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Congenital anomalies

2 directions:

gastrointestinal anomalies

craniofacial anomalies:

temporomandibular region

clefts

I

"...Dear Authors M.Pilmane, L.Ozoliņa, Z.Ābola, A.Pētersons, V.Popkovs, A.Dabužinskiene, J.Vētra,

On behalf of the executive editor of the journal Medicina (Kaunas), we would like to inform you that the manuscript entitled "Growth factors, their receptors, neuropeptide-containing innervation and matrix metalloproteinases in the proximal and distal ends of esophagus in children with esophageal atresia" has been accepted for publication in one of the nearest issues of the journal "Medicina"..."

The pathogenesis of esophageal atresia (EA) remains unknown despite relatively high incidence of this anomaly in population that affects one newborn from 3000 alive born children.

...growth factors, cell adhesion molecules, genes and apoptosis...

Aim of study was examination of relative occurrence of growth factors, their receptors, neuropeptide-containing innervation and tissue degradating enzymes – matrix metalloproteinases in proximal and distal parts of esophagus with EA.

- ***Materials:*** **15 newborns (9 boys and 6 girls; 21 hours to 1 month).**
- **Diagnosis: 13 cases - EA with distal tracheoesophageal fistula (EA/distal TEF); while in 2 cases - EA/proximal TEF.**
- **Control group - 12 specimens of oesophagus were enrolled, obtained from newborns, whose death reason was not related to gastrointestinal pathology.**
- ***Methods:*** **Immunohistochemistry**

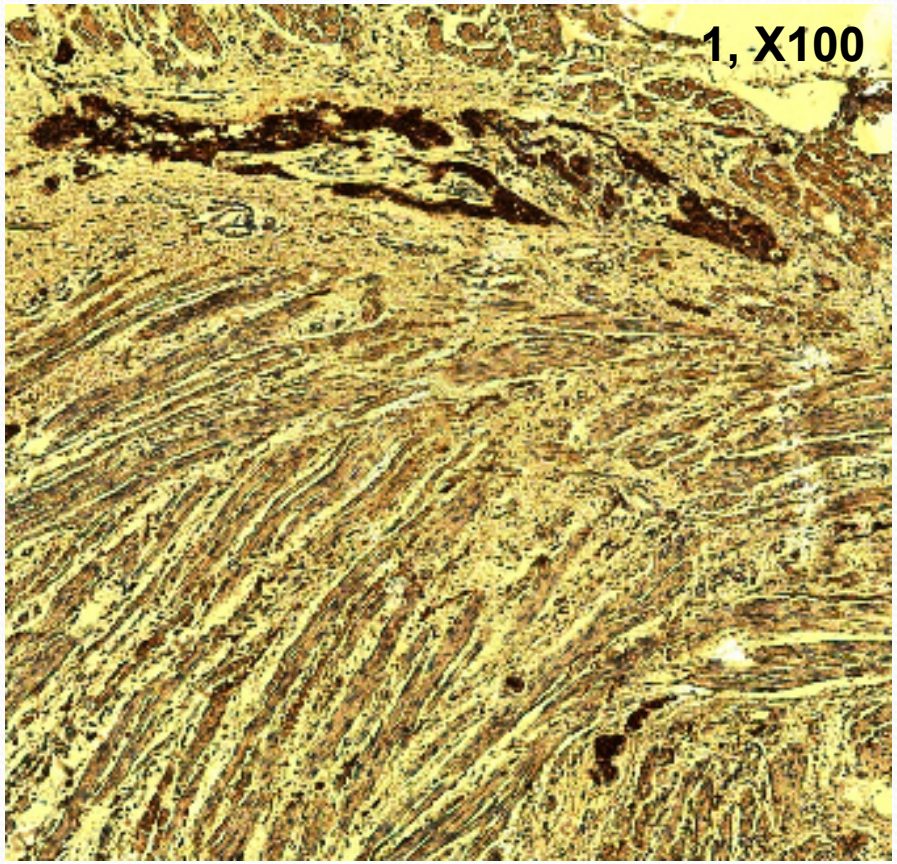
- **Nerve growth factor receptor, NGFR (code M3507, working dilution 1:150, *Dako*, USA);**
- **Protein gene product 9.5, PGP 9.5 (code Z5116, w.d. 1:200, *Dako*, Denmark);**
- **The first fibroblast growth factor receptor, FGFR1 (code ab 10646, w.d. 1:100, *Cambridge Science Park*, UK);**
- **Beta transforming growth factor, TGFβ (code ab 1279, w.d. 1:1000, *Cambridge Science Park*, UK);**
- **Vascular endothelial growth factor, VEGF (code M7273, w.d. 1:50, *Dako*, Denmark);**
- **Epidermal growth factor receptors, EGFR (code M3563, w.d. 1:200, *Dako*, USA);**
- **Matrix metaloprotease-2, MMP-2 (code AF902, w.d. 1:50, *RD Systems*, UK).**

