Case Presentation

18-02-2005

Dr E F Post

On Presentation

- 45 yo male
- C/O * diplopia
  * headache
  * TMJ pain (L)
- PMHx/ Meds (-)
- Athlete
- Social (-)
- PENT *M+G left 2004
  - (L) OME

Examination

- JACCOL
  - * 2x3 cm (L) II
- Ear
  - * UMG (L)
- Nose / Throat
  - * tender pterygoid (L)
  - * mild trismus
- CNS
  - * ↓ CN V², VI, VII±
  - * ↓ red (L) eye

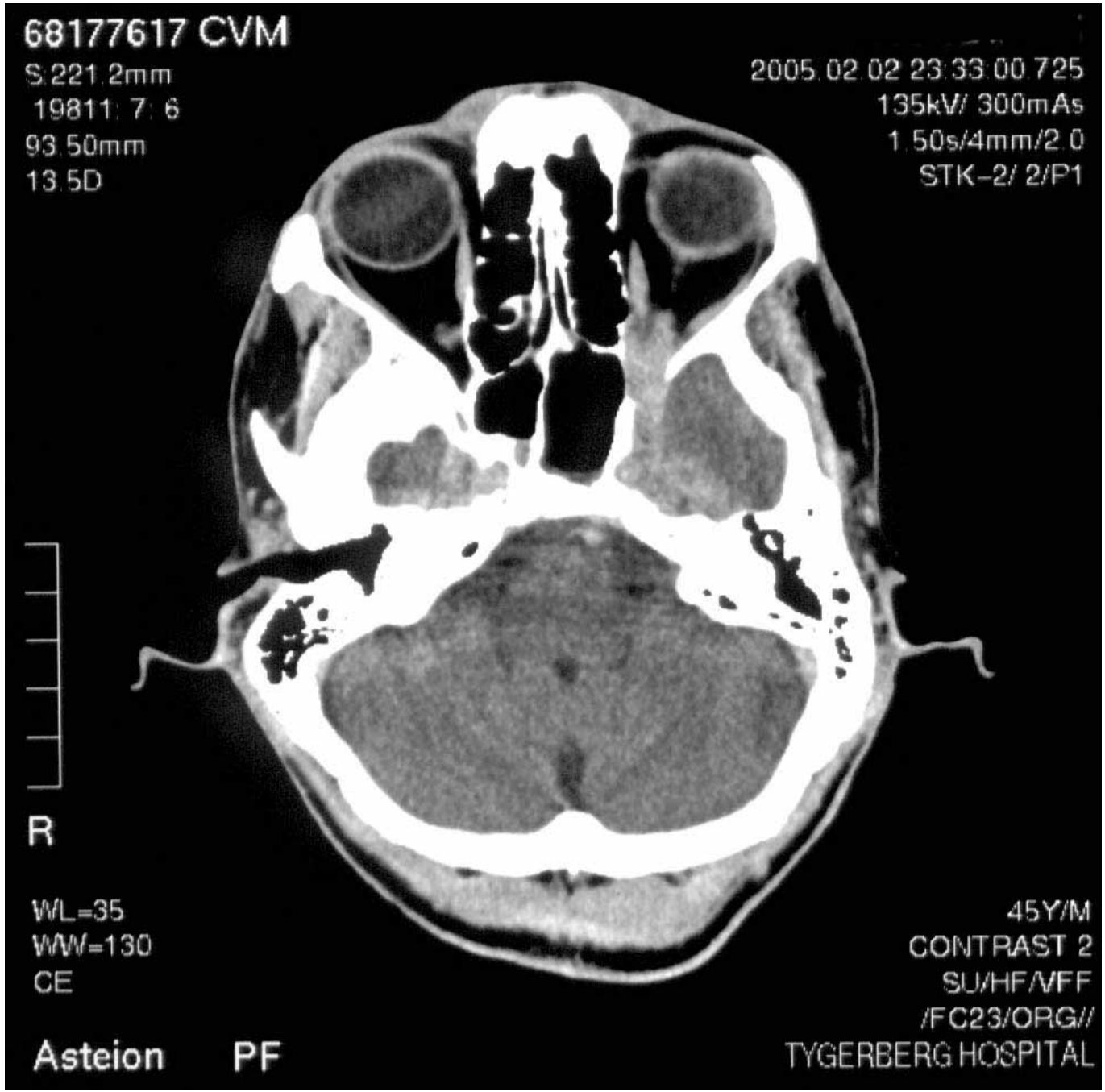
Further examination / SI

- Scope — Nasopharynx irregular, friable, bleed (L) > Nose NAD
- FNA — turbid fluid
- Bloods — NAD
- CXR
- Biopsy
- CT scan

Results

- Biopsy — Nasopharyngeal Ca
  - » Infiltrating carcinoma
  - » No keratinisation
  - » Dense surrounding lymphocytic infiltrate
- FNA — necrotic tissue, no malignancy
- CXR — Metastases
- CT — * posterior orbit / cavernous sinus / skull base/ infratemporal fossa

