Chievitz' juxtaparotid organ, free from cancer

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INTRODUCTION: *Up to the half of twentieth century, Chievitz organ was considered an embryonal organ, disappearing with growth. But Zenker, in 1953, demonstrated the existence of this organ in adult life, too*[4].
REVIEW*: In this article we review the embryology, the macroscopic and microscopic anatomy, the ultrastructure, the functional significance and the pathology of the Chievitz'Juxtaparotid Organ (CJO). The CJO is not a macroscopic apparent organ, but it looks like a nerve. The CJO takes connections with buccinator muscle, at the level of the parotid duct, and the medial pterygoid muscle. The cell parenchyma is enveloped by the connective tissue, that is divided into three layers*[15, 16]*: the inner layer –"stratum fibrosum internum"-, composed of collagenous and elastic microfibrils; the middle layer - "stratum nervosum" – containing a lamellar inner core and Ruffini SNF*[5]*; the external layer - "stratum fibrosum externum", that is a collagen capsule. The parenchymal cells show a rich enzyme activity. The parenchymal cells may play the same role as glomus cells of the 1st type and Merkel cells*[20, 21]*. When a surgical resection is performed for an oral carcinoma, the CJO may be present in the specimen*[25]*. The CJO may be wrongly diagnosed as perineural invasion by carcinoma*[26, 27, 28].
CONCLUSION:*We report that Chievitz' organ is the only organ in which the cancer does not occur.*

KEY WORDS: Chievitz' organ, Juxtaoral organ, Parotid gland

Introduction

Juxtaparotid or juxtaoral organ was called, by Broman, Chievitz' organ[1] .
Chievitz J.H. was a Danish Anatomist who studied the development of the parotid gland in 1885 and found a longitudinal epithelial structure in human embryo, connected with the ductus parotideus[2].

Juxtaoral organ was the term proposed by Salzer and Zenker owing to the topography of this organ, in spatium buccotemporale[3].
Up to the half of twentieth century, Chievitz organ was considered an embryonal organ, disappearing with growth. But Zenker, in 1953, demonstrated the existence of this organ in adult life, too[4].

Review

EMBRYOLOGY

Chievitz' Juxtaparotid Organ appears earlier than Parotid Gland, in embryos of very small dimensions, 1 cm in length (cm 0.75 to 1.2), whilst Parotid appears later, in embryos of 2 cm in length (cm 1.6 to 2)[5].

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The development of Chievitz and Parotid Organs presents the same genetic mutations[6] and in view of its proximity to Parotid Gland, D'Andrea V.[7], for the first time, called the Chievitz Juxtaparotid Organ (CJO), changing Juxtaoral with Juxtaparotid.
The commissura buccalis is formed by the fusion of maxillary and mandibular walls. The anlage of the Chievitz organ corresponds to epithelium of the commissura buccalis, from which it gradually separates[7].
The epithelium of the oral cavity and the parotid duct don't have connections with the Chievitz' organ[5,8].
The development of the CJO may be separated in three parts[7]:
– the oral part descends orocaudally to the site where the parotid duct penetrates the buccinator muscle;
– the middle part crosses the buccalis nerve;
– the dorsal part is related to the oral part of medial pterygoid muscle.
The oral part of the CJO disappears in the course of the embryologic development, which led some authors to wrong conclusion that this organ was a rudimentary one.
The epithelial components of CJO are step by step surrounded by the mesenchymal components of the organ. In humans, the CJO does not involve and it exists throughout life[5,9]. The CJO has been reported in many other species, but it is most organized and differentiated in humans.
The CJO is richly innervated from the buccal nerve.

Macroscopic Anatomy (Fig. 1, Fig. 2)

The CJO is a spindle shaped structure, 7 to 17 mm long and 1 to 2 mm wide. It is situated in spatium buccotemporale, limited by the medial surface of the mandible and the buccinator muscle, which is on its medial side.
The buccalis nerve innervates the CJO by 2 to 4 thin branches. The CJO is not a macroscopic apparent organ, but with a dissecting microscope it can be showed as a flat, white solid strand of tissue. It looks like a nerve.
The CJO takes connections with buccinator muscle, at the level of the parotid duct, and the medial pterygoid muscle.
At dissection the CJO may be confused with connective tissue fibers as it is contained in the fascia buccotemporalis.

