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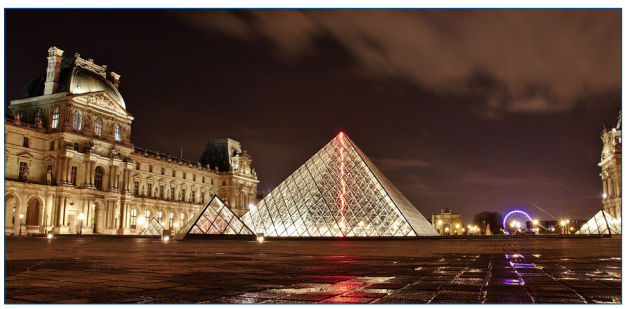

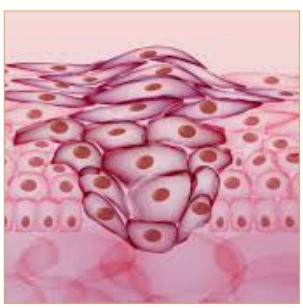
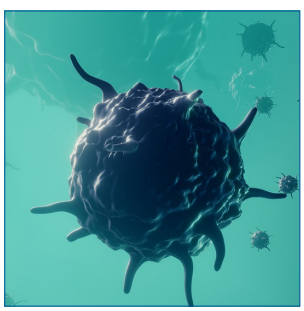

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July 05-06, 2019 | Paris, France

Retinal image analysis for diabetics and hypertension

Patil Sarika B and **B P Patil**
Sinhgad College of Engineering, India

Retinopathy is an acute disease to retina of a human. Retina of a person gets affected due to lifestyle diseases like diabetics and hypertension known as diabetic and hypertensive retinopathy respectively. Diabetic retinopathy is the leading cause of global blindness. The World Health Organization has launched "Vision 2020", a global initiative for the prevention of avoidable visual impairment by the year 2020. Early detection of features often not directly discernible by clinical investigation has the potential to reduce the global burden of diabetes and cardiovascular disease. Fundus photography has made it possible to analyse human retina noninvasively. Engineering tools such as digital image processing combined with advanced machine learning allow identification and automated classification of features like optic disk, macula and blood vessels, lesions and retinal blood vessel changes named microanurysms, haemorrhages, cotton wool spots, hard exudates, venous beading in digital images of the retina. Online databases like DRIVE, HRF, VICAR, Image ret along with ground truths are made available for researchers to work on and compare their results with state-of-the-art methods.

Speaker Biography

Patil Sarika is pursuing PhD in Medical Image Processing under Savitribai Phule Pune University, Pune. She has completed her master's in engineering in June 2008 from SPPU, Pune. She is professor of SPPU University, Pune. She has over 15 publications on her name in various national and international conferences and journals (SNIP and SJR Index). One paper is published in Scopus Indexed journal - Journal of Intelligent and Fuzzy Systems, IOS Press, Netherlands. She has worked on project funded by University of Pune Rs.2,50,000 in image processing. Implemented and proposed various algorithms for various feature and lesion detection in retina using image processing. Till now 11 students have completed their projects at master's degree under her guidance.

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Telogen-pattern hair loss as a presenting symptom of GAPO syndrome

Burhan Ahmed[1] and **Sami Girtli**[2]
[1]Clinique Dermatologie, Pakistan
[2]Harvard University, USA

GAPO syndrome is the acronym for Growth retardation, Alopecia, Pseudoanodontia and Optic atrophy. In children, androgenetic alopecia is rarer and its prevalence is not well known. I present to the audience a unique case of GAPO syndrome that presented to us with androgenetic pattern alopecia starting as early as two years of age and progressing within a year to Hamilton–Norwood type VII. I will explore the possible other reasons for such condition and importance of including GAPO syndrome as a differential in diagnosis when a dermatologist, pediatrician or plastic surgeons gets a case like this.

Speaker Biography

Burhan Ahmed, MD, MACP, MSc is currently a consultant dermatologist at Clinique Dermatologie in Pakistan and editor-in-chief at Medicalopedia.org. He completed his residency from Michigan State University in 2015 and masters in dermatology from University of South Wales, UK in 2018.

