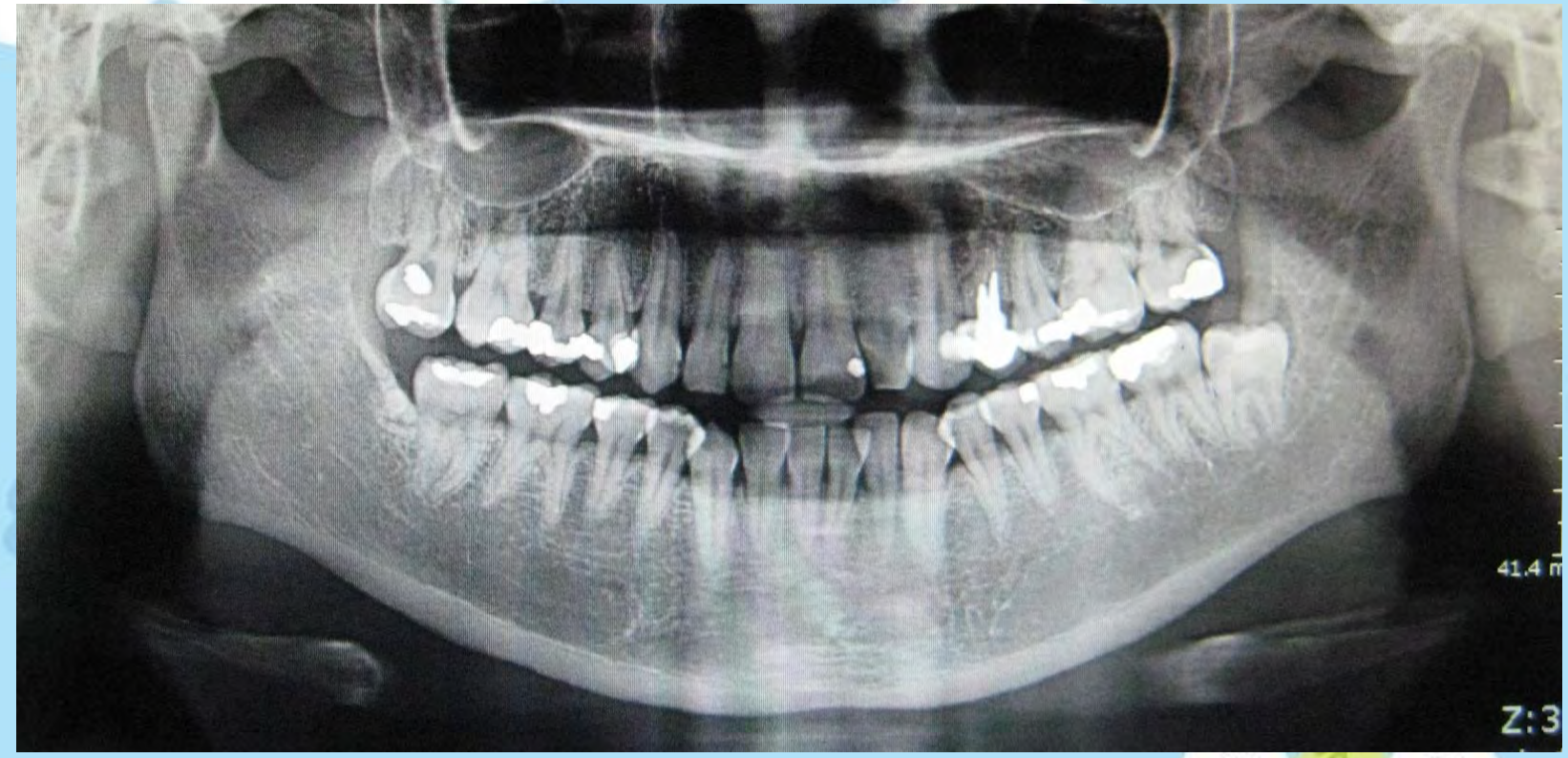
2013/08/13

Image finding – Panorex(102/08/13)