CXR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93.50mm
13.5D
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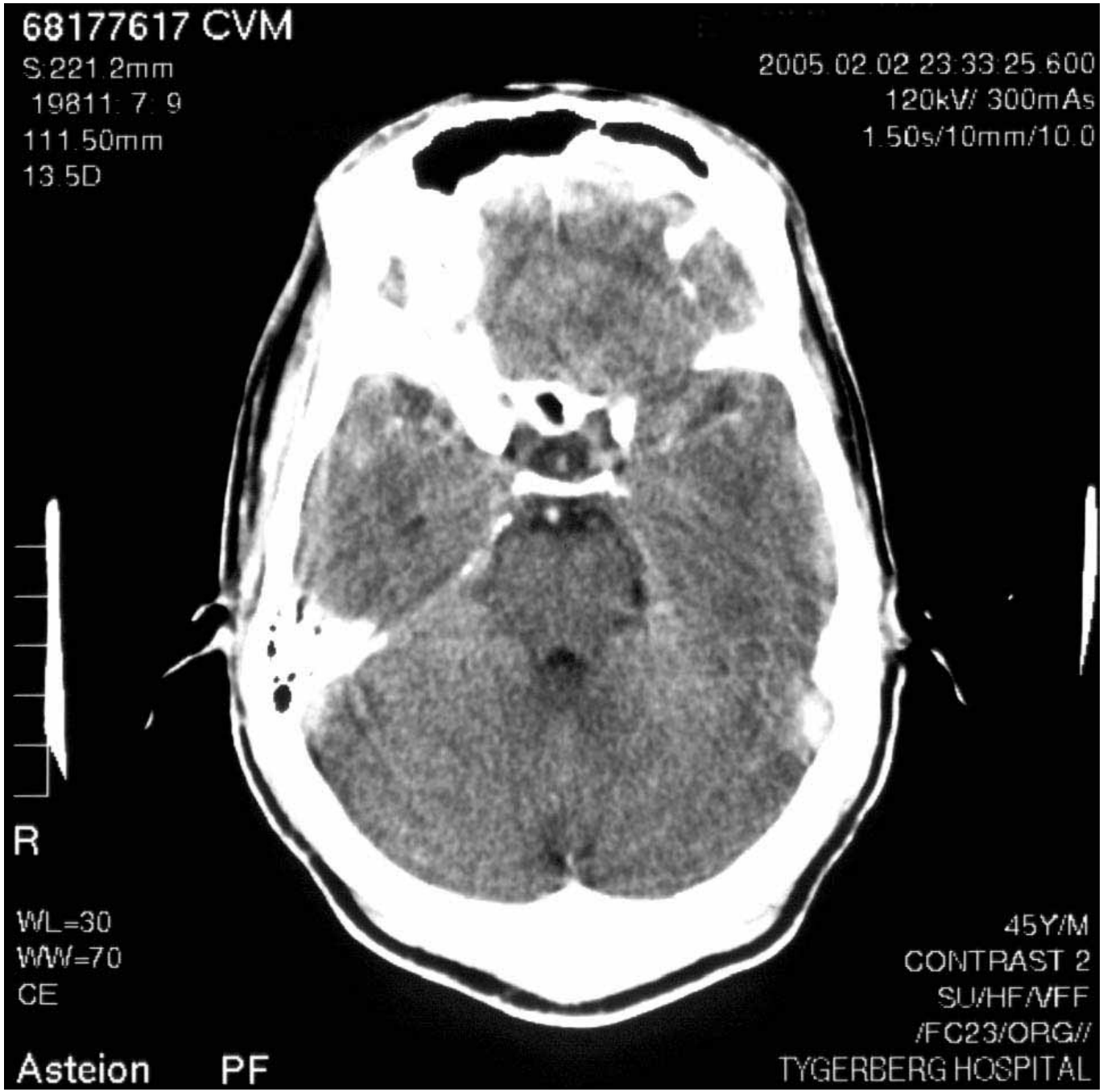
1.50s/4mm/2.0
STK-2/ 2/P1
R
W/L=35
W/W=130
CE
45Y/M
CONTRAST 2
SU/HF/VFF
/FC23/ORG//
Asteion PF
TYGERBERG HOSPITAL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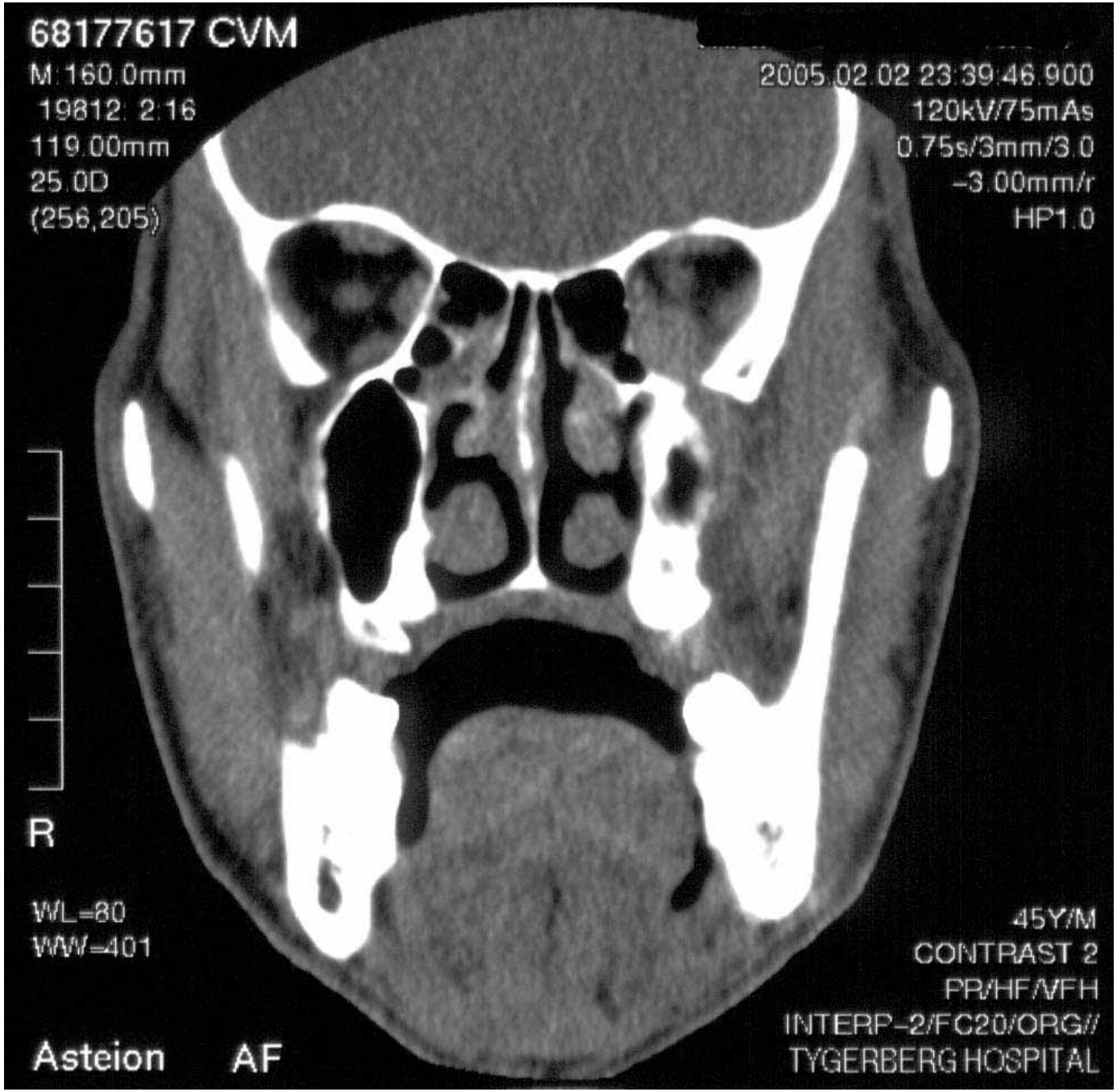