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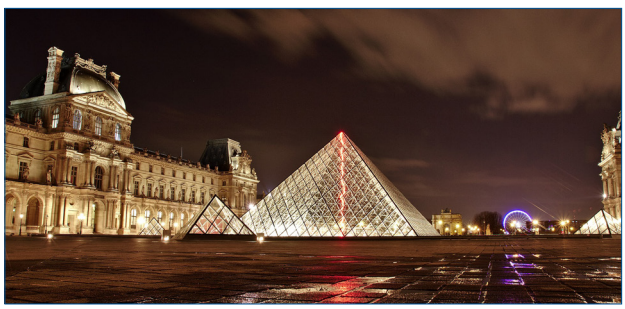

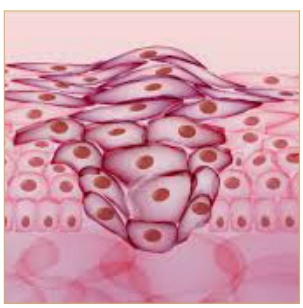
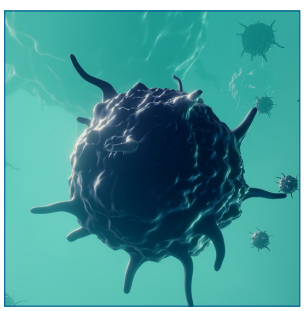

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Prevalence of periodontal disease and adverse events in pregnancy in high risk pregnant

Ana Paula de Lima Oliveira
Federal University of Uberlândia, Brazil

Periodontal disease during pregnancy can lead to adverse outcomes such as preterm delivery, low birth weight and preeclampsia. In this context, the dental monitoring of pregnant women with periodontal disease is very important. Our study aimed to evaluate periodontal health in a group of high-risk pregnant women (cardiac, hypertensive, diabetic, among others) who attend the clinic of pregnant women at the Hospital das Clínicas de Uberlândia - HCU-UFU, Brazil. Examinations of plaque index, depth of probing, mobility, bleeding on probing and the gingival margin level was measured to evaluate the degree of loss of periodontal insertion and the severity of periodontal disease. Oral hygiene instruction procedures were performed and prophylaxis in pregnant women and supra and subgingival scaling when necessary. At the end, the patients' medical records were evaluated to see if any adverse outcome occurred during pregnancy or delivery. The majority of pregnant women presented periodontal disease (78.8%), with higher values for periodontitis and gingivitis. Most of the pregnant women presented some type of problem at delivery (58.33% of the patients) and 57.14% of these women who had problem at delivery had periodontal disease. Although the results show that most high-risk pregnant women with periodontal disease presented with adverse events during labor. However studies with a larger sample size were necessary to confirm the relationship between periodontal disease and adverse pregnancy events.

Speaker Biography

Ana Paula de Lima Oliveira is a PhD in Periodontology. She completed the research scholar program in Periodontology at the Forsyth Institute, Boston, USA and studied oral microbiology and oral immunology at Harvard Dental Medical School in Boston, USA (2009). She is currently a professor of periodontology at faculty of dentistry of Federal University of Uberlândia, Minas Gerais/Brazil, where she does research in the area of periodontal diseases and systemic disturbance.

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AnnexinA7 knockdown could suppress cell proliferation and metastasis in gastric cancer

Xin Li
Chengde Medical University, China

Gastric cancer is one of the most deadly disease around the world. However, the mechanism of it is still unclear. AnnexinA7 is one of the calcium-dependent phospholipid binding protein which is involved in the cell membrane dynamics and cell signal transduction. Whether AnnexinA7 play any role in the development of gastric cancer is still unknown. In this study, RNA interfering was performed to silence AnnexinA7 in gastric cancer cell lines MGC-803 and MKN-45. Cell proliferation was detected by MTT method, while cell metastasis was examined by wound healing assay and trans well assay respectively. Western blotting was employed to detect the expression of the EMT marker genes and the key genes in the ERK signal pathway. Our results indicated that AnnexinA7 acted as an oncogene suppressor and could suppress cell proliferation and metastasis in gastric cancer which might via ERK signal pathway.

Speaker Biography

Xin Li has completed her PhD at the age of 36 years from Hebei Medical University, China. She is the professor of Chengde Medical University, China.