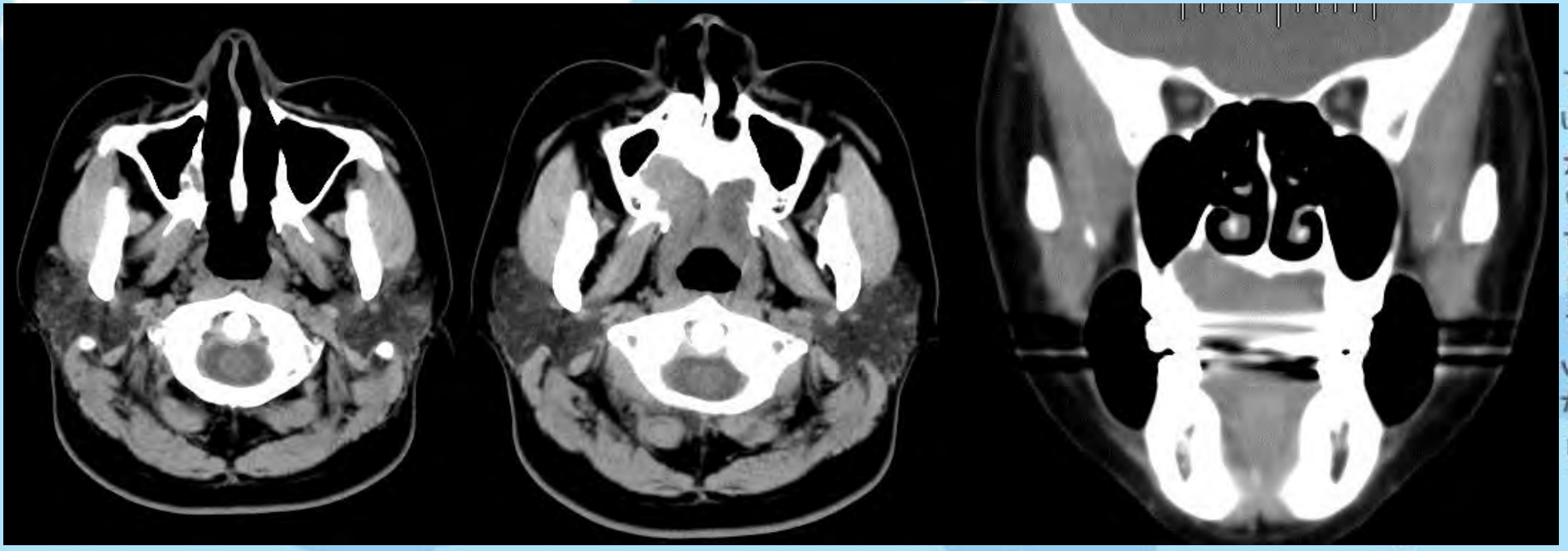
No particular finding

Dental Finding(102/08/13)



Missing:Tooth 18, 28, 48
OD filling:Tooth 14,15,16,17,21,25, 26, 27,
35, 36, 37, 45, 46, 47
post and crown: Tooth 24

CT scan (102/08/29)



<Axial view> <Coronal view>

There is a soft tissue density lesion invade into sinus floor and nasal area,result in bony destruction, measured up approximately 2cm in diameter.

Past Dental History

- Experiences of general routine dental treatment
- Attitude:cooperative

Personal History

- Risk factors related to malignancy
  - Alcohol drinking (-)
  - Betel quid chewing (-)
  - Cigarette smoking (-)
- Special oral habits: Denied

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Working Diagnosis

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Peripheral or Intrabony

	Peripheral	Intrabony	This case
Mucosal lesion	+	-	+
Induration	+	-	-
Bony expansion	-	+/-	-
Destruction of sinus floor	+/-	+/-	+

→ Peripheral

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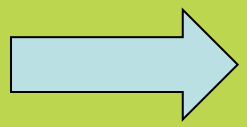
Inflammation

	Inflammation	This case
Redness	+	+
Swelling	+	+
Local heat	+	–
Pain	+	–



Cyst or Neoplasm

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Cyst

	Cyst	This case
Aspiration	+	undo
Fluctuation	+/-	+
Well-defined border	+	+
Bone expansion	+/-	-

