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Anatomy

RECENT ADVANCES IN CRANIOSYNOSTOSIS AND FUTURE PROSPECTIVE

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ABSTRACT

Objective: Craniosynostosis (CS) is the premature ossification and genetically heterogeneous in conditions. We aim to focus on recent advances with future prospective on Craniosynostosis.

Material and Methods: We observed (since1990 to till 2017) through different databases of world literature and add our experience with recent advances and future prospective in Craniosynostosis in both the group (syndromic and non syndromic) and additional anomalies.

Results: The pathologies result from complete loss of gene function, biochemical mechanisms involving haploinsufficiency, dominant gain-of-function and recessive hypomorphic mutation (RHM). X-linked cellular interference process been implicatedfew of the genes involved could predicted based on their expression patterns. Genes play much wider roles in embryonic development or cellular homeostasis (CH). Here we argue that they fit into a limited number of functional modules active at different stages of cranial suture development (CSD).

Conclusion: Recent advances in neurosurgery, neuromonitoring and neurointensive care (NIC) have dramatically improved the outcome in patients affected by surgical lesions of central nervous system (CNS). Most of these techniques were applied first in the adult population; paediatric patients present a set of inherent challenges.Recently their developing and maturing neurological and physiological status, apart from the CS disease process and phenotypic pattern.

KEYWORDS : craniofacial; craniosynostosis; gene mutations; malformation; skull sutures; recent advances;prospective

INTRODUCTION

Craniosynostosis (CS) is the premature ossification of one or more skull sutures [1].It is a clinically and genetically a group of heterogeneous congenital anomaly (HCA), affecting approximately one in 2,500 live births globally. In Indian scenario 1:1000 [2-3]. CS occurs as an isolated congenital anomaly, that is, nonsyndromic craniosynostosis (NCS) [4]. The major causes of the disease are genetic, and environmental. Other causes remain largely unknown [5]. Researcher believe that some of the midline NCS cases may be explained by two loci inheritance,approximately in 25-30% of the patients[6]. In craniofacial disorders, upper airway obstruction (UAO) is one of the primary causes for morbidity and mortality, in the neonatal period, including Pierre Robin sequence, which is high risk for obstructive sleep apnea syndrome (OSAS)[7-8-9]. Nonsyndromic craniosynostosis (NSC) is basically associated with significant learning disability, later in life [10].This small cohort supportedby the primary goal of surgery in allowing for more normalized brain growth [11]. Largesample, and correlating degree of normalization with cognitive performance in NSC, is warranted [12]. In this article, we discuss the recent advances in our understanding of the embryology of craniofacial conditions, and we focus on the use of animal models to guide rational therapies [13]. Further Genetics and biochemistrymay lead for further future prospective of Craniosynostosis (CS) and other additional anomalies [14-15].

MATERIALAND METHODS

We observed (since1990 to till 2017) through different databases of world literature and add our experience with recent advances and future prospective in CSin both the group (syndromic and non syndromic). We provides current approaches in craniofacial surgery for treating states of bone excess and deficit, recent advances in our understanding of the molecular and cellular processes underlying craniosynostosis, a pathological state of bone excess (PSOBE) and current research efforts in cellular-based therapies (CBT) for bone regeneration and its recent advances and future prospective for craniosynostosis (CS) amongst both the group.

RESULTS

Recently, new approach to dissect the underlying causes from investigation of clinical samples, and recent advances in high-throughput DNA sequencing have dramatically enhanced the human subject as the preferred as model [16-17-18]. Most CS, investigation of mechanisms requires more conventional model organisms (CMO) [19].Inmouse, similarities in cranial suture development (CSD) present a framework for classifying genetic causes of craniosynostosis (CS) [20].Current understanding of cranial suture biology with molecular and developmental pathogenesis and pathologies result from complete loss of gene function (CLOGF) [21]. Biochemical mechanisms involving haploinsufficiency, dominant gain-of-function and recessive hypomorphic mutations (RHM) and X-linked cellular interference process are important [22]. Expression patterns of the genes play much wider roles in embryonic development or cellular homeostasis at different stages of cranial suture development (CSD) [23-24].CS defining as the potential avenuesfordevising pharmacological approaches for newmolecular targetedtherapy (MTT) [25].