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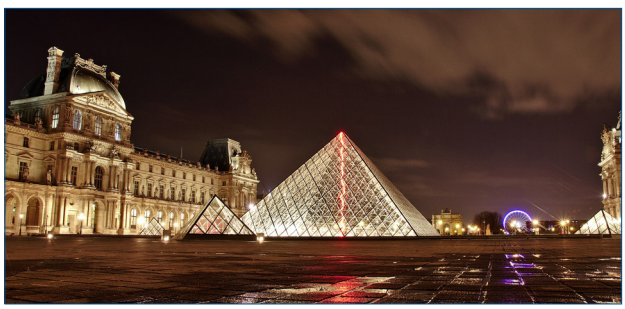

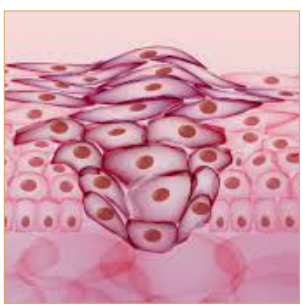
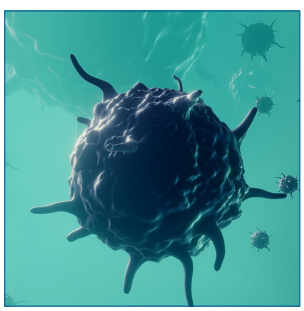

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Psychological features of breast cancer in Mexican women

Tania Romo-González T, Antonia Barranca-Enríquez, Iván Montes-Nogueira I, Rosalba León Díaz, Yolanda Campos-Uscanga, Gabriel Gutiérrez-Ospina, Ángel J Sánchez-García and **Carolina Palmeros Exsome**
Universidad Veracruzana, Mexico

Breast cancer (BC) is one of the oncological diseases most frequently diagnosed in adult women worldwide. As with other cancer types, BC is thought to emerge after genetically susceptible stem epithelial cells display uncontrolled proliferation after being chronically exposed to stressful environmental conditions that may include altered hormonal profiles, metabolic status and/or surrounding environmental settings. This scenario, nonetheless, fails to recognize the role that psychological factors play on BC origin, progression and outcome. We study if some psychological traits may predispose Mexican women to develop BC and also explore the "relative weight" that emotional suppression and repression and stress symptoms have on the likelihood of women developing BC by establishing, through network analyses, the way these psychological traits interact with well accepted BC-risk environmental, genetic and physiological factors. Our results indicated that women diagnosed with benign or malign breast pathology share low restraint, low global stress symptoms, low physical stress symptoms, low restraint-defensiveness composite and high distress before diagnosis. This outcome was independent of the educational level, as well as of family, reproductive and nutritional histories, supporting that the weight of the psychological traits is greater than that of the latter variables, at least in our sample. Also, the results show that the psychological traits, as expected, adopt a network organization, in which BC patients had the most disconnected distribution, followed by the benign breast pathology (BBP) group. Breast pathology according to the resulting network seems to disconnect emotions from the stress response. Addtionally, the variance found between groups can only be explained by psychological traits, that is, in this sample only certain psychological traits increase the susceptibility to BC but none of the most recognized clinical factors do.

Speaker Biography

Tania Romo-González is a pharmaceutical biologist by the Universidad Veracruzana (UV), with a Doctorate (Honorary Mention) in basic biomedical research from the National Autonomous University of Mexico (UNAM), a postdoctoral stay at the Biomedical Research Institute, UNAM, period 2012-2013. She has been an associate professor in the master in neuroethology and full professor at the Faculty of Biology of the Universidad Veracruzana. Her areas of interest are psychoneuroimmunology, health-disease processes, prevention of drug use. She has directed thesis at the bachelor's and master's level. She is National Researcher Level I of the National System of Researchers (SNI) 2013-2015. Professor with desirable profile PROMEP. 2012-2015. She has published articles in national and international journals, as well as book chapters in national publishers.

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Improvement in quality of life through the use of mandibular advancement Herbst appliance in patient with obstructive sleep apnea

Ana Carolina Costa Stival, Danilo Cassiano Ferraz, Thalles Eduardo Ribeiro, Allyne Jorcelino Daloia de Carvalho, Anahi de Paula Melo, Jéssica Ribeiro Damasceno, Kássia Gabriela Silva Ribeiro, Rafael Antonio Veloso Caixeta, Ana Paula de Lima Oliveira and **Paulo Cezar Simamoto Junior**

Federal University of Uberlândia, Brazil

Obstructive sleep apnea (OSA) is a disorder caused by partial or total upper airway obstruction during sleep. It is believed that pharyngeal airway obstruction improves with mandibular advancement by using oral appliances. Patient with 23 years, male, bring forward the clinic at University of Uberlândia an obstruction during sleep, was diagnosed OSA with the help of polysomnography. Additionally, it was necessary a laryngoscopy performed by a doctor for diagnosis of partial or total obstruction upper airway. Herbst therapy was chosen, which consists in preparation of a device for mandibular advancement. The patient had to use the appliance for 6 months in an attempt to prevent obstruction. After this period, it was applied a questionnaire which evaluates the patient's quality of life after using Herbst appliance. To colloborate this analysis, it was performed a final polysomnography. The results presented significant differences on the quality of life of this patient. Therefore, the Herbst appliance could be used in cases of upper airway obstruction as an alternative to conventional treatment for this type of disorder.