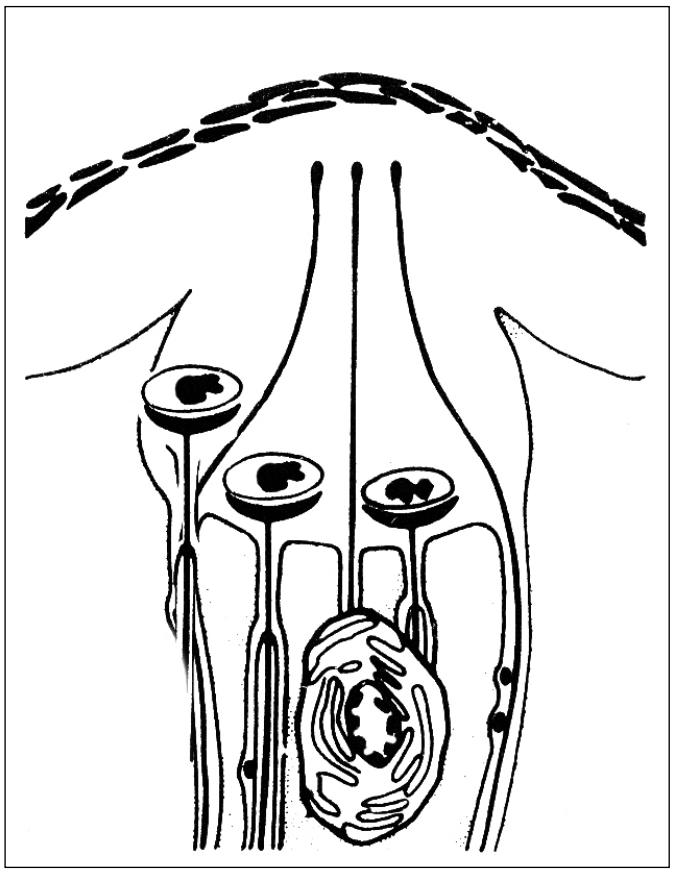

Fig. 1: Chievitz juxtaparotid organ.

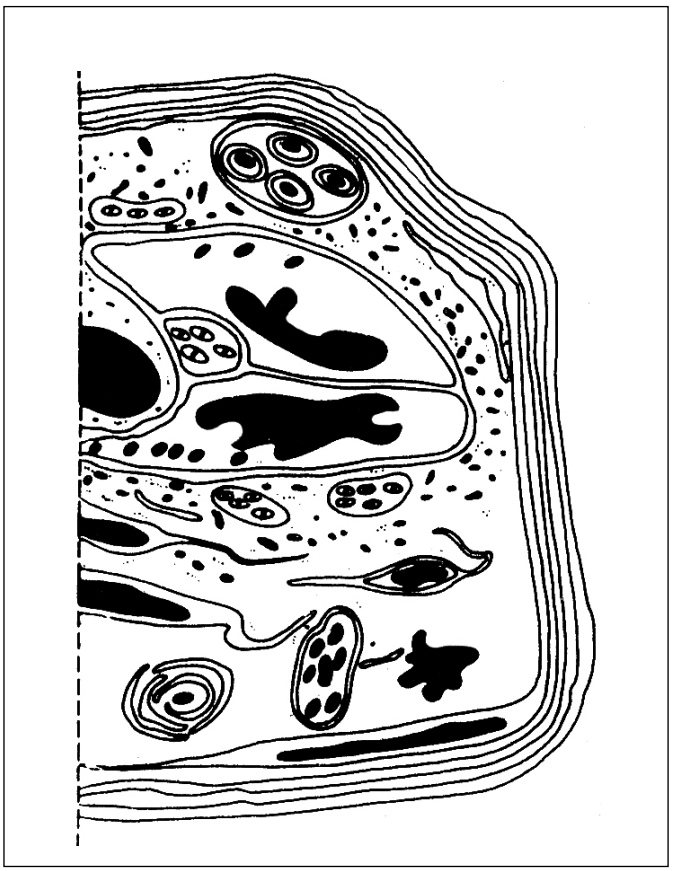

Fig. 2: Chievitz juxtaparotid organ.