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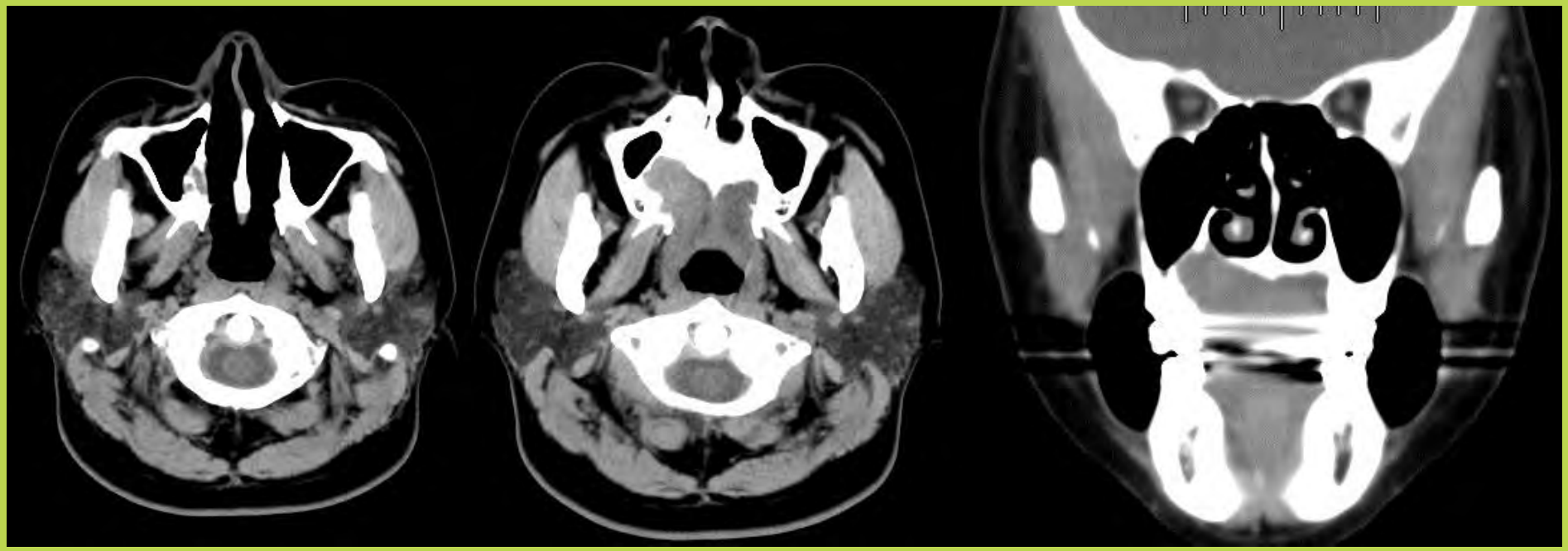
Neoplasm

	Benign	Malignant	This case
Border	Well-defined	Ill- defined	Well-defined
Sclerotic margin	+	-	-
Destruction of bone	+/-	+	++
Pain	-	+	-
Induration	-	+	-
Lymphadenopathy	-	+/-	-
Progress	Slow	Fast	Slow
Metastasis	-	+/-	No clear evidence

CT scan (102/08/29)



<Axial view> <Coronal view>

There is a soft tissue density lesion invade into sinus floor and nasal area,result in bony destruction, measured up approximately 2cm in diameter.

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Differential Diagnoses

- Mucoepidermoid carcinoma, low grade
- Polymorphous low-grade adenocarcinoma
- Pleomorphic adenoma
- Acinic cell adenocarcinoma
- Adenoid cystic carcinoma

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Mucoepidermoid carcinoma

	Our case	Mucoepidermoid carcinoma
Gender	Female	Slight female or equal
Age	26	20~70
Site	Palatal side	Parotid gland, minor gland Lower lip, floor of mouth, tongue, palate and retromolar pad areas
Pain	-	Early stage: -
Swelling	+	+
Drainage	-	-
induration	-	+
Consistency	rubbery	Firm or hard
Shape	Smooth, dome-shaped	Dome-shpaed
duration	8 years (since 2003 November founded)	slow