Speaker Biography

Ana Carolina Costa Stival is a coordinator at Ministry of Science and Technology in Brazil and she completed her education at Federal University of Rio Grande do Sul in Brazil.

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Inflammatory radicular cyst

Denildo De Magalhães, Karine Regina Tolesano Loureiro , Rafael Pires Vaz, Isabella Resende Vieira, Gabriel Sousa Lima, Jessica Stephanie Martins, Thalita Braga Nazario and **Ana Paula de Lima Oliveira**
Federal University od Uberlandia, Brazil

Patient, 27 years old, male, brown-skinned was referred to the Federal University of Uberlândia's Dental care unit for an endodontic treatment of the left maxillary central incisor. Intraoral clinical and radiographic examination suggested a hypothesis of diagnosis compatible with chronic apical periodontitis. The treatment was performed in two sessions, using manual instrumentation system according to the goerig technique combined with replacement of the intracanal medication in between sessions. The obturation was satisfactory and the tooth was restored with a pin-retained metal ceramic crown. Six months posterior to the treatment, the patient returned presenting clinical signs of a fistula. Radiographic examination sustained the hypothesis of chronic apical periodontitis (cyst or granuloma). It was suggested the patient should undergo an apicectomy surgery followed by an excisional biopsy of the lesion preserving the restorative prosthetic treatment and discarding the possibility of an endodontic retreatment. After the flap was lifted, it became possible to identify a crack in the root, which was confirmed by the colorimetric method. The sample was stored in 10% formaldehyde and sent to histopathological analysis at the Federal University of Uberlândia's pathological laboratory. The results suggested inflammatory odontogenic cyst, root cyst type. Six months posterior the procedure, the fistula returned and the tooth was kept on follow up. In this case, the parendodontic surgery represented the most conservative plan of treatment. It is important to emphasize the need to send the biopsied tissue to histopathological analysis to confirm the diagnosis and help the patient's condition preservation.

Speaker Biography

Denildo de Magalhães, PhD and MSc in Dentistry from the University of São Paulo, Brazil. He is currently a full professor at the Federal University of Uberlândia in the faculty of dentistry in the area of Periodontics.

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Proliferative verrucous leukoplakia

Karine Regina Tolesano Loureiro, Larissa Ayres Scagliarini Alvares, Juliana Prado Domingues, Laura Aguiar Pastori, Aline Rodrigues Renovato, Suzanna dos Santos Silva, Ana Paula de Lima Oliveira, Paulo Cézar Simamoto Júnior and **Denildo de Magalhães**

Federal University of Uberlandia, Brazil

Verrucous carcinoma and proliferative verrucous leukoplakia resemble histopathologically at some stage of their evolution making the differential diagnosis between both diseases much more difficult and, as for the final diagnosis, it often depends on clinical, epidemiological and histopathological data. A 58-year-old female patient was admitted to the University's Dental Care Unit complaining about oral lesions which had developed in the last 6 months. At clinical examination, it was possible to observe the edentulous mandible presenting smooth and non- homogeneous white plaques, with a papillary surface, erythematous areas and multifocal lesions. Incisional biopsy was performed in five distinct sites of the edentulous mandible and the samples were stored under same conditions in 10% formaldehyde and sent to histopathological analysis at the Federal University of Uberlândia's pathological laboratory. Histological sections revealed: Mucosa epithelium presenting hyperkeratosis and mild dysplasia. Mucosal epithelium presenting hyperkeratosis, marked papillomatosis and mild dysplasia, compatible with verrucous hyperplasia with mild dysplasia. Mucosal epithelium presenting hyperkeratosis, focal papillomatosis, slight dysplasia, suggesting the presence of invasion area (microinvasive squamous cell carcinoma). Summing up, proliferative verrucous leukoplakia diagnosis relied on clinical and histopathological data. The patient was referred to the Cancer Hospital for further treatment. However, this clinical case report illustrates the aggressive and relentless manner that is the carcinogenic evolution of this condition emphasizing the need of these patients to have a solid support system.

Speaker Biography

Karine Regina Tolesano Loureiro, PhD student and MSc in dentistry from the Federal University of Uberlandia. She is a specialist in oral maxillofacial surgery and traumatology and implantodontics from Pontifica Universidade Católica de Minas Gerais - Brazil.