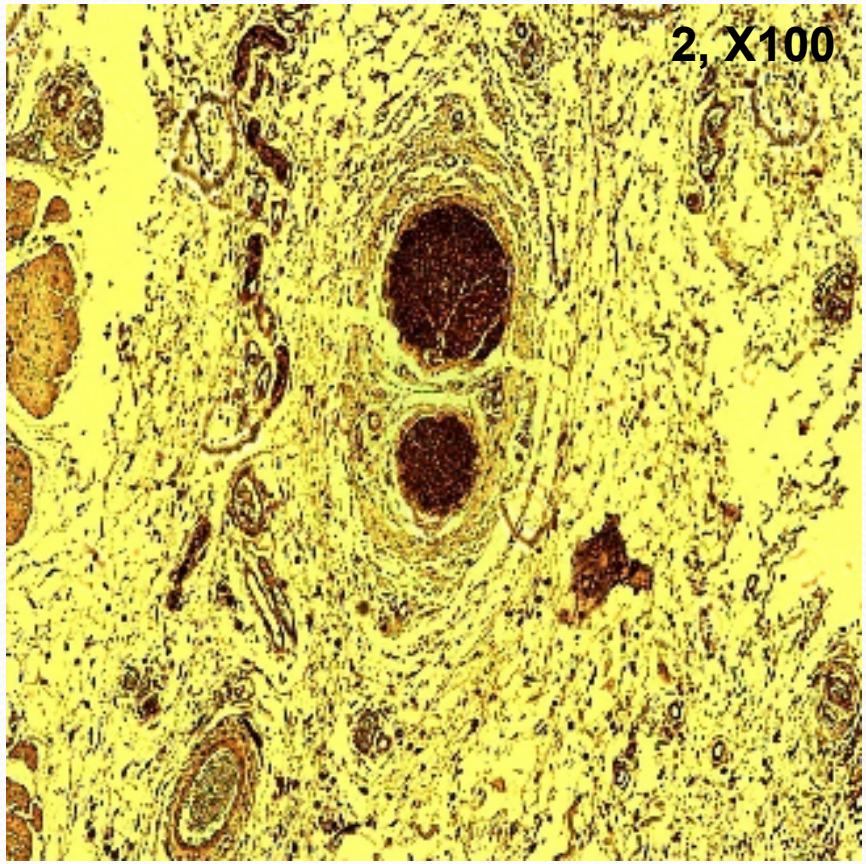
Using nonparametric Kruskal-Wallis Test statistical significant differences between groups showed the relative occurrence of PGP 9.5 (χ^2 = 7.847; p = 0.020), TGFβ (χ^2 = 20.609; p = 0.001), EGFR (χ^2 = 17.662; p = 0.001) and MMP-2 (χ^2 = 6.002; p = 0.050).

Table 1. Relative occurrence of growth factors, their receptors, innervation markers, and tissue degradating enzymes in EA and controls.

Material/ /Factors	NGFRp75	PGP 9.5	TGFβ	FGFR	VEGF	EGFR	MMP-2
Proximal esophagus; n=2	+++	++	0/+	++++	0	0-0/+	++
Distal esophagus; n=13	+++/++++	+++	0/+	++++	0	0-0/+	+++/ /++++
Control; n=12	+++/ /++++	++/ /++++	+++/ /++++	++++	0	++	+++

In EA, moderate and numerous PGP 9.5-containing nerve fibres and bundles were detected around blood vessels and in the Auerbah´s plexus (Fig. 1). The proximal esophagus showed moderate, but distal part - numerous PGP 9.5-containing nerves. In controls, the numerous and abundant number of PGP 9.5-containing nerves was seen (Fig. 2).