Polymorphous low-grade adenocarcinoma

	Our case	Polymorphous low-grade adenocarcinoma
Gender	Female	2/3 Female
Age	26	60~80
Site	Palatal side	Exclusively minor salivary gland (65% palate)
Pain	-	-, occasionally bleeding or discomfort
Swelling	+	+
Drainage	-	-
induration	-	+
duration	8 years (since 2003 November founded)	slow

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Pleomorphic adenoma

	Our case	Pleomorphic adenoma
Gender	Female	Slight female
Age	26	All ages (common in the third to sixth decades)
Site	Palatal side	Major salivary glands (most in parotid salivary gland, less in sublingual gland), minor salivary(33%~43%)
Pain	-	-
Swelling	+	+
Drainage	-	-
Consistency	rubbery	Firm
Induration	-	+
Shape	Smooth, dome-shaped	Single irregularly shaped, bosselated surface
Duration	8 years (since 2003 November founded)	Slow

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Acinic cell adenocarcinoma

	Our case	Acinic cell adenocarcinoma
Gender	Female	60% woman
Age	26	40 (20~70)
Site	Palatal side	Parotid gland(85%), minor gland(9%)
Pain	-	-, sometimes + or tenderness
Swelling	+	+
Drainage	-	-
induration	-	+
Shape	Smooth, dome-shaped	Smooth surface
Duration	8 years (since 2003 November founded)	Slow

Adenoid cystic carcinoma

	Our case	Adenoid cystic carcinoma
Gender	Female	Equal or slight female
Age	26	Middle age adult
Site	Palatal side	Major and minor salivary gland (ex. palate)
Pain	-	+, sometimes facial nerve paralysis
Swelling	+	+
Drainage	-	-
induration	-	+
Shape	Smooth, dome-shaped	Smooth surface or ulcerated
Duration	8 years (since 2003 November founded)	slow

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Treatment Course

Treatment Course

- Excisional biopsy, under GA 102/09/27
- Surgical plan:

  cyst enucleation+tooth16 extraction
- Follow up: Wound healing and bone density evaluation

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- 102/08/13-
  1. Taking pano
  2. Arrange CT scan on 102/08/29
  3. Arrange CT scan report on 102/09/10
- 102/08/29-
  -CT scan by OOO醫師
- 102/09/10
  1. CT report
  2. EKG diagnosis: normal
  3. Arrange OP under GA on 102/09/27
     : Cyst enucleation+tooth16 extraction

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- 102/09/25
  Admission
- 102/09/27
  OP Day
- 102/09/30
  Discharge
- 102/10/07
  Suture remove

- 102/09/27 OP day

  bone tumor excision

  (and simple odontectomy of tooth 38)

- 102/10/14

  F/U+開立診斷證明書
- 102/10/15

  Pathology report:

  Mucoepidermoid carcinoma, low grade

Pathologic diagnosis

- 102/10/02

  The immunohistochemical stains demonstrate:

  S-100 protein: negative.

- 102/10/03

  Microscopic examination:

  CK(+), p63(+), HMB45(-), SMA(-).

- 102/10/07

  Microscopic examination:

  The histochemical studies demonstrate:

  Mucicarmine(+), PAS(+), PASD: focally positive.

- 102/10/9'13

  Pathologic diagnosis:

  Oral cavity, gingiva, tooth 14-17 area , excision, mucoepidermoid carcinoma, low grade (pT1cNocMo,stage I)

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Discussion

Mucoepidermoid carcinoma

What's mucoepidermoid carcinoma ?