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Comparative study of GATA3 and CD147 overexpression in urinary bladder carcinoma: Diagnostic and prognostic implications

Nehal Abd El-Ghaffar Heabah, Mohammed Farid Aref, Mohamed Alaa Mokhtar, Mohamed Moustafa Shareef and **Ahlam Mohamed Abo El-Enain**

Tanta University, Egypt

Introduction: Urinary bladder carcinoma is an international health problem and the most common urologic malignancy, particularly in males. Many efforts were made to investigate the role of GATA3 and smoothelin as diagnostic markers for bladder carcinoma and CD147 (EMMPRIN) as a prognostic and potentially therapeutic one.

Aim of the work: This study aimed to study the immunohistochemical expression of GATA3, smoothelin and CD147 (EMMPRIN) in urinary bladder carcinoma and its available morphological variants and to correlate the immunohistochemical results of these markers with the available clinicopathological parameters.

Materials and methods: Paraffin blocks from 85 cases of urinary bladder carcinoma patients including: 69 cases of urothelial carcinoma (UC), 10 cases of squamous cell carcinoma (SCC), 5 cases of adenocarcinoma and one case of neuroendocrine small cell carcinoma were stained by GATA3, smoothelin and CD147 immunohistochemical markers.

Results: GATA3 exhibited high sensitivity (87%) and specificity (100%) as a diagnostic marker for urothelial carcinoma. Strong nuclear GATA3 expression (+3) had been found in all cases of low grade urothelial carcinoma, plasmacytoid, microcystic, micro-papillary and clear cell urothelial carcinoma while showed a range of sensitivity as a marker for urothelial carcinomas with variant morphologic features as squamous and sarcomatoid differentiation.

A statistically significant relations was found between GATA3 expression and tumor grade and stage, so that reduction in GATA3 expression was associated with high-grade and muscle invasive bladder carcinoma. Smoothelin proved an important diagnostic utility, allowing distinction of the muscularis propria MP (positive smoothelin expression) from the muscularis mucosa MM (negative smoothelin expression). The sensitivity and specificity of smoothelin in detecting MP invasion in the current study was 100%. Regarding CD147 expression, positive CD147 staining was significantly associated with high tumor grade and muscle invasion.

Conclusion: GATA3 acts as a valuable tool for confirming the urothelial origin of microcystic, micropapillary, plasmacytoid and clear cell variants of urothelial carcinoma. Also, decreased GATA3 expression is associated with high tumor grade and MP invasion. It is important to use smoothelin immunohistochemistry as a routine in all cases of TURBT specimens for accurate staging and subsequent optimal patient management. CD147 positive expression is significantly related to high grade and advanced stage of bladder carcinoma.

Speaker Biography

Nehal Abd El-Ghaffar Heabah has completed her Master from Tanta University. She works as an assistant lecturer: Faculty of Medicine, Tanta University, Egypt from 2015-till present. She performed Master thesis entitled: "An immunohistochemical and image analysis study of fragile histidine triad (FHIT) protein expression in colorectal adenoma and carcinoma", January 2015 and Medical Doctoral thesis entitled: "Immunohistochemical Study of GATA3, Smoothelin and CD147 Expression in Urinary Bladder Carcinoma", March 2019.

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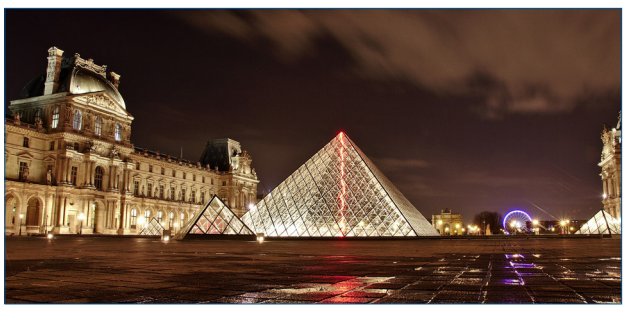

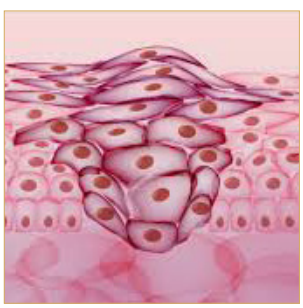
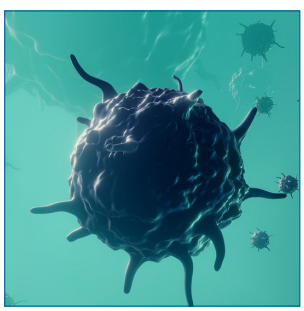