Asteion
PF
TYGERBERG HOSPITAL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HP1.0
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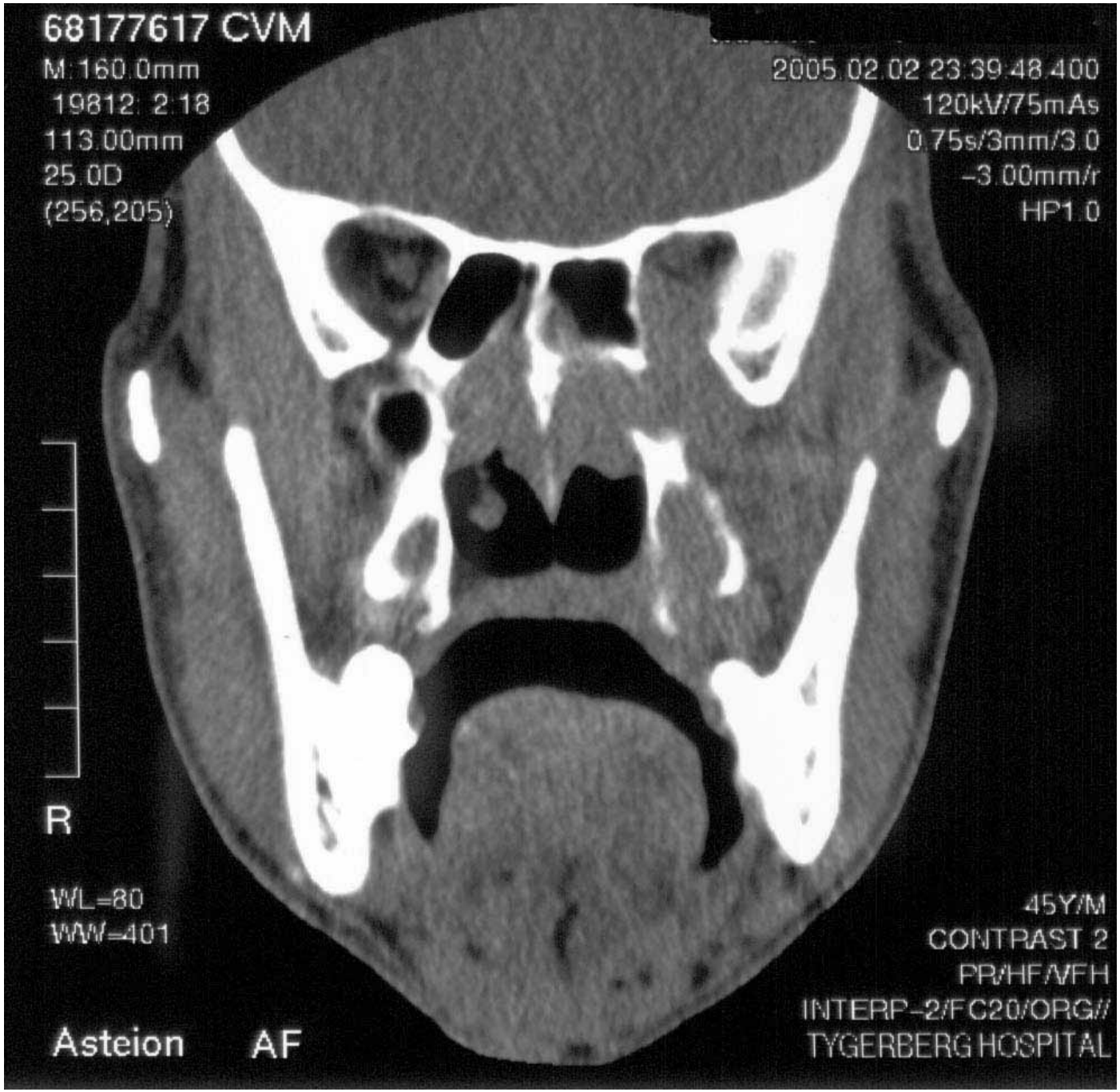
TYGERBERG HOSPITAL
Asteion
AF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TYGERBERG HOSPITAL
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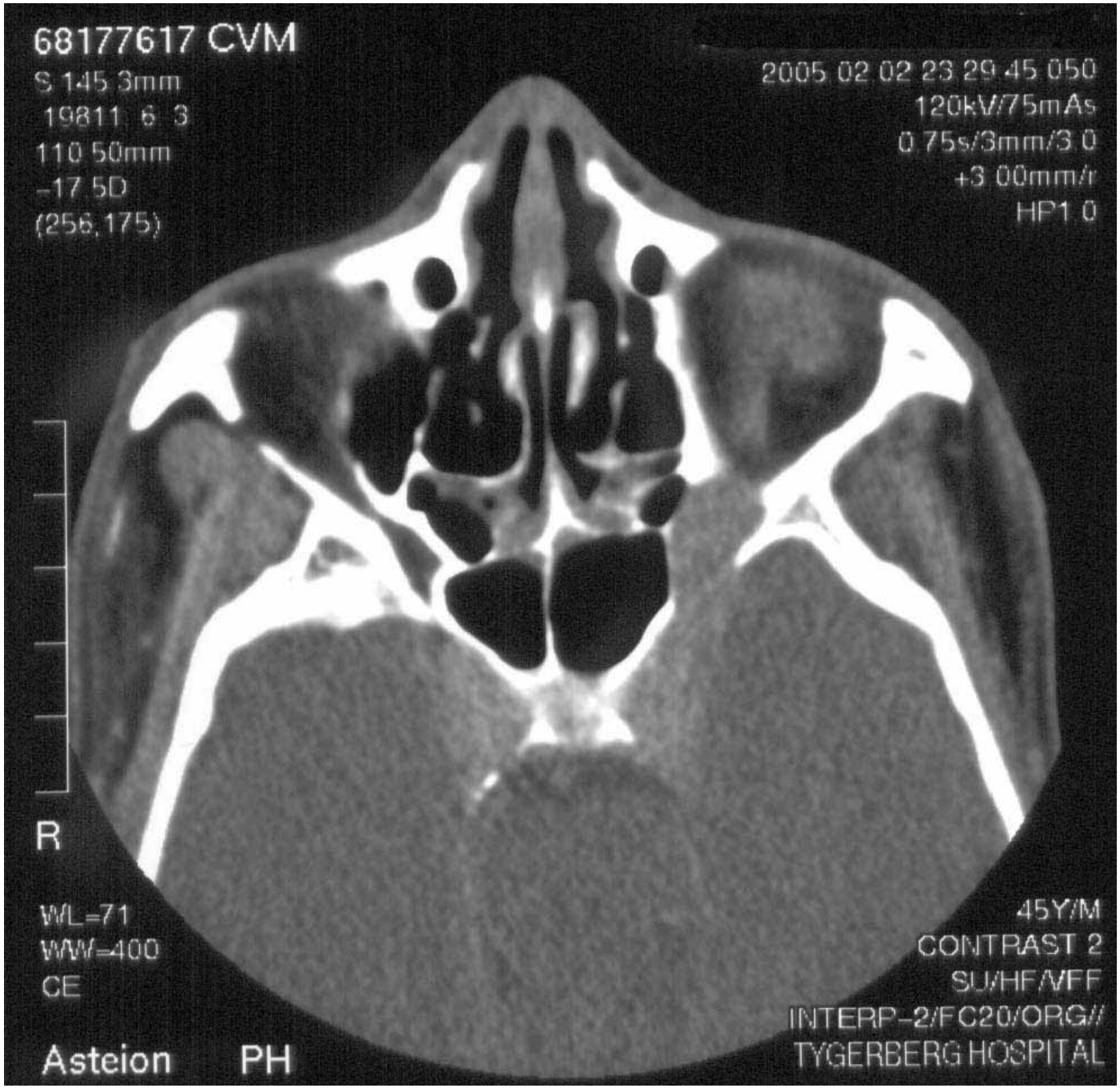