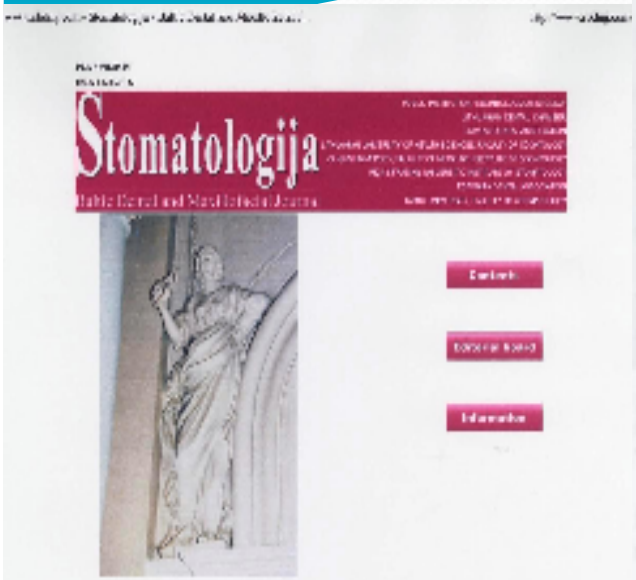




CONCLUSIONS

- **The decrease of PGP 9.5-containing neuronal structures in proximal esophagus supports insufficient innervation of this part of organ in EA.**
- **Low expression of TGFβ and almost absence of EGFR in EA may deal with disturbances in cell growth, proliferation and differentiation indicating significant role of these substances in morphopathogenesis of EA.**
- **Decrease of MMP-2 cells in EA affected proximal esophagus indicates the possible decrease of tissue adaptive/ regenerative reactions.**
- **FGFR, NGFR and VEGF seem not to characterize EA pathogenesis.**

II TMJ...



24-Nov-2011

...Dear Dr. Pilmane:

The manuscript, entitled "Apoptosis of temporomandibular joint disc with internal derangement involves mitochondrial-dependent pathways. An “in vivo”study" has been submitted to Acta Odontologica Scandinavica.

I would be grateful if you would kindly agree to act as a reviewer for this paper...

Sincerely,

Prof. Peter Holbrook

Editor, Acta Odontologica Scandinavica

Stomatologija, Baltic Dental and Maxillofacial Journal, 13: 96-101, 2011

Growth factors, genes, bone proteins and apoptosis in the temporomandibular joint (TMJ) of children with ankylosis and during disease recurrence

Mara Pilmane, Andrejs Skagers

SUMMARY

Aim of study was complex detection of appearance and distribution of growth factors, facial bone growth stimulating genes, ground substance proteins and apoptosis in bone of ankylotic TMJ in primary and repeatedly operated children.

Materials and Methods. Ankylotic tissue was obtained during the arthroplastic surgery from two 6 years old children (boy and girl) with osseous type of disease. The girl underwent the repeated surgery in TMJ due to the same diagnosis in age of 12 years. Ankylotic tissue was proceeded for detection of BMP2/4, TGFβ, Msx2, osteopontin, osteocalcin immunohistochemically, and apoptosis.

Results demonstrated massive bone formation intermixed by neochondrogenesis, the lack of BMP 2/4, but abundant number of TGFβ-containing cells in bone of all tested cases. Despite rich osteopontin positive structures in bone obtained from both – primary and repeated surgery, osteocalcin demonstrated variable appearance in 6 years aged children, but was abundant in joint 5 years later during disease recurrence. Expression of Msx2 varied widely before, but with tendency to decrease stabilized until few positive cells in bone of 12 years old girl. Apoptosis practically was not detected in primarily operated TMJ, but massively affected the supportive tissue in girl with recurrent ankylosis.

Conclusions. The lack of BMP2/4 expression in ankylotic bone proves the disorders in cellular differentiation with simultaneous compensatory intensification of cellular proliferation and/or growth by rich expression of TGFβ leading to the remodelling of TMJ.

Mainly rich distribution of osteocalcin and osteopontin indicate the intensive mineralization processes of ankylotic bone.

Persistent Msx2 expression is characteristic for the supportive tissue of recurrent ankylosis of TMJ and indicates the persistent stimulation of bone growth compensatory limitated by massive increase of programmed cell death.

Key words: growth factors, osteopontin, osteonectin, apoptosis, temporomandibular joint, children.