- A tumor usually occur in salivary glands
- The most common malignant salivary gland neoplasm
- It can mimic most other tumors of the glands

→often considered in the differential diagnosis

Epidemiology

- Seen throughout all adult age groups
- Most common in 20-70 years of age
- Most common malignant salivary gland tumor in children
- Overall, MEC account for :
  2.8-15.5% of all salivary gland tumors
  - 10%(US), 1~2%(UK) of major salivary gland tumors
  - 15~23%(US), 9%(UK) of minor salivary gland tumors
- In the parotid gland they are the most common malignant primary neoplasm
- A slight female predilection has been described
- Radiation therapy to head and neck has been implicated as a risk factor

Clinical presentation

- Most frequently arise in the parotid gland
- Painless swelling
- With or without facial nerve involvement
- These tumours can however be found anywhere there are salivary glands
- Overall distribution across various glands is as follows :
- Major salivary glands : ~ 50%
  - parotid gland : ~ 40%
  - submandibular gland : ~ 7%
  - sublingual gland : ~ 3%

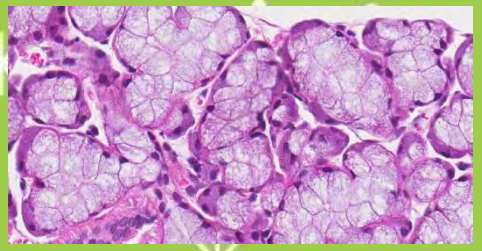
Clinical presentation

- Minor salivary glands : ~ 50%
  - Palate : most common
  - Retromolar area
  - Floor of the mouth
  - Buccal mucosa
  - Lip
  - Tongue
  - Other: anywhere in the proximal aerodigestive tract, the lacrimal glands and even in the bronchi
- Presentation will depend on the anatomic location

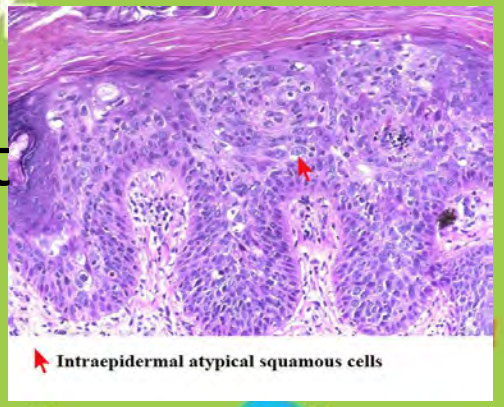
Pathology

- The tumours are composed of a mixture of :

1. Mucus secreting cells (*muco-*)
2. Squamous cells (*-epidermoid*)



3. Lymphoid infiltrate often also present



- Histology will often show clear mucin containing cells which stain reddish pink with the musicarmine stain

Pathology

- Mucoepidermoid tumours are graded histologically into :

1. Low grade :
   a. Well differentiated cells with little cellular atypia
   b. High proportion of mucous cells
   c. Prominent cyst formation
2. Intermediate grade : intermediate features
3. High grade :
   a. Poorly differentiated with cellular pleomorphism
   b. High proportion of squamous cells
   c. Consists of solid island

Grading systems

AUCLAIR ET AL (1992)	Point value
Intra cystic component<20%	2
Neural invasion present	2
Necrosis present	3
Four or more mitoses per 10 high-power fields	3
Anaplasia present	4
Grade	Total point score
Low	0-4
Intermediate	5-6
High	7-14

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Grading systems

Brandwein ET AL(2001)	Point value
Intra cystic component<25%	2
Tumor front invades in small nests andislands	2
Pronouced nuclear atypia	2
Lymphatic or vascular invasion	3
Bony invasion	3
Greater than four mitoses per 10 high-power fields	3
Perineural spread	3
Necrosis	3
Grade	Total point score
Low	0
Intermediate	2-3
High	4 or more

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Radiographic features

- Radiographic appearances **largely depend on grade**, making preoperative imaging important in planning and counselling.
- **CT**