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R
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TYGERBERG HOSPITAL
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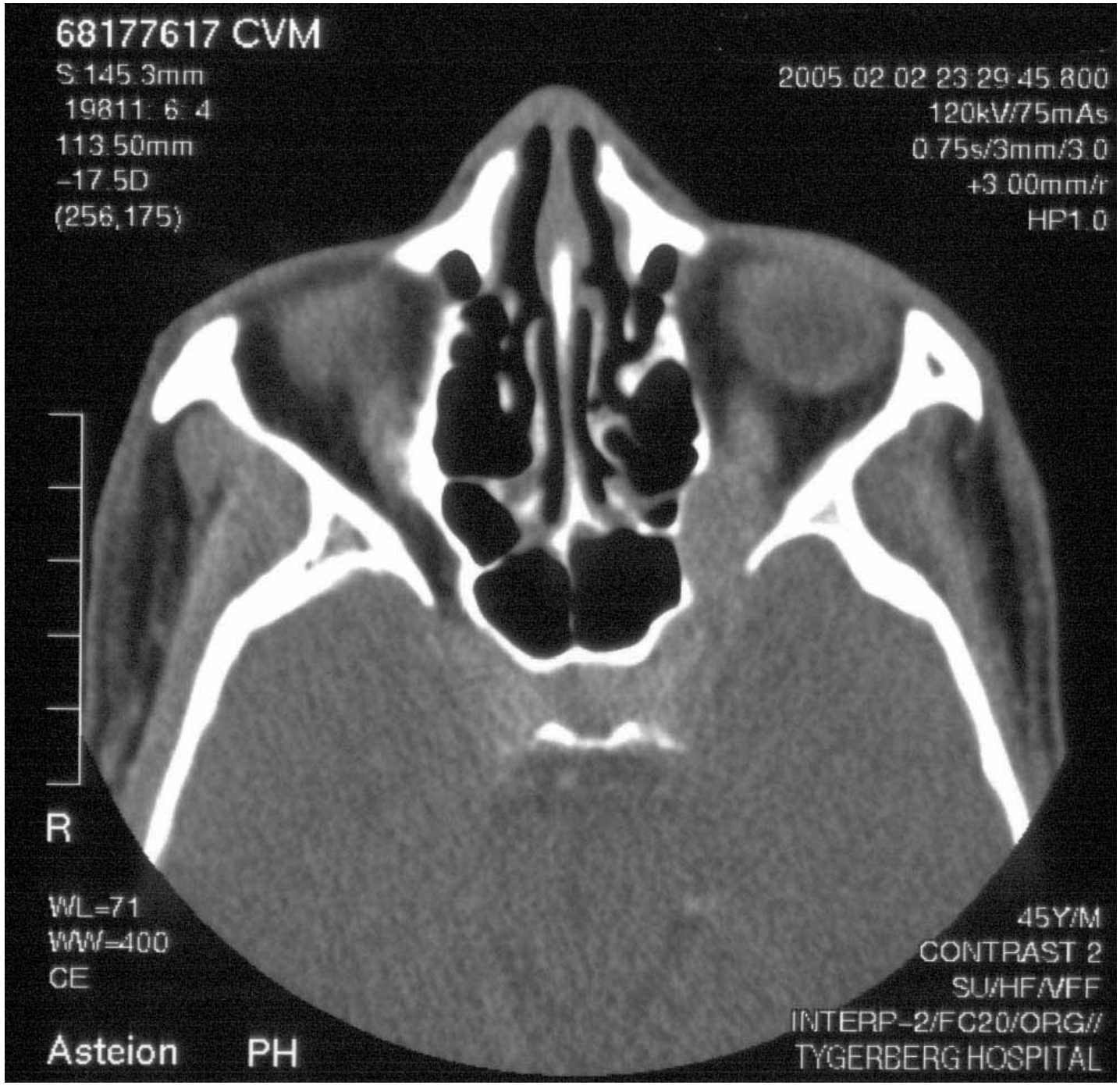
PH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WL=71
WW=400
CE
45Y/M
CONTRAST 2
SU/HF/VFF
INTERP-2/FC20/ORG//
TYGERBERG HOSPITAL
Asteion
PH