Microscopic Anatomy

The epithelial parenchyma of the CJO is surrounded by connective tissue stroma which is divided into three strata:
– stratum fibrosum internum = inner connective tissue stratum, composed of connective tissue fibers and some elastic fibers;
– stratum nervosum = loose connective cellular tissue which contains nerve fibers[10] and sensory structures;
– Stratum fibrosum externum = collagenous fibers.
The central part of the CJO is formed by cells derived from ectoderm of the cavum oris. The cells of the first type are the most and contain granular vesicles, the cells of the second type are the less and possess long processes interposed among the first type cells[11,12,13].
In the stratum nervosum there are different kinds of cells, like mast cells, lymphocytes, fibrocytes, pigment cells, but the most important are the sensory nerve structures (SNS). The stratum nervosum is irrorated by capillaries.
The epithelial nests of cells rest on a basement membrane and are found not just around but also within nerves. The nerve fibers penetrate the CJO in many points. Single nerve fibers are present among the epithelial cells. The most penetrating nerve fibers reach the stratum nervosum, where they are forming different kinds of SNS: simple arborizations, glomerular SNS, lamellar simple sensory corpuscles and, maybe the Ruffini SNS[5].

Ultrastructure

Epithelial cells of the CJO are of two different kinds.
Epithelial cells of the first type are the most, resemble keratinocytes, are polygonal in shape, have a diameter 7 to 13 micron, have large granular vesicles in cellular processes. They contain cytoplasmic granules, inclusions, tonofibrils and are interconnected by desmosomes and tight junctions.
Epithelial cells of the second type are the less, resemble dendritic cells, send long processes among the first type cells, contain a rich endoplasmic reticulum, lacking desmosomes and tonofibrils. They are always separated,by means of the epithelial cells of the first type, from the basal lamina.
The cell parenchyma is enveloped by the connective tissue, that is divided into three layers[15,16].
Its inner layer is the "stratum fibrosum internum", composed of collagenous and elastic microfibrils. This inner layer is separated from the cellular parenchyma by lamina basalis and has a thickness of about 50 nm.
The middle layer is the "stratum nervosum": it is the thicker layer. It contains different sensory structures and myelinated and nonmyelinated nerve fibers. The cell population consists of fibroblast, lymphocytes, mastcells, melanin containing cells. There are also collagenous microfibrils and numerous capillaries.
Inside the "stratum nervosum" the nerve fibers form different kinds of sensory nerve formations – SNS. These are glomerular sensory corpuscles, simple lamellar corpuscles with a lamellar inner core and Ruffini SNF[5]. The dendritic zones of these SNF contain numerous mitochondria.
The external layer is the "stratum fibrosum externum": it is composed by concentrically arranged connective tissue lamellae, among them occur collagenous and elastic microfibrils. This outer collagen capsule is connected to the fascia buccotemporalis.

Functional Significance of the Chievitz Organ and Its Classification.

The parenchymal cells show a rich enzyme activity, indicating a high metabolism[15]. These enzymes are alkaline phosphatase and carbonic anhydrase or esterases[17]. They are similar to those found in ductal cells of the salivary glands[17].
Within cells, neurosecretory – like granules have been found[18]; this finding, joining a close relationship between parenchyma and nonmyelinated nerves, suggests a neurosecretory function of the CJO[5,15].
A secretory function of parenchymal cells in CJO was described by Mayr[19] and Zenker[5]. The parenchymal cells of the 1st type in CJO may play the same role as glomus cells of the 1st type and Merkel cells[20, 21], that is the modulation of afferent fibers activity in the organ.
As to the chemoreceptors or chemosensors, there is a constant relation of glomus cells of the 1st type to the afferent nerve fibers. These cells modulate the activity of the dendritic zones. An analogy can be found in Merkel complexes in the skin, too.
The parenchymal cells of the 1st type in CJO, the glomus cells of the 1st type in glomus caroticus and Merkel cells in the epidermis are the cells of neuroectodermal origin and represent, or may represent in the case of CJO, the paraneurons.
As the CJO seems to be fully developed already in newborns, it indicates its important function as a mechanosensor of this region connected with nutrition reflexes. CJO contains different kinds of sensory nerve formations (SNF), i.e. intraepithelial fibers, simple arborizations, maybe Ruffini SNF, glomerular SNF, simple lamellar corpuscles, showing multimodal mechanosensory function for this organ. According to the accumulation of sensors of different kinds, the CJO belongs to complex sensory nerve formations[22,23].

Pathology

The CJO is localized in the soft tissues of an area that is commonly the site of oral cancer surgery[24]. When a sur-

gical resection is performed for an oral carcinoma, the CJO may be present in the specimen[25]. The CJO may be wrongly diagnosed as perineural invasion by carcinoma[26-28]. Several authors stressed the chance of mistake between CJO and a carcinoma or a schwannoma[24,25,27,29,30].

