

63th European Ophthalmic Pathology Society (EOPS) Meeting

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Location: Basel Switzerland
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Case number: 406774
Material distributed: 1 glass slide
Title of Case Presentation High-grade undifferentiated carcinoma of the left hemifacial area with orbital extension and involving the eyeball

Clinical History and gross findings:

A 51-year-old man resident in Spain, 700 km away from Valencia, came to our hospital (November 2024) with a large tumour affecting the left hemifacial area with orbital growth, completely enveloping the eyeball and extending to the frontoparietal region.

Complete tumour resection of such lesion is a major surgical challenge that is unaffordable in most hospitals. A famous plastic surgeon, responsible for the first complete facial transplant in Spain and with extensive experience in highly complex surgeries, works in our centre.

The surgical procedure starts with anaesthesia through tracheostomy, with radical oncological resection plus left parotidectomy and left cervical lymphadenectomy of levels 2A and 2B.

Surgical limits are evaluated by intraoperative frozen biopsy study of the parotid, ethmoid sinus, infraorbital nerve and lateral pterygoid edges. All of these resection margins appear free of tumour on frozen sections.

The parotid resection measures 3.5 x 2 cm, remitted separately from the main specimen and does not appear macroscopically infiltrated. The cervical lymphadenectomy included a 9 x 5 cm adipose fragment bloc from which 17 lymph nodes were identified, 13 of which showed tumour metastasis. The largest of the metastases measured 1.5 cm in diameter.

The main tumour specimen measures 16x14x9 cm and weighs 785 grams. Externally, there are lobulated raised nodules of soft consistency that bulge the skin surface, especially in the left parietal area with a nodule larger than 9 cm. The specimen includes the upper and lower eyelids. On section, the eyeball is completely enveloped by the tumour but without perforation of the sclera. There is significant compression of the eyeball and in the anterior region the space of the anterior chamber appears reduced.

Despite the large surgical resection, tumour remnants had spread to the right hemifacial area and their removal was postponed to a second surgical procedure. This was performed at the end of December 2024: A new tracheostomy was performed for anaesthesia on top of the previous tracheostomy with placement of a nasogastric tube. Oncological resection is performed en bloc including right partial mandibulectomy (level 47), resection of the right jugal mucosa and right masseter muscle, right premaxillary oncological resection. Intraoperative frozen sections of the surgical margins of the resection of the left nasal region, the subcutaneous area of the right cheek and the right tonsil mucosa were again studied intraoperatively and found to be free of tumour. The resection is received fragmented in two portions: the tumour in the right mandibular region measures 10 x 6.5 x 4.5 cm, which macroscopically reveals a neoplastic area of 3.7 x 3.5 cm. The premaxillary tumour is removed in a fragment measuring 6 x 5.5 x 3.1 cm and macroscopically includes a neoplastic area of 3.4 x 3.1 cm.

Previous diagnosis from his local hospital was limited to a small biopsy with a report of poorly differentiated adenocarcinoma. Expression of cytokeratin 7 with negativity for other common IHC markers was in support of this diagnosis. The origin of the neoplasm does not appear determined.

Microscopic study

Sections of the tumour show neoplastic growth of epithelial type. It is diffusely distributed and consists of large cells. They have reinforced membranes with homogeneous eosinophilic cytoplasm and markedly atypical pleomorphic nuclei with prominent eosinophilic nucleoli. There is mitotic activity with a rate of around 20 mitoses per 10 high magnification fields. No clear keratinization is seen. There is minimal dyskeratosis. There are areas of loss of cellular cohesion and foci of necrosis. The morphology of the lesion corresponds to a poorly differentiated carcinoma. The left parotid gland and right submaxillary gland have preserved morphology without neoplastic infiltration. The lesion does not infiltrate the masseter muscle and is contiguous with the epithelium of the jugal mucosa. The resection limits are free both in the region of the right mandibular angle and in the lesion in the premaxillary area, although focally less than 1 mm. from the tumour. The margins studied intraoperatively in the subcutaneous region of the right cheek and the right tonsillar mucosa are all free of lesions.

The immunohistochemical study shows intense expression of cytokeratin AE1-AE3 and CK7. p40 and p63 (markers of squamous cell carcinoma) are weakly and focally expressed. Neuroendocrine markers were negative. S100, actin, desmin and cd 34 are all negative.

Final diagnosis: undifferentiated carcinoma most probably from sinonasal origin with rapid expansion to the left hemifacial region, orbit, left fronto-parietal cranial region and right mandibular region.

Discussion:

Microscopic study in multiple sections, and without particularly heterogeneous patterns, suggested most probably an epidermoid carcinoma. However, it was difficult to find confirmatory evidence for this type of lesion. There were no sarcomatoid areas as in more dedifferentiated SCC, no dyskeratosis features and no expression of SCC IHC markers. The expression of CK AE1AE3 alone confirmed carcinoma, but CK7 expression did not allow glandular orientation in the absence of other markers. Undifferentiated carcinoma is classically described in salivary gland (ours had no involvement) and sinonasal tumors and this seemed to be the most probable origin of our case.

These tumor not infrequently presents with stage 4 disease and involves the skull base and orbit [1], being our case among those with huge local extension. Although lymph node metastasis were assessed, no visceral metastasis were known at the time of surgery.

Overall, 5 and 10 year relative survival rates for SNUC patients were publish among 34.9% and 31.3%, respectively. It seems there is survival benefit from surgery combined with radiation therapy [2] which justifies the ambitious surgical procedure undertaken with our patient, even if it is not curative but palliative and extends his survival. Aggressive surgical procedures have been employed with some success [3]. Maybe immunotherapy can improve survival [4] as in many other settings.

References:

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- 3.- Zielinski V, Laban S, Tribius S, Schafhausen P, Veldhoen S, Knecht R, Clauditz T, Muenscher A. Management of sinonasal undifferentiated carcinoma with intracerebral invasion: Clinical experience at a single institution and review of the literature. *Ear Nose Throat J.* 2016 Jan;95(1):23-8. PMID: 26829682.
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