Staged / Plan

- T4N0M1 Nasopharyngeal Carcinoma

- Chemo therapy,
- Radiotherapy

NASOPHARYNGEAL CA

- Key points:
  - Clinical blind spot
  - Late presentation
  - ALWAYS scope NP if
    - metastasis neck nodes
    - OME in adult
  - Need tissue diagnosis of NP mass

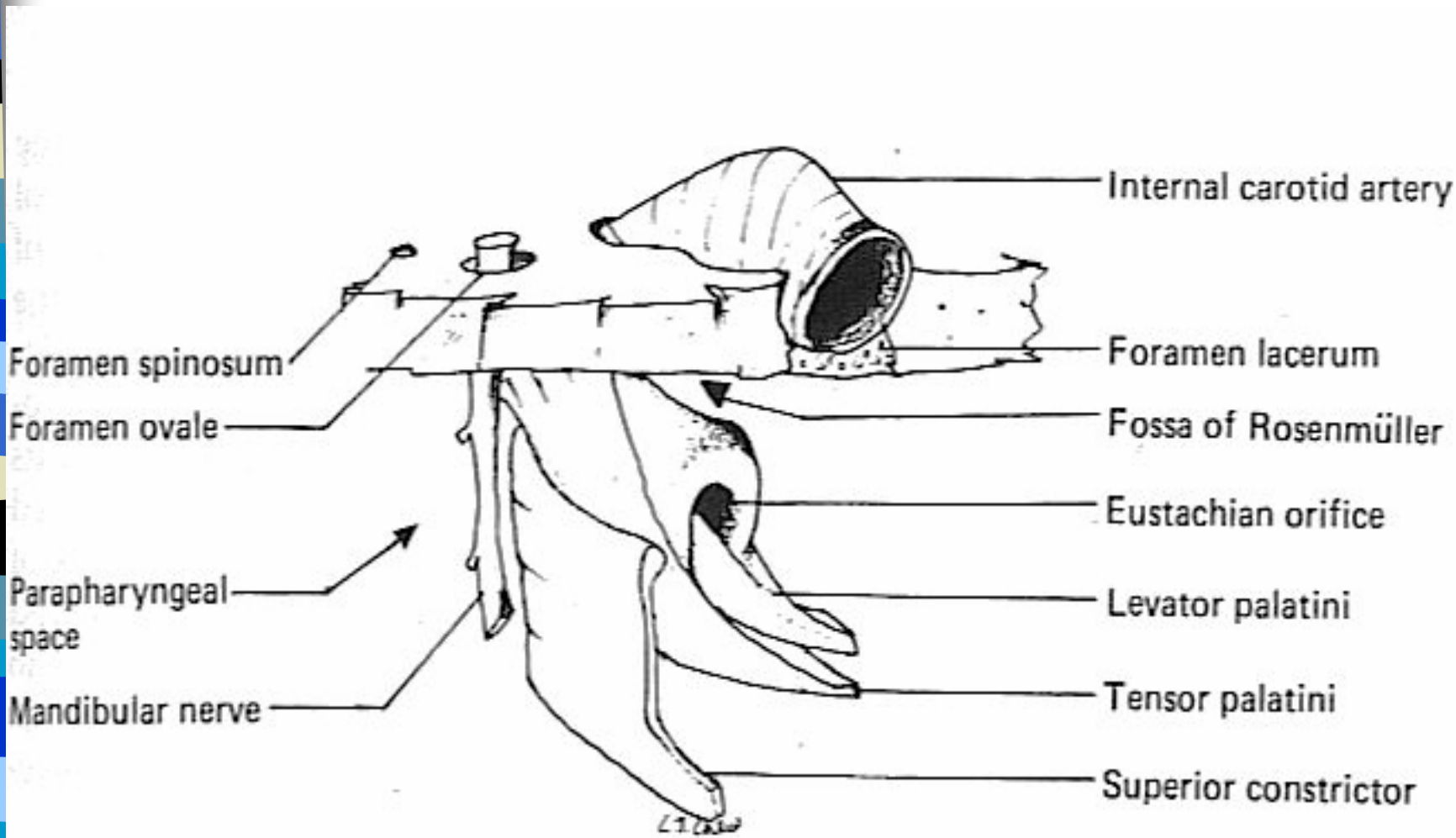
Histopathology

- “Lymphoepithelioma” - lymphocytes
- Cervical node metastasis characteristic cytology
- 3 histological types / WHO
  - 1) Squamous cell carcinoma – well / mod / poor diff
  - 2) Non-keratinising
  - 3) Undifferentiated / lymphoepithelial

  - 75% type 1 + 2

Anatomical site

- Order of Hz
  - Lateral wall (fossa of Rosenmuller)
  - Superior-post wall
  - > 1 wall (80% unilat)
  - Anterior wall


Internal carotid artery
Foramen spinosum
Foramen lacerum
Foramen ovale
Fossa of Rosenmüller
Eustachian orifice
Parapharyngeal space
Levator palatini
Mandibular nerve
Tensor palatini
Superior constrictor

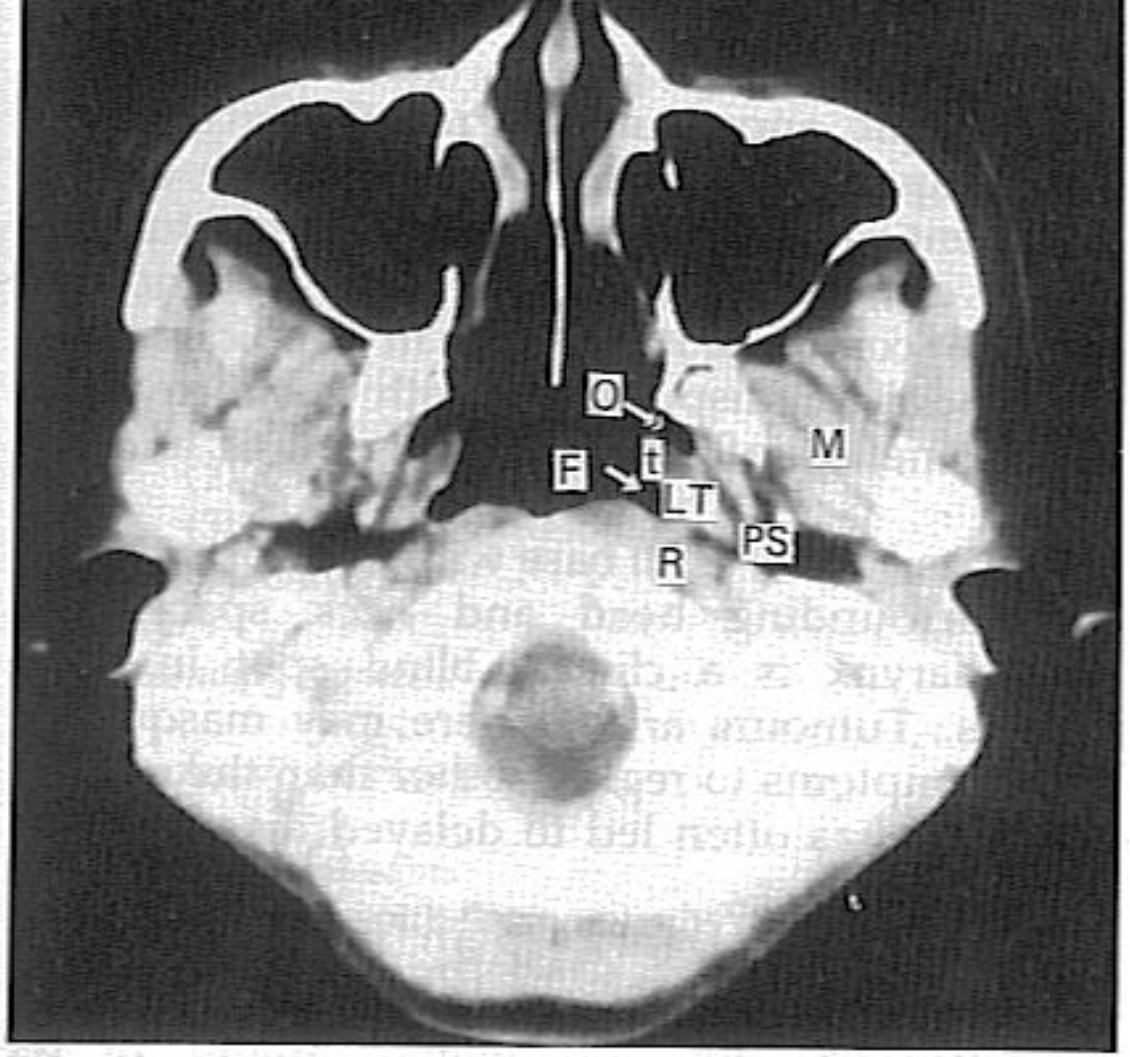


Figure 19.2 Computerized axial tomogram of the fossa of Rosenmüller showing its anatomical relations to the parapharyngeal space and infratemporal region.
O: eustachian opening; R: lateral retropharyngeal space; t: torus tubarius; F: fossa of Rosenmüller; LT: levator and tensor palatini; PS: parapharyngeal space; M: lateral pterygoid muscle

Differential of NP malignancy

- Epithelial
  - NP carcinoma, AdenoCa, Adenoid cystic Ca
- Lymphoid and Haemopoetic
  - Malignant lymphoma, Hodgkin's disease, Burkitt's lymphoma, Plasmacytoma
- Bone and cartilage
  - Chondrosarcoma, Osteosarcoma
- Soft tissue
  - Fibrosarcoma, Rhabdomyosarcoma
- Miscellaneous
  - Malignant melanoma, Chordoma, Craniopharyngioma

Environment

- Obscure aetiology
  - Genetic
  - Environment – Chinese in USA ↓ 3rd generation
    Chinese lifestyle
- Factors: EBV

Epidemiology

- 90% NP cancers = NP carcinoma
- SE Asia NP Ca: other Ca = 99:1
- China / Hong Kong / SE Asia: 50x ↑
- M:F = 3:1
- Age: Plateau (20 – 40)
  Bimodal low risk : < 15, high risk rare < 15

Environmental Factors ???