Conclusion

Zenker[5] reported that no tumors have been found in the CJO. Now we confirm that CJO is an organ free from cancer.

Riassunto

INTRODUZIONE: Fino alla metà del XX secolo, l'organo di Chievitz è stato considerato un organo embrionale, che scompare con la crescita. Zenker, invece, nel 1953, ha dimostrato l'esistenza di questo organo anche nella vita adulta.
STUDIO: In questo articolo descriviamo l'embriologia, l'anatomia macroscopica e microscopica, l'ultrastruttura, il significato funzionale e la patologia dell'organo iuxtaparotideo di Chievitz'(CJO). Il CJO non è un organo macroscopicamente evidente, ma ha l'aspetto simile ad un nervo. Il CJO prende collegamenti con il muscolo buccinatore, a livello del condotto parotideo e con il muscolo pterigoideo mediale. Il parenchima cellulare è avvolto da tessuto connettivo, che è diviso in tre strati:lo strato interno - "strato fibrosum internum" -, composto da microfibrille di collagene; lo strato intermedio - "stratum nervosum" - contenente un nucleo interno lamellare e strutture nervose di Ruffini; lo strato esterno - "stratum fibrosum externum", che è una capsula di collagene. Le cellule parenchimali contengono enzimi, quali la fosfatasi alcalina e l'anidrasi carbonica, con una ricca attività enzimatica, simile a quella delle cellule duttali delle ghiandole salivari. Il CJO presenta, inoltre, un'importante funzione meccanosensore di questa regione. Quando viene eseguita una resezione chirurgica per un carcinoma orale, il CJO può essere presente nel pezzo operatorio. Il CJO può essere erroneamente diagnosticato come invasione perineurale da carcinoma.
CONCLUSIONE: Sulla base della revisione della Letteratura, tuttavia, si può definire che l'organo di Chievitz è l'unico organo in cui il cancro non si verifica.

A special **acknowledgment** is dedicated to the memory of Prof. Lubomir Malinovsky

References

1. Broman I: *Uber Chievitz Organ und dessen Bedeutung. Ergebn.* Anat EntwGesch, 1914; 22:603-62.

2. Chievitz JH: *Beitrage zur Entwicklungsgeschichte der Speicheldrusen.* Arch Anat Physiol Anat, 1885; 9:401-36.

3. Salzer GM, Zenker W: *Das juxtaorale Organ*. Bibl Anat fasc 3 Basel: Karger S, 962.

4. Zenker W: *Organon bucco-temporale (Chievitzsches Organ); ein nervos-epitheliales Organ beim Menschen*. Anat Anz, 1953; 100 Erg. H.2: 257-62.

5. Zenker W: *Juxtaoral organ (Chievitz's organ). Morphology and clinical aspects*. Baltimore: Urban & Schwarzenberg; 1982.

6. Gruneberg H: *Exocrine glands and the Chievitz organ of some mouse mutants*. J Embryol Exp Morph, 1971; 25:247-61.

7. D'Andrea V, Malinovsky L, Biancari F, Spyrou M, Dibra A, Malinovska V, Hees H, Gallenzi P, Cristalli MP, Di Mateo FM, De Antoni E: *The Chievitz Juxtaparotid Organ*. G Chir, 1999; 20(5): 213-17.

8. Ramsay AJ: *Persistence of the organ of Chievitz in the human.* Anat Rec, 1935; 63:281-93.

9. Kramer EB, Zenker W: *Neuroepithelial structures in the oral cavity.* Am J Clin Pathol, 1974; 62:571-73.

10. Zenker W: *Die nervosen Elemente des Chievitz'schen Organs.* Verh Anat Ges, 1959; 56:249-58.

11. Mayr R, Salzer GM: *Elektronenmikroskopische Untersuchungen am juxtaoralen Organ des Menschen.* Z Zellforsch, 1967; 81:135-54.

12. Mayr R: *Neue Untersuchungen uber das juxtaorale Organ*. Verhandl Anat Gesellsch, Erg.H.zum 121 Band Anat Anz 1968; 361-65.