➢ Low grade tumors

a. Well circumscribed masses
b. Usually with cystic components.
c. Solid components enhance & calcification is sometimes seen

have appearances similar benign mixed tumor

➢ High grade tumors

a. Have poorly defined margins
b. Infiltrate locally
c. Appear solid

Radiographic features

- **MRI**

➢ Again, imaging is dependent on grade

➢ **Low grade** tumors have similar appearances to benign mixed tumor :

a. **T1** - low to intermediate signal ; low signal cystic spaces

b. **T2** - intermediate to high signal ; cystic areas will be high signal

c. **T1 C+ (Gd)** - heterogeneous enhancement of solid components

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Radiographic features

- **MRI**

物質	訊號	
	MRI T1WI	MRI T2WI
Water (or CSF)	Low（暗）	High（亮）
Edema	Mid-low（灰暗）	High（亮）
Acute blood clot /Hemorrhage	Mid（灰）	Mid-low（灰暗）
Sub-acute or late blood clot / Hemorrhage	High（亮）	High（亮）
Bone cortex / Calcification	Low（暗）	Low（暗）
Bone marrow	High（亮）	High（亮）
Cartilage	Mid（灰）	Mid-low（灰暗）
Fat	High（亮）	High-Mid（灰亮）

mas &
new year!

Radiographic features

- **High grade** tumours on the other hand have lower signal on T2 and poorly defined margins and infrequent cystic areas.

a. **T1** - low to intermediate signal

b. **T2** - intermediate to low signal

- It is essential to image the cranial nerves with fat saturated post contrast T1 sequences to assess for perineural spread, and as such the base of skull should be imaged up to and including the cavernous sinus and inner ear

Immunohistochemical Analysis

- Enhance accuracy
- Investigate subjects
  - Cell nature and differentiation status
  - Cell proliferation
  - Tumor protein expression

Merry Xmas &
AHappy new year!

Immunohistochemical Analysis of Salivary Gland Tumors: Application for Surgical Pathology Practice

Toshitaka Nagao, Eiichi Sato, Rie Inoue, Hisashi Oshiro, Reisuke H. Takahashi, Takeshi Nagai, Maki Yoshida, Fumie Suzuki, Hiyo Obikane, Mitsumasa Yamashina and Jun Matsubayashi

Acta Histochem. Cytochem. 45 (5): 269–282, 2012

Table 1. *Summary of the useful immunohistochemical markers of salivary gland tumors in general surgical pathology practice*

Markers [antibodies]	Positivity in normal salivary gland parenchymal cells	Uses and significance for salivary gland tumors
Pan-cytokeratin (CK) [AE1/AE3]	Both luminal and abluminal cells	Epithelial marker; differential diagnosis between myoepithelioma/myoepithelial carcinoma or "undifferentiated carcinoma" and non-epithelial tumors
Epithelial membrane antigen (EMA)	Luminal cells	Ductal (luminal) cell marker; apical staining pattern; bubbly positive in sebaceous cells
Carcinoembryonic antigen (CEA)	Luminal cells	Ductal (luminal) cell marker
α-Smooth muscle actin (SMA)	Myoepithelial cells	Myoepithelial marker (high specificity, very useful)
Calponin	Myoepithelial cells	Myoepithelial marker (high specificity, very useful)
Muscle-specific actin (MSA) [HHF35]	Myoepithelial cells	Myoepithelial marker (high specificity)
p63	Myoepithelial and basal cells	Myoepithelial marker (note: also positive for basal and squamous epithelial cells)
CK14	Myoepithelial and basal cells	Myoepithelial marker (note: also positive for basal and squamous epithelial cells)
Glial fibrillary acidic protein (GFAP)	Myoepithelial cells (variable)	Myoepithelial marker (low sensitivity); highly positive in pleomorphic adenoma and myoepithelioma
S-100 protein	Variable	Myoepithelial marker (good for screening, low specificity)
Vimentin	Myoepithelial cells	Myoepithelial marker (good for screening, low specificity)
Ki-67 [MIB-1]	Few cells	Cell proliferation marker; differential diagnosis between benign and malignant tumors; prognostic factor
p53	Negative	Differential diagnosis between benign and malignant tumors; prognostic factor
HER2/*neu*	Negative to weakly positive in ductal cells	Highly overexpressed in salivary duct carcinoma; diagnosis of non-invasive carcinoma ex pleomorphic adenoma; expected use for molecular targeted therapy
α-Amylase	Acinar cells	Positive in acinic cell carcinoma (low sensitivity)
Androgen receptor (AR)	Negative	Often positive in salivary duct carcinoma; diagnosis of non-invasive carcinoma ex pleomorphic adenoma; expected use for molecular targeted therapy
Gross cystic disease fluid protein-15	Luminal cells	Often positive in salivary duct carcinoma (low specificity)
Mitochondria	Striated duct cells	Strongly positive in oncocytic cells
Renal cell carcinoma/CD10	Negative	Diagnosis for metastatic renal cell carcinoma
Melan A	Negative	Diagnosis for metastatic malignant melanoma
Lymphoid cell markers	Negative	Diagnosis for malignant lymphoma
EBER *in situ* hybridization	Negative	Positive in lymphoepithelial carcinoma