- EBV ↑ AB; viral genome in tumour
- Chemical cigarettes , Chinese herbal meds

  EBV act. plant

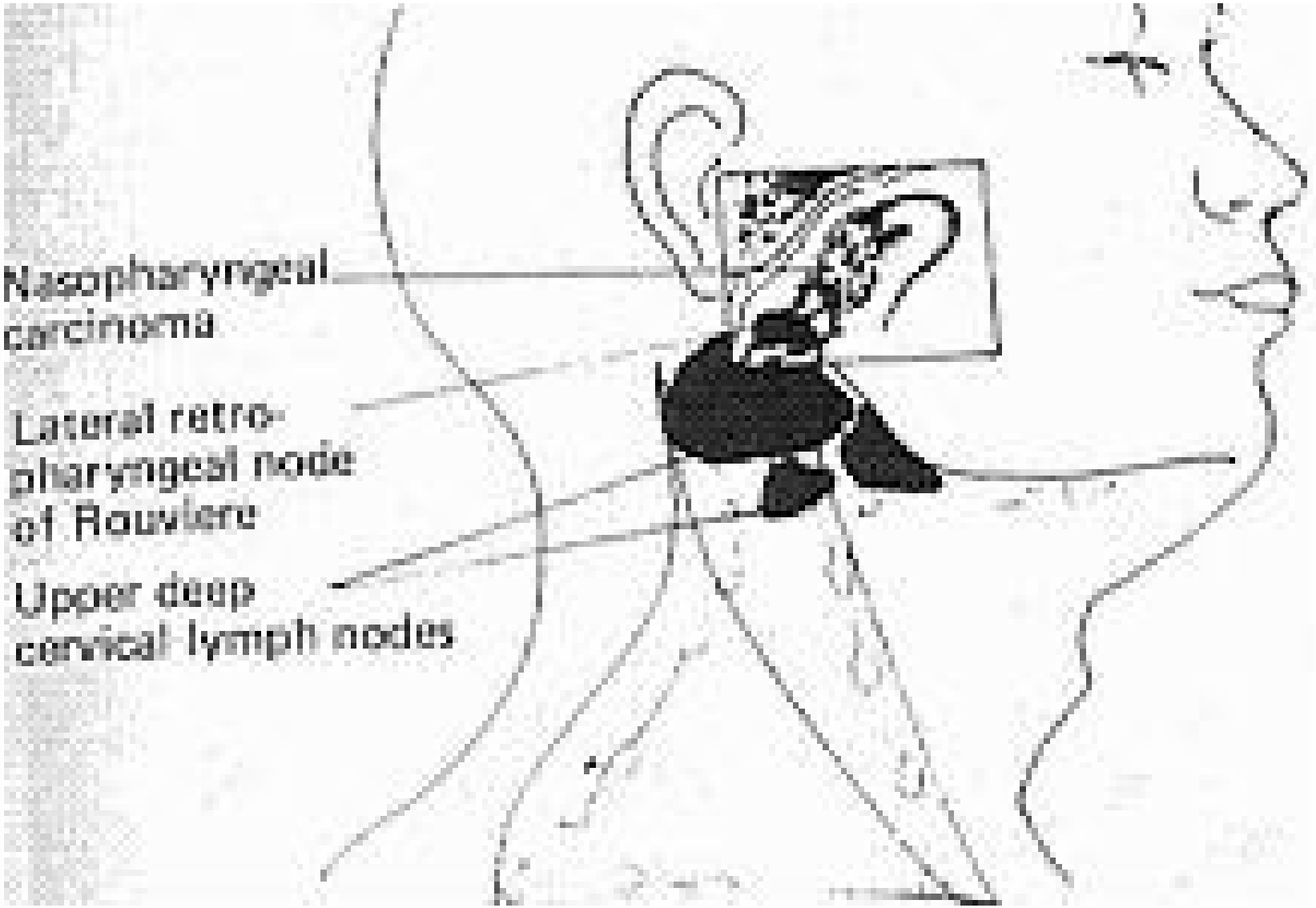
  salted fish, nitrosamines

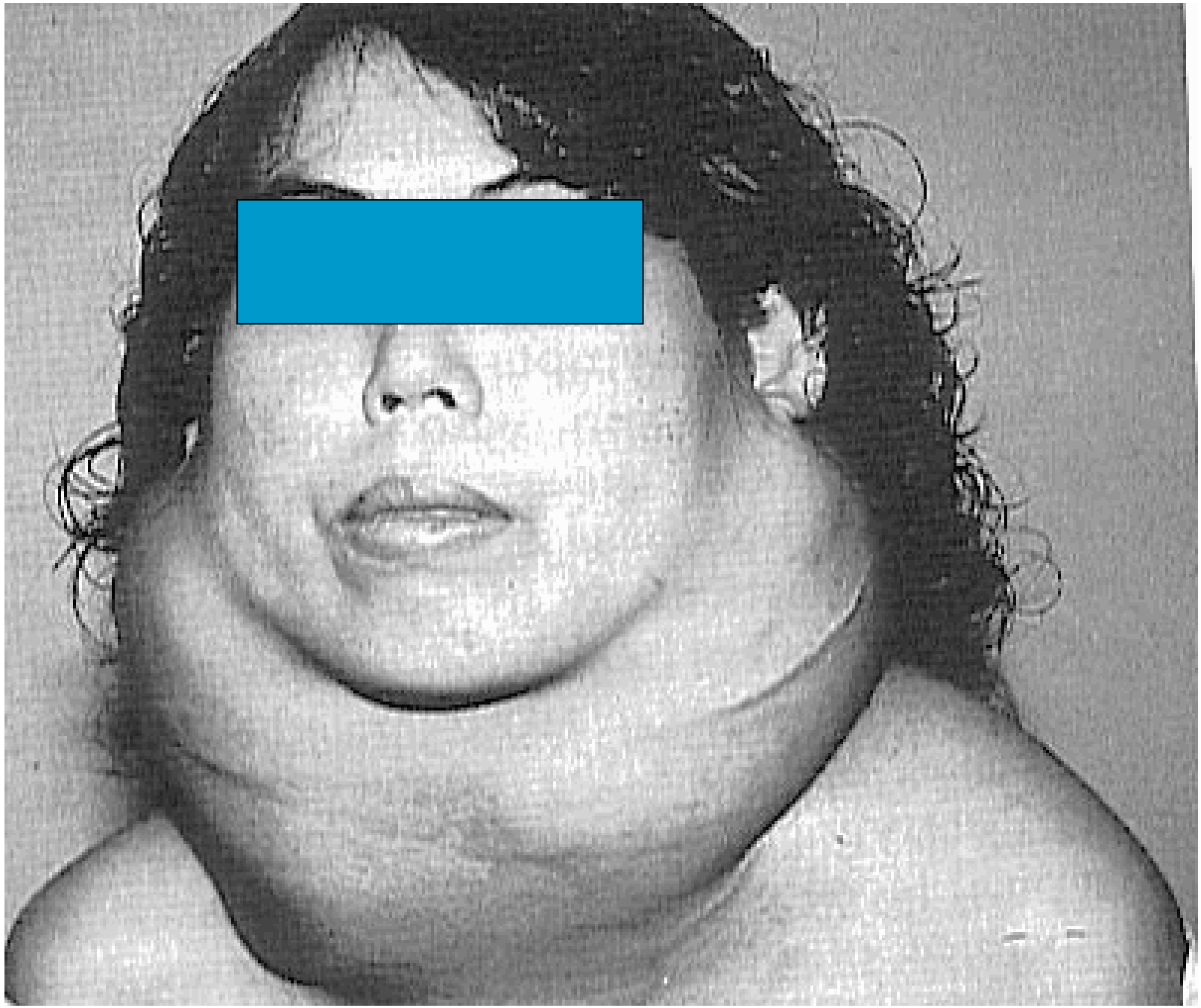
  incense
- Work industrial fumes, chemicals – activate EBV?
- Other socio-economic