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Surgical and non-surgical management and treatment of glioblastomas

Alain L Fymat
International Institute of Medicine & Science, USA

Glioblastoma is the common brain tumor in adults. It remains an unmet need in oncology. To gauge the difficulties encountered in devising treatment lines, I will first review the morphology of brain cancers, their different biological types and their associated risks. It is important to grasp how a diagnosis of a suspected such tumor could be arrived at in both the initial and the very often recurring case, and what are the prognoses in these several instances. I will also detail the various treatments that have been devised so far for primary tumors and their metastases in both cases of monotherapies or combination therapies and for recurring tumors after treatment. For each such therapy, the treatment results obtained in clinical trials and other reported practices will also be discussed and summarized. At the outset, however, it must be recalled that the use of cytotoxic drugs (chemotherapy) is essentially an educated trial-and-error approach with one approved drug or a combination of a number of such drugs. It does not rely on the deep understanding of the tumor biology nor does it consider the braiding of both normal and cancerous cells that is embedded in our genome. As a result, it has historically provided little durable benefit with tumors recurring within several months, even in the case of more accessible tumors located outside the brain; for brain tumors, the access is even more difficult because of the presence of the brain protective barriers, compounding the difficulties. More effective therapies involving other options are required either in isolation or more likely in combination. Of these other options, the following will be considered: Surgery, conformal radiotherapy, boron neutron therapy, intensity modulated proton beam therapy, antiangiogenic therapy, alternating electric field therapy, without neglecting palliative therapies. Research conducted in these and other options will also be reviewed to include microRNA, immunotherapy, adjuvant therapy, gene therapy, stem cell therapy and intra-nasal drug delivery.

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Maxilla compound odontoma: Case report

Lair Mambrini Furtado
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The present paper aims to report the clinical case of a 12-year-old male patient that went to the buccomaxillofacial surgery and traumatology service from Federal University of Uberlândia – Minas Gerais - Brazil, by his dentist recommendation, seeking for evaluation of a radiopaque lesion in the upper canine region perceived during radiographic exams for investigation of prolonged retention of the permanent tooth. In the anamnesis, drug allergies were denied and a convulsive episode for over a year was reported. At the clinical examination, there was an increase in volume at the site evaluated and there was no pain symptomatology. After the tomography analysis, it was possible to detect a predominantly hyperdense image composed of several denticles in the right premaxilla region. The indicated treatment was surgical center exertion under general anesthesia by nasotracheal intubation. Material was collected for histopathological examination, which later confirmed the diagnosis of compound odontoma. Two weeks after surgical removal, the patient was in good general condition, without complains, with reduced edema and without phlogistic signs. After four months, tooth 53 was still present and the patient was instructed to discuss with orthodontist the possibility of permanent tooth traction.

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Recurrent EP300-BCOR fusions in pediatric gliomas with distinct clinicopathologic features

Sanda Alexandrescu

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BCOR is an epigenetic regulator and is genetically altered by mutation, deletion, or gene fusion in a range of cancers. "Central nervous system high-grade neuroepithelial tumor with BCOR alteration" is a recently described entity with characteristic internal tandem duplications within exon 15 of the BCOR gene (hereafter CNS HGNET-BCOR ex15 ITD). In this case series of three patients, we report the clinicopathologic, molecular (arrayCGH, RNA fusion analysis and targeted exome sequencing) and methylome features of gliomas with novel EP300-BCOR in-frame gene fusions, thus expanding the spectrum of BCOR alterations seen in CNS tumors. The gliomas in this series arise in children (age 10-18), involve the supratentorial compartment and have an infiltrative pattern of growth and a myxoid/microcystic background with frequent psammomatous calcifications and prominent chicken-wire vessels. All three cases had areas with low-grade morphology and two of them demonstrated histologic high-grade transformation. In contrast to CNS HGNET-BCOR ex15 ITD, they lack perivascular pseudorosettes. On methylation studies and a t-distributed stochastic neighbor embedding (tSNE) plot they cluster perfectly together, away from CNS HGNET-BCOR ex15ITD, consistent with a different entity. Gliomas with EP300-BCOR fusions and high-grade histology can demonstrate relatively rapid regrowth after debulking or subtotal resection. In conclusion, our study demonstrates that EP300-BCOR gliomas are a unique entity and calls for a more specific nomenclature for the existing HGNET-BCOR, as not all BCOR-altered gliomas are high-grade.