Markers of mucoepidermoid carcinoma

- Squamous epithelial cell
  - p63
  - CK14

Cheuk, W. and Chan, J. K. (2007)
Advances in salivary gland pathology.

- Prognostic factor
  - Ki-67

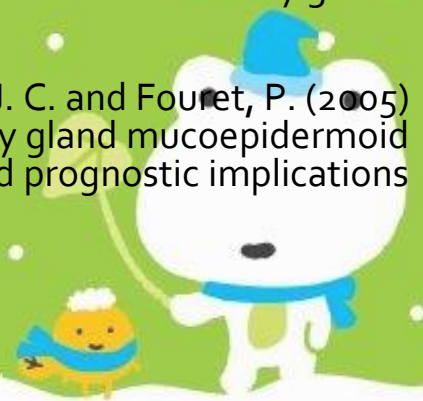
Skalova, A. and Leivo, I. (1996)
Cell proliferation in salivary gland tumors.

  - p27

Okabe, M., Inagaki, H. et al. (2001)
Prognostic significance of p27 and Ki-67 expression in mucoepidermoid carcinoma of the intraoral minor salivary gland.

  - MUC1

Handra-Luca, A., Lamas, G., Bertrand, J. C. and Fouret, P. (2005)
MUC1, MUC2, MUC4, and MUC5AC expression in salivary gland mucoepidermoid carcinoma: diagnostic and prognostic implications



Treatment

- Dependent on grade and location

➢ low grade (well circumscribed)

a. wide local excision

b. preservation of the facial nerve

c. without the need for neck dissection or adjuvant radiotherapy

➢ high grade (poorly circumscribed)

a. complete parotidectomy

b. often with sacrifice of the facial nerve

c. neck dissection (as nodal metastases are common)

d. adjuvant radiotherapy

Prognosis

- Also very dependent on grade
- Low grade tumours having a 90 - 98% survival and a low local recurrence rate
- High grade tumours having 30 - 54% survival and a very high local recurrence rate
- Has a predilection for perineural spread

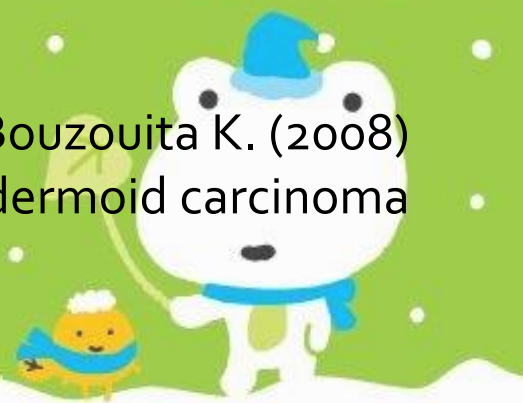
→careful and long term follow-up is required

Retention Cyst? Mucoepidermoid Carcinoma?

- What lead to a retention cyst?
  ➔ Partial blockage of a duct of the seromucous gland

- Mucoepidermoid Carcinoma may play a role in the obstruction of a salivary gland duct and caused a retention cyst

Kermani W, Belcadhi M, Mani R, Abdelkéfi M, Sriha B, Bouzouita K. (2008) Parotid retention cyst revealing a mucoepidermoid carcinoma