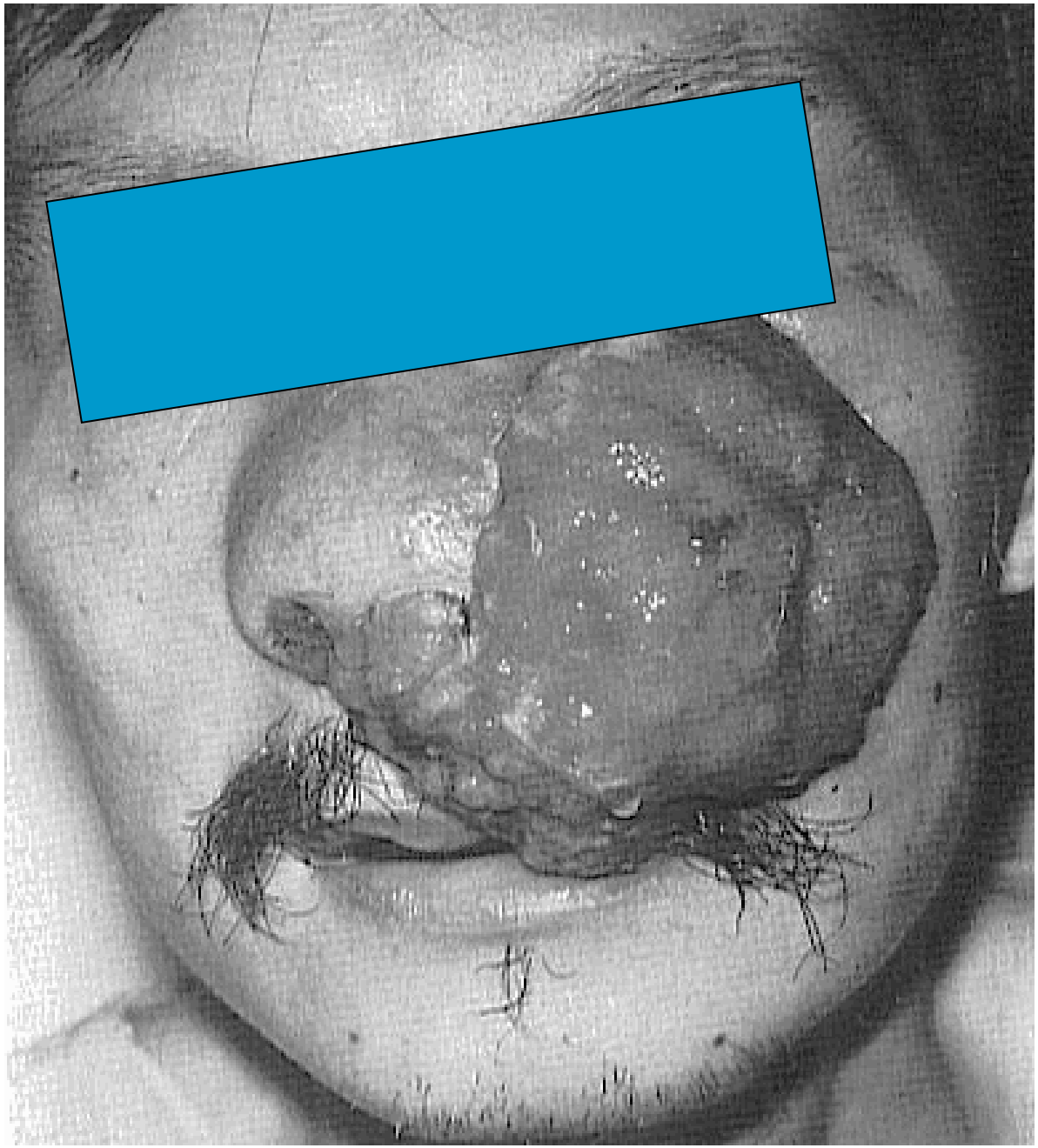
  heavy metals

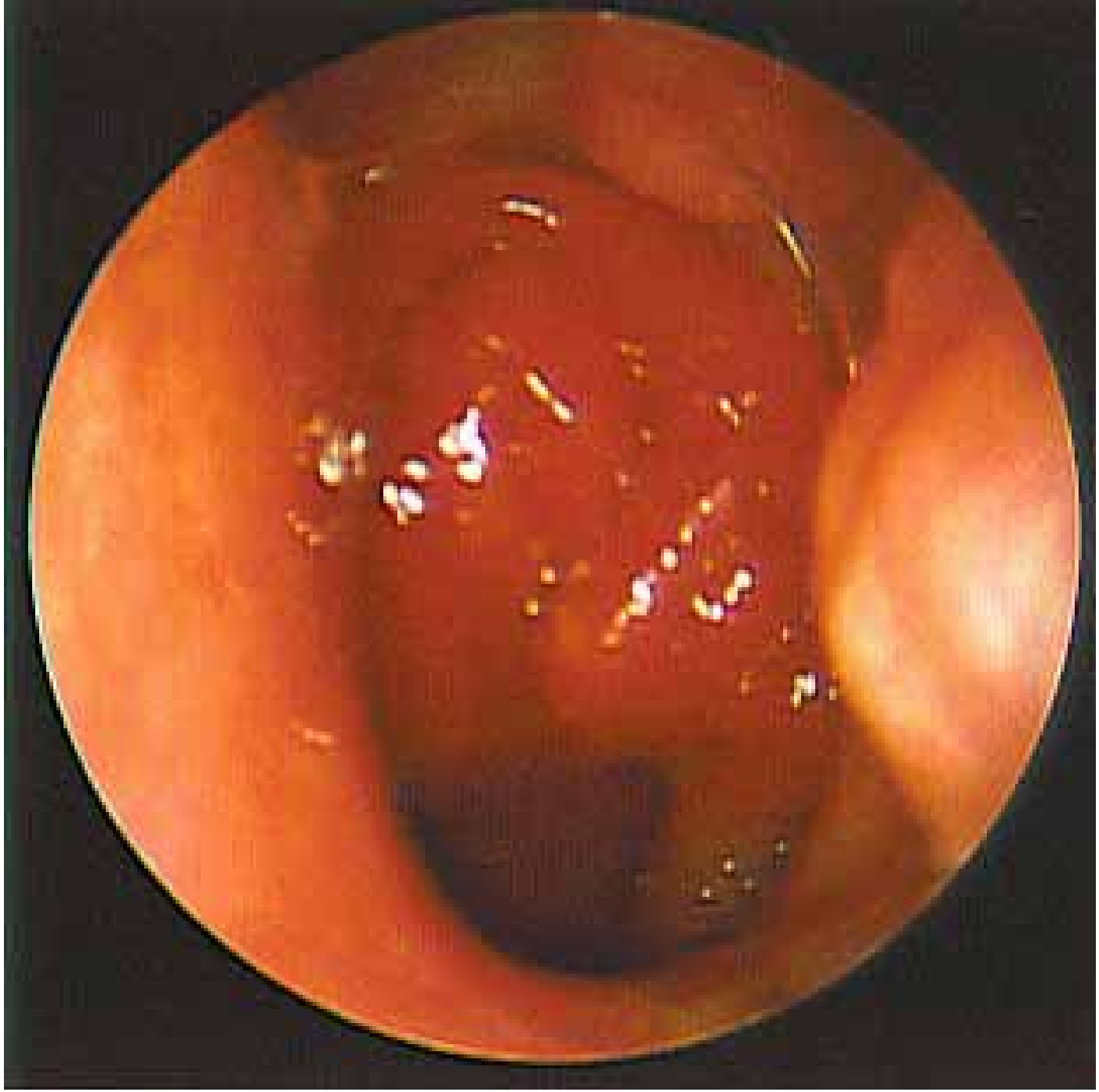
Clinical features

- 60% Cervical LA early
  - 1st Rouviere (retro pharyngeal)
  - 2nd JD / apical II
  - Also level V, parotid (Para pharyngeal)
- 40% Epistaxis / Nasoresp Sx late
  - Blood stained rhinorrhoea
  - Obstruct / epistaxis = advanced
- 30% Audiological Sx
  - Tinnitus / OME: 1° may be insignificant initially
  - **China + OME = NPCa**


Nasopharyngeal carcinoma
Lateral retro-pharyngeal node of Rouviere
Upper deep cervical lymph nodes







Clinical features

- 20% Neurological Sx
  - All CN, 50% = V, VI, IX, X
  - Pain / headache = erosion BOS
  - Trismus = pterygopalatine fossa
- Cranial nerves
  - **Retroparotidian Syndrome** = IX – XII
  - **Petrosphenoidal Syndrome** = III – VI (+ II)
- Metastases
  - 30% - thoracolumbar
    lung / liver

Local Spread

- Anterior
  - Nasal cavity, Pterygopalatine fossa, Apex of orbit
- Posterior
  - Retro pharyngeal space / node of Rouviere,
- Lateral / Para pharyngeal:
  - Poststyloid
    - Carotid sheath, IX – XII, Cervical sympathetic
  - Prestyloid compartment:
    - mandibular nerve, pterygoid mm, parotid deep lobe
- Superior
  - Sphenoid, optic n., petrous apex, foramen lacerum – cavernous sinus: III - VI
- Inferior
  - Oral cavity, retrotonsillar

Special investigations

- Biopsy
- FNA
- X-rays
- CT:
  - Submucosal infiltration
  - Small NP mass : tip of the tumour iceberg
  - BOS and occult nodes
  - MRI also useful

Classification / UICC (2002)

Nasopharynx	
T1	*Nasopharynx*
T2	*Soft tissue*
T2a	Oropharynx/nasal cavity without *parapharyngeal* extension
T2b	Tumour with parapharyngeal extension
T3	Bony structures, paranasal sinuses
T4	Intracranial, cranial nerves, infratemporal fossa, hypopharynx, orbit, masticator space
N1	Unilateral *node(s)* ≤6 *cm, above supraclavicular* fossa
N2	Bilateral node(s) ≤6 *cm, above supraclavicular* fossa
N3	(a) >6 cm (b) in supraclavicular fossa

Ebstein-Barr Virus

- Act on B lymphocytes receptors, in lymphoepithelium
- Childhood ⇒ seroconvert ⇒ harbour virus

- Chicken:egg? Ca with↓ immunity: EBV 1st