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An overall view of the new genetic developments that changed the classification of tumours of central nervous system

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University of Montreal School of Medicine, Canada

The last WHO classification of tumours of the nervous system of 2016 stresses the importance of genetic alterations that permitted the inclusion of new diagnostic categories. This is the case of tumours of the diffuse astrocytic type: Identification of mutations in the genes IDH-1 and IDH-2, either by immunohistochemistry or by genetic evaluation of mutations are important tools that have prognostic implications. A new entity has been added to this group with mutation of the H3K27M gene – diffuse midline glioma. The diagnosis of an oligodendroglial tumour needs the presence of co-deletions of the chromosomes 1p and 19q and mutation of the IDH-1 gene. Deletions or translocations resulting in BRAF fusion proteins are pathognomonic of pilocytic astrocytomas; Mutation of the FGFR1 are found in midline pilocytic astrocytomas. Many molecular alterations have been described in the ependymoma group: Cytogenetic aberrations, fusion genes involving the RELA or YAP1 genes are found in supratentorial ependymomas whereas for the spinal cord group present with genome wide polyploidy. These characteristics have prognostic implications. MGMT promoter methylation was described in all choroid plexus papilloma and mutations of the TP53 gene was found in almost all choroid plexus carcinoma and those exhibiting loss of the chromosome 12q are associated to a shorter survival. MYCN gain and overexpression of genes of the WNT signaling pathway were described in central neurocytomas. Medulloblastomas may be genetically or histologically defined with important prognostic implications. Finally, inversion on chromosome 12q13 generates the fusion of the NAB2 et STAT6 genes and induces the nuclear expression of STAT6 necessary for the diagnosis of the solitary fibrous tumour/hemangiopericytoma. Since 2016 a number of new genotype varieties of tumours of the central nervous system have been added.

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Tyramid amplification system, an old and unappreciated powerful immunohistochemistry problem solving weapon. Hints for a simple and easy use of it

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The tyramide amplification system was first used in immunohistochemistry in the decade of 1990, but has never been very popular in spite of its capacity to increase in an extraordinary way the sensitivity and specificity of the regular immunostaining. The tyramide principle of action is based on the reactivity of this molecule with horseradish peroxidase (HRP) enzyme which causes a catalytic reporter deposit in close vicinity to the epitope of interest. With this system we are able to use primary antibodies at a very high dilution which makes our immunolabeling more specific and also less expensive. It is also capable of detecting molecules that are very scarce or small or the ones that give weak signaling in our tissue, as it highly increases the size and intensity of the signal, enabling us to visualize a very precise and enhanced label without loss of resolution or increase in background. Other advantage of this amplification system includes the possibility to do a dual immuno-labeling with primary antibodies made in the same species, like the use of two primaries from mouse. Regarding the protocol of use of this technique, it is very important to utilize specific washing and protein blocking buffers to prevent having background or non specific binding. To do the tyramid system more versatile is recommendable to have HRP conjugated streptavidin (SA-HRP) which would favor the use of secondary biotinylated antibodies and to have HRP conjugated anti-fluorescein, that would allow to continue with the amplification step of an already fluorescein labeled slide with a weak signal. Finally the anti-fluorescein-HRP could be used with a fluorescein conjugated tyramid reagent to do a chromogenic detection without the need of a fluorescence microscope.

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Combinatory FK506 and minocycline treatment alleviates prion-induced neurodegenerative events via caspase-mediated MAPK-NRF2 pathway

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Transcription factors play a significant role during the symptomatic onset and progression of prion diseases. We previously showed the immunomodulatory and nuclear factor of activated T cells' (NFAT) suppressive effects of an immunosuppressant, FK506, in the symptomatic stage and an antibiotic, minocycline, in the pre-symptomatic stage of prion infection in hamsters. Here we used for the first time, a combinatory FK506+minocycline treatment to test its transcriptional modulating effects in the symptomatic stage of prion infection. Our results indicate that prolonged treatment with FK506+minocycline was effective in alleviating astrogliosis and neuronal death triggered by misfolded prions. Specifically, the combinatory therapy with FK506+minocycline lowered the expression of the astrocytes activation marker GFAP and of the microglial activation marker IBA-1, subsequently reducing the level of pro-inflammatory cytokines interleukin 1 beta (IL-1β) and tumor necrosis factor alpha (TNF-α) and increasing the levels of anti- inflammatory cytokines IL-10 and IL-27. We further found that FK506+minocycline treatment inhibited mitogen-activated protein kinase (MAPK) p38 phosphorylation, NF-kB nuclear translocation, caspase expression and enhanced phosphorylated cAMP response element-binding protein (pCREB) and phosphorylated Bcl2-associated death promoter (pBAD) levels to reduce cognitive impairment and apoptosis. Interestingly, FK506+minocycline reduced mitochondrial fragmentation and promoted nuclear factor–erythroid2-related factor-2 (NRF2)-heme oxygenase 1 (HO-1) pathway to enhance survival. Taken together, our results show that a therapeutic cocktail of FK506+minocycline is an attractive candidate for prolonged use in prion diseases and we encourage its further clinical development as a possible treatment for this disease.