13. Jeanneret-Gris B*: Ultrastructure de l'organe juxta-oral*. Arch Anat microsc Morphol experiment, 1980; 69:197-214.

14. Pantanowitz L, Balogh K: *Significance of the juxtaoral organ (of Chievitz*). Head Neck, 2003; 25:400-405.

15. Zenker W, Salzer GM: *Die Histologie des Chievitz'schen Organs.* Acta Anat 1961; 44:286-321.

16. Jeanneret-Gris PB: *Ultrastructure de l'organe juxta-oral.* Arch Anat Microscop, 1980; 69:197-214.

17. Muller E, Zenker W: *Enzyme-histochemistry of the juxtaoral organ in man (Organ of Chievitz).* Histochemistry, 1981; 71:279-90.

18. Klacsmann PG, Taxy JB: *Juxtaoral Organ of Chievitz.* Am J Surg Pathol, 1980; 4:307-09.

19. Mayr R: *Morphologische Hinweise auf eine rezeptorische Funktion des juxtaoralen Organs*. Verh Anat Ges, 1979; 73:1043-45.

20. Hartschuh W, Weihe E, Reinecke M: *The Merkel cell.* In: Bereiter-Hahn J, Matoltsy AG, Richards KS (eds): *Biology of the Integumentum. Vol. 2. Vertebrates.* Berlin, Heidelbergh: New York-Tokyo: Springer Verlag, 1986; S.606-20.

21. Hartschuh W, Weihe E, Yanaihara N: *Immunohistochemical analysis of chromogranin and multiple peptides in the mammalian Merkel cell: further evidence for its paraneuronal function?* Arch Histol Cytol, 1989; 52, Suppl: 423-31.

22. Malinovsky L: *Mechanoreceptors and free nerve endings.* In: Bereiter-Hanh J, Matoltsy AG, Richards KS (eds): *Biology of the Integumentum. Vol. 2. Vertebrates*. Berlin-Heidelberg, New York, Tokyo: Springer Verlag, 1986; 535-60.

23. Malinovsky L: *A contribution to the nomenclature of peripheral sensory structures (sensory nerve endings*). Z. Mikrosk, Anat Forsch, 1990; 104:170-16.

24. Tschen JA, Fechner RE: *The juxtaoral organ of Chievitz.* Am J Surg Pathol, 1979, 3:147-50.

25. Sciubba JJ, Sachs SA: *Schwannoma of the inferior alveolar nerve in association with the organ of Chievitz.* J Oral Pathol, 1980; 9.16-28.

26. Barnes L, Peel RL: *Head and neck pathology: A text-atlas of differential diagnosis.* New York: Igaku-Shoin, 1990; 146-47.

27. Geist ET, Adams TO, Carr RF: *The organ of Chievitz: its importance in the microscopic diagnosis of oral carcinoma.* J Oral Med, 1984: 177-79.

28. El-Mofty SK: *Pseudoneoplastic lesions of the head and neck*. In: Wick MR, Humphrey PA,Ritter JH,(eds.): *Pathology of pseudoneoplastic conditions*. Philadelphia: Lippincott-Raven Publishers; 1997; 69-96.

29. Danforth RA, Baughman RA: *Chievitz's organ:a potential pitfall in oral cancer diagnosis*. Oral Surg Oral Med Oral Pathol, 1979; 48:231.

30. Mirko T, Molnar P: *The juxtaoral organ. A pitfall for pathologists.* J Pathol, 1981; 133:17.

Commento e Commentary

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L'aggiornamento anatomo-istologico rappresentato da questo studio rappresenta una nota culturale interessante, misconosciuta com'è dalla maggior parte dei chirurghi, se non dagli anatomisti e dagli embriologi, forse per il suo scarso-nullo impatto nella patologia.
La conclusione degli Autori, che si tratterebbe di una struttura-organo esente totalmente da possibili evoluzioni neoplastiche appare però quanto meno appartenente più alle ipotesi che non alle assolute certezze, perché è più facile fare affermazioni in positivo che dimostrare quelle in negativo. Per dare conferma a quella affermazione bisognerebbe fare una ricerca retrospettiva di tipo istopatologico su una adeguata casistica di patologia neoplastica maxillo-parotidea.

* * *

The anatomical and histological remainder represented by this study is an interesting cultural note, as it is misunderstood by most surgeons, if not by the anatomists and embryologists, perhaps for his poor-zero impact on any known form of pathology.
The conclusion of the authors, that it would be a structure-body totally free from possible neoplastic developments appears, however, at least most belonging to the hypothesis that to absolute certainties, because it is easier to make statements in positive than to demonstrate them in negative. To give confirmation to that statement should be made a retrospective histopathological study on an adequate number of neoplastic specimen in the maxillo-parotid field.