- EBV markers / DNA / Ag in tumour cells
- Antibodies: Immune response against
  - **IgA** + IgG to VCA (viral capsid antigen)
  - IgA + IgG to EA (early antigen)
  - Antibody to EBNA (nuclear antigen)
  - Antibody-dependent cellular cytotoxicity antibodies (kill cell)

- 90% NPCa = ↑antibody titres
  - Undiff Ca always EBV
  - Well diff no EBV DNA or EBNA

Immunology

- Cell-mediated immunity in NPCa
  - Antigen overload ⇒ Immunosuppresion
    - » ↓ viral T-cell activity >50%
    - » ↑ suppressor T-cell activity

- Diagnostic markers – titre rel. to tumour load
  - IgA/VCA = 95 % sensitivity
  - IgA/EA = ↑ specific (almost nil false +)
  - IgG/VCA + IgG/EA
  - Use: Stage of Dx / Effect of Rx/ Clinical course/ Survival

Immunology

- Prognosis
  - Good if antibody-dependant cellular cytotoxicity antibody titre
  - 1/ $\propto$ mean titres of VCA and IgA EA
- Screening
  - High risk groups: IgA/VCA. If $\uparrow \Rightarrow$ clinical and biopsy
- Occult 1° with Nodes: Serology IgA
  - (+) $\Rightarrow$ multiple Bx NP
  - (-) $\Rightarrow$ Immunohistological markers on node

Immunogenesis

- Genetic susceptibility to NPCa
  - High risk southern China
  - High risk in emigrant Chinese
  - Family clustering of NPCa
  - Increase risk in genetic admixture with Chinese
  - Low risk in Indians in China
- Genetic markers: HLA
  - A2, BW46, B17
  - HLA assoc. with haplotypes A2-BW46 and AW19-B17
  - Different survival and frequency distributions

Treatment / Prognosis

- Just radiotherapy (2000) = Ca Sensitive
  - (-) neck = 65 % 5 yr-survival
  - Stage III (N2,T2a-3) = 10 – 43% “
  - Stage IV (T4,N3) = 0 – 30 % “
  - 80% of bilateral LA developed distant metastases
  - Distant metastases * 1yr survival = 10%
    * 3month median survival
- Surgery
  - Biopsy
  - Radio resistant cervical nodes

Treatment / Prognosis

- Chemotherapy combined Radiotherapy
  - Taiwan study, T4N0-2
    - RoRx 41% $\Rightarrow$ C/RoRx 65% survival
  - USA study: stage III + IV, at 3 years
    - Cysplatin during RoRx and then 3 adjuvant courses of cysplatin and 5-fluorouracil
    - Survival 76% vs. 46%
    - Reduced distant metastases 35% vs. 13%