Development of the craniofacial region is a remarkably complex and tightly orchestrated process with genetic and environmental insults frequently results in craniofacial anomalies [26]. In our knowledge of theircell fate in etiology and pathogenesis is still scarce, limiting our efforts for preventing diseases [27]. New standardized protocols have been developed to guide clinical and surgical interventions on the most recent research advances on craniofacial conditions [28], from genomics and epigenetics to ontology and medical care are discussed with emphasis on the most common anomalies (CA) of the craniofacial region like(facial clefts, craniosynostosis, craniofacial microsomia, facial dysostosis, Robin sequence, jaw and dentition anomalies, and anterior neural tube defects) [29-30].As a phenotypic variability and the importance of standardized terminology to better distinguish between phenotypes, new technologies for genetic diagnosis, and the use of mouse models to study these conditions, complex phenotypic and genetic aspects are highlighted [31-32].Recent advances in neurosurgery, neuromonitoring and neurointensive care have dramatically improved the outcome in patients affected by surgical lesions of central nervous system (CNS) [33]. Although most of these techniques were applied first in the adult population, paediatric patients present a set of inherent challenges because of their developing and maturing neurological and physiological status, apart from the CNS disease process [34-35-36].Syndromic craniosynostose (SCS) and (CBT) exhibits variable clinical and genetic heterogeneity condition [37]. The fibroblast growth factor receptor genes (FGFR1, FGFR2, FGFR3 (encoding fibroblast growth factor receptors), TWIST1 (functions as an upstream regulator of FGFRs) and EFNB1 (gene encoding fibrillin1) [38-39-40]. Recently, advances in molecular genetics have led to a discover of other genes implicated in different craniosynostosis syndromesas a priority [41-42].The transcription factor Twist (TWIST) plays vital roles during embryonic development

through regulating/controlling cell migration [43]. The transcriptional activities of Twist support cancer cells to disseminate from primary tumours and subsequently establish a secondary tumour growth (STG) in distant organs [44-45]. Recent advances in Twist regulation and activity, with a focus on phosphorylation-dependent Twist activity, potential upstream kinases contribution of these factors in transducing biological signals from upstream signalling complexes (USC) [46-47-48]. Rcent advances in particular areashave new light on the phosphorylation-dependent regulation (PDR) of the Twist proteins promotes or suppresses among the scene [49]. The Twist activity (TA) now leading to differential regulation of Twist transcriptional targets and thereby influencing the cell fatein easiest way in the cell fate (CF) [50-51].

DISCUSSION

Recent studies have demonstrated the impressive improvements in treatment outcome with the use of tyrosine kinase inhibitors (TKIs) [52]. High-resolution genomic profiling (HRGP), of genetic alterations and gene expression has revolutionized our understanding of the genetic basis of CS[53-54]activating mutations of Janus kinases, and rearrangement of the lymphoid cytokine receptor gene CRLF2 [55].Recent progress in elucidating the molecular and cellular mechanisms governing bone formation will have significant role in developing advanced therapies for the treatment of pathological states of bone excess and deficit (BEAD) and reengineering the bone access [56-57-58]. The health caresystem (HCS) are built on the evolution of technology fetal medicine technology(FMT), prenatal imaging (PI) / allow us to see and diagnose abnormalities [59-60].The oral and maxillofacial surgeon on the fetal diagnosis and treatment team required for correct deformity [61].

Recent advances in molecular genetics have led to a better understanding of the role of specific genes (fibroblast growth factor receptor (FGFR) and Twist as the root cause of cranial bone malformations (CBMF) and osteoblast abnormalities (OA)[62-63-64].The list of genes that are involved in CS includes those coding FGFR and a ligand of ephrin receptors (ER) [65-66].Genes encoding transcription factors, FGFR, MSX2 and TWIST genes are equally involved in skull formation, odontogenesis, providing a explanation for associations of CS and tooth malformations[67-68].Bone ridging seen on the ectocranial and endocranial surfaces of fused sagittal suture (FSS) pattern are not observed stenosis of coronal and lambdoid sutures [69-70]. This making it specific to sagittal suture only [69]. Thus there is a complex arrangement of the structure of the human cranium and the process of craniosynostosis, with some differences in final structure depending on the affected suture [70-71].
Fibroblast growth factor receptor (FGF) signalling pathway is involved in evolution and playscrucial roles in developmentof CS [72]. FGF signal pathway plays important role in suture and synchondrosis regulation (SR) [73]. FGF receptors relate to syndromatic and non-syndromatic CS basically located (Fgf10/Fgfr2b signal loop) is critical for palatogenesis and submandibular gland formation (SMGF) through mutation [74-75].