醫學倫理討論

醫學倫理

- 醫學倫理：一種道德思考、判斷和決策，以倫理學的觀點出發，以期能做出對病人最有利益、最能符合道德倫理規範的醫療決策

Tom Beauchamp &James Childress 六大原則- 1979

1.行善原則(Beneficence)：即醫師要盡其所能延長病人之生命且減輕病人之痛苦。

2. 誠信原則(Veractity)：即醫師對其病人有「以誠信相對待」的義務。

3. 自主原則(Autonomy)：即病患對其己身之診療決定的自主權必須得到醫師的尊重。

4. 不傷害原則(Nonmaleficence)：即醫師要盡其所能避免病人承受不必要的身心傷害。

5. 保密原則(Confidentiality)，即醫師對病人的病情負有保密的責任。

6. 公義原則(Justice)，亦即醫師在面對有限的醫療資源時，應以社會公平、正義的考量來協助合理分配此醫療資源給真正最需要它的人。

行善原則(Beneficence)

- 行善原則包括不傷害原則的反面義務(不應該做的事)和確有助益的正面義務(應該做的事)，包括維護和促進病人的健康、利益和福祉，為基本倫理原則，也是醫護人員的基本義務
- 臨床意義

(1) 勿施傷害：不得故意對他人施予傷害或惡行

(2) 預防傷害：應該預防傷害或惡行

(3) 移除傷害：應該移除傷害或惡行

(4) 維持善行：應該致力於行事或維持善行

誠信原則(Veractity)

- 是否有清楚的向病人說明清楚疾病病程、治療計畫、預後、風險？
- 對於病人疾病嚴重程度是否有誠實的通知，盡到告知的義務？

自主原則(Autonomy)

- 一位具理性思考能力的病人，在完全瞭解醫療處置方針的利弊得失下，有權決定自己的行為，包括決定及選擇醫療專業人員和治療方式
- 臨床意義

(1) 病人之自主行為不應遭受他人之操控或干預

(2)指醫療人員應提供充分且適當之資訊，以促成病人針對診療方式主動作一抉擇

不傷害原則(Non-maleficence)

- 原則：

  不殺害病人、不能侵害病人權益和福祉以及平衡利害得失，使痛苦減到最低

- 臨床意義

(1)醫療上是必須的，或是屬於醫療適應症範圍，因所施行的各種檢查或治療而帶來的傷害應符合不傷害原則

(2)權衡利害原則→ 兩害相權取其輕

(3)保護病人的生命安全

保密原則(Confidentiality)

- 告知的對象

1. 本人為原則
2. 病人未明示反對時, 亦得告知其配偶與親屬
3. 病人為未成年人時, 亦須告知其法定代理人
4. 若病人意識不清或無決定能力, 應須告知其法定代理人.配偶.親屬或關係人
5. 病人得以書面敘明僅向特定之人告知或對特定對象不予告知

公義原則(Justice)

- 原則：

強調資源合理分配、賞罰分明以及合乎正義之事。醫療上公平原則指基於正義與公道，以公平合理的態度來對待病人、病人家屬和受影響的社會大眾

- 臨床意義

(1) 公平地分配不足的資源

(2) 尊重病人的基本權利

(3) 尊重道德允許的法律及法律之前人人平等

(4) 先來先服務與急重症優先

臨床案例討論

原則	臨床討論
行善原則(Beneficence)	是否施行的治療是出自善意，是對病患的生活品質有所幫助?
誠信原則(Veractity)	是否有讓病患簽署同意書並詳實說明術後可能併發症
自主原則(Autonomy)	有讓病患簽署同意書並得到病人的支持
不傷害原則 (Non-maleficence)	有沒有讓病患承受非正常手術所造成的傷害 還有我們所做的檢查是否為必要的
保密原則(Confidentiality)	對於病患病情的保密，已及他的資料是否會被使用來研究用途是否有告知
公義原則(Justice)	是否讓病患有可以接受到完整的治療的權益，以及術前術後照護有無不足之處

誠信原則與自主原則

不傷害原則

Tx. of OO醫院

- 2003/11/24 incisional biopsy under LA in OO Hospital

  -0.7x0.4X0.2 retention cyst
- 2004/02/05 Excisional biopsy under LA in OO Hospital

  -0.8x0.6x0.3 retention cyst
- 2004/02/12 dexatin application
- 2004/03/27 F/U

  -No evidence of recurrence


The end
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