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Study the clinicopathological characteristics of primary malignancies of GIT in patients ≤ 40 years of age and association of a positive family history

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Background: Gastrointestinal (GI) malignancies have been on the rise in the young. This age group is associated with advanced stages at presentation and aggressive histologies. Kashmir has a considerable burden of GI cancers as compared to the rest of the country with gastric, esophageal and colorectal malignancies in the lead, but their comprehensive profile in a young Kashmiri population has not been gauged so far.

Objective: To study the clinicopathological characteristics of primary malignancies of GIT in patients ≤ 40 years of age and association of a positive family history.

Study design: A 5 years observational study, divided into 1.5 years of prospective and 3.5 years of retrospective analysis, extending from 2013-2017.

Methods: The relevant details of cases fulfilling the inclusion criteria were noted as per the proforma. Resection specimens and biopsies were received and processed, archived samples were retrieved and the cases analysed. Staging, wherever applicable was done as per 8th AJCC guidelines. Frequency distribution tables, bar diagrams and pie charts were used for data presentation.

Results: 511/5676 cases (9%) of total registered primary GI malignancies were present in our study group. The leading sites were Anorectum (149, 29.1%), stomach (124, 24.3%), esophagus (113, 22.1%) and colon (104, 20.3%). Adenocarcinoma was the leading histology (388/511, 75.9%), followed by squamous cell carcinoma (92/511, 18%), neuroendocrine tumors (13, 2.5%) and 8 (1.6%) cases each of GISTs and lymphomas. Mean duration of complaints was 6.4±7.2 months. Majority cases had advanced stages (III-IV) at presentation and aggressive histologies in the form of poorly differentiated lesions and signet ring cell carcinomas. 44/511 (8.6%) of the total study cases had a documented positive family history.

Conclusions: Cases presented with nonspecific and protracted symptomatology, advanced stages and poorly differentiated lesions. Familial association could imply a hereditary component or aggregation of shared environmental risk factors or both.

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Experimental facilities pave the rainbow access of the herbal melanin

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Backgrounds: Melanin is a polymer found in most organisms acts as natural biological, antioxidants factor by reducing oxidative stress and inflammatory reaction of cells. It is playing a vital role as an antioxidant agent as well as its scavenging activities on free radicals. Also, melanin acts as immunoprotective polymers preventing the tissues and cells via its absorbable acts against ultraviolet and/or other radiation and thus prevents any injured of the cells. Recently, melanin has been extracted from the *Nigella sativa* seeds (NSM) and thus researched for biomedical applications such as natural protective agent with therapeutic effectiveness and targeted as a natural therapeutic or drug delivery. This work presents a general view of NSM extracts as a promising agent due to its therapeutic outcomes using *in vivo* and *in vitro* methods. Using of this type of melanin could play an important role through the biological needs and/or could pave the way as an active field of research including biochemistry, biomedical, dermatological, cosmetic therapies and microbiological points of view, as well as health care industry.

Methods: In the current study, the latest published works were studied to analyze the trend and pattern of the NSM extracts and the impacts of machine learning methods. Applications of histopathological methods and preclinical imaging computerized techniques such as computed tomography (CT) and nano CT Scans were also investigated for the prediction and interpretation of the amelioration effects of the NSM extracts via *in vivo* and *in vitro* clinical models.

Results: The results showed that NSM produced significant pathological and morphological changes in dose-and time-dependent manners in different organs architecture during both *in vivo* and *in vitro* experiments. In therapeutic development phases, it is well known the advantages of computerized data outcomes and it can be of importance related databases led to the success of the whole pharmacotherapy modalities and/or provide to the scientific field a new key transformative paradigms that can revolutionize the treatment of diseases and hence medical care.

Conclusion: Experimental *in vivo* and *in vitro* researches are valuable but also expensive and in some cases, researchers may suffer from limitations. But a well understanding of the therapeutic effects of this herbal extracts might pave the way and thus provides a robust means a better designing for much more effective natural medicinal agent or therapeutic products and also grantees the patient safety.

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