The principle of abnormal skull growth due to restriction of skull growth at the fused sutures [76], and the realization by Moss that the sutures at the skull base are equally affected, have been the main intellectual driving forces behind the majority of cranial expansion procedures in children with craniosynostosis (CS) diseases [77-78].The main subtypes of craniosynostosis and craniofacial dysostosis presented, including specific clinical features presently available surgical options[79].

Development and new application of various vehicles and tissue engineered constructs to deliver different cytokines, gene products andshort segment DNA, to treat CS [80]. Such therapy based on gene product may be used an adjuncts to surgeryand manage postoperative resynostosis [81]. Study of TWIST, FGFR-1, FGFR-2 and FGFR-3 genes in a cohort of patients with CS led to the diagnosis of Saethre-Chotzen syndrome (SCS) [82]. It is a newly diagnosed a new micro deletion disorder (MD) and reports the first example of a gene-environment interaction (GEI)[83].

Basic to Clinical approachthrough animal model and organism:

Many laboratories are investigating murine cranial suture biology as a model for human cranial suture development and fusion [84]. Normal murine cranial suture biology(MCSB) is very complex [85]. Evidencessuggestthat the dura mater provides the bimolecular blueprints, which guide the fate of the pleuripotent osteogenic fronts(POF) [86]. We have very little understanding the fundamental mechanisms of cranial suture fusion (CSF) [87]. Interestingly, recent advances in premature human and programmed murine suture fusion (PMSF) have revealed unexpected results[88].We present recent advances in the understanding of mechanisms of CS, with particular emphasis on the biology of programmed cranial suture fusion (PCSF) in rodents [89-90].Several surgical techniques have been described for correction of scaphocephaly [91].

Advances in the field of craniofacial surgeryhave allowed more extensive operative procedures [92].For the treatment of cranial vault anomalies (CVA) aim of surgical treatment is to prevent early refusion of the parietal bones [93].After the sagittal craniotomy associated with the widening of the biparietal diameter [94]. In children with older than 6 months, these procedures result are unsatisfactory, and provides only a partial correction of the malformation [95]. Therefore operative techniques of total cranial vault (TCV) reshaping are reported in the literature [96].Additionally occipital remolding is useful in young infants with a marked skull deformity. This technique will provide good results[97-98].Recently, human genome initiative has accelerated positional cloning efforts toward identification of a number of genes responsible for human developmental anomalies (HAD) [99-100-101].

CURRENT STATE OF KNOWLEDGE AND FUTURE PROSP ECTIVE

Premature fusion of the metopic suture is an uncommon form of craniosynostosis (CS)[102].The reported withan incidence of less than 10% among the various forms of craniosynostoses[103]. The most obvious deformity associated with premature fusion of a single suture with its prominent frontal keel, narrow forehead, and close-set eyes [104]. We discuss the timing and long-term results, of surgery [105]. Frontal bone advancement (FBA) and compensatory craniofacial growth (CCG) changes in rabbits with experimental coronal suture immobilization (CSI) very nicely [106]. Clinical advances in the surgical correction of coronal suture synostosis (CSS) involve the overcorrection of a frontal bone segment (FBS) to allow for unrestricted expansion of skull [107]. Animals those underwent frontal bone advancement (FBA) exhibited normal overall craniofacial growth by 18 weeks of age, compared with control animals [108].However, surface dysmorphology (SD) of the head in Apert syndrome known for a century [109]. A computer-assisted medical imaging technology (CAMIT) allows in vivo nondestructive "dissection." [110].Presently, the surgical correction of brachycephalic airway syndrome (BAS) in dogs has been reported good long-term outcomes [111-112].

CONCLUSION

Recent advances have been achieved in craniofacial surgery (CS) , improved the strategies for addressing states of bone excess (BE) and bone deficit (BD) in the craniofacial region (CR) are needed. The biomolecular events involved in craniosynostosis (CS and NSCS) and cellular-based bone tissue engineering (CBBTE) soon be added to the armamentarium of surgeons treating craniofacial dysmorphologies as an emerging cellular base therapy (CBT) for resolve these types of diseases as a priority in future management and early planning for patient benefit and research.

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Conflict of Interest: Nil

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