IN MEMORIAM MARIO COMPORTI 1935-2014 (CO-EDITOR-IN-CHIEF SINCE 2009)

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Mario Comporti was born in Siena and earned a high school diploma (Classical studies) at the local *Liceo Classico Enea Silvio Piccolomini.* He was proud of this title, and always firmly considered classical studies an essential aspect in the education of young generations. Mario attended as a student at the University of Siena the Institute of Medical Pathology managed by Cesare Bartorelli, and was positively impressed by the ability of many physicians of the Institute to connect the scientific research with the medical-care activity. That was the time period when research first captivated him, to follow him for the rest of his subsequent life. Comporti graduated with honours in 1960, and then worked as Assistant professor at the Institutes of General Pathology of Siena and Turin. In 1966 he was Research Associate at the Department of Physiology of the University of Tennessee, US. He moved in 1968 to the University of Pisa, where he was first Assistant professor and then Full Professor and Director at the Institute of General Pathology. In 1973 he moved to the University of Siena, where he was appointed Director of the Institute of General Pathology. In 1999, following the replacement of Institutes with Departments, Comporti was the Director of the Dept. of Physiopathology and Experimental Medicine till 2005. He retired in 2010. He was Regional Director of the National Foundation for Cancer Research (NFCR) from 1979 to 1986, and then of the Association for International Cancer Research (AICR). Comporti was a member of NATO Science Committee and Visiting professor at the J.A.Burns School of Medicine, US. He was awarded with Gold Medal of Merit for Culture and Science by the Italian Ministry of Education, and was the President of the Italian Society of Pathology for two terms of office. He was a member of the Editorial Board of important international journals as well as a Honorary Member of the Oxygen Club of California. He served as reviewer for illustrious international journals and was popular for his ability to fairly evaluate the others' works.

Freshly graduated, in 1965, Mario Comporti published two pieces of research whose titles were *'Inhibition of lipid peroxidation by CCL_4 in vitro and in vivo'* and *'Stimulation of the lipid peroxidation of rat liver homogenates by low concentration of CCL_4 in vitro'* respectively. These papers represent the original observation about the unsuspected relationship between certain hepatotoxic chemicals and lipid peroxidation. lt should be noted that in the latter of the aforementioned publications only Comporti's name appears, and that the co-author of the former did not publish any further work on this subject. Therefore, Comporti alone sensed the importance of a phenomenon that now - half a century later – we know to be involved in a multitude of pathological processes, such as atherosclerosis, cell death, carcinogenesis, etc. The concept embodied in that phenomenon subsequently expanded, and has been then globally interpreted as 'oxidative stress'. In the newborn child, oxidative stress is at the root of many serious complications of prematurity such as retinopa-

Mario Comporti.

thy, anoxic-ischemic and haemorrhagic brain injury, and bronchiolar-pulmonary dysplasia.

Once he had settled in Pisa at the beginning of 1970's Mario could build up his own research team, including three young and enthusiast co-workers: Angiolo Benedetti, Alessandro Casini – both MD's – and Marco Ferrali, PhD. The intense experimental studies carried out during the following decade by these four – with the help of several who gradually joined the group after moving to the Institute in Siena – led to a series of crucial observations concerning the mechanisms in initiation, propagation as well as termination of phospholipid peroxidation in the liver and other tissues of living animals. At that time one major focus of the research was the formation of diene conjugates in polyunsaturated fatty acids of cell membranes. This led Mario to establish scientific contacts with other scientists active in the same field, among which a leading position was then occupied by Richard O. Recknagel of Case Western University, Cleveland; close scientific as well as human exchanges thus started between the two, including several visits to the respective labs. Those were years of intense and passionate research work, and the atmosphere at the Institute truly was one of elation. Identification of the molecular species originating from degradation of peroxidised membrane phospholipids became soon a major research objective: mostly a matter of painstakingly accurate chromatographic separations, whose results were detailed in a series of timely publications. It was thus observed that products originating during phospholipid peroxidation were carbonyls in nature, and sufficiently stable to diffuse through a dialysis membrane and produce cytotoxic effects at a distance. Crucial scientific contacts had been established through the NFCR network: among those Trevor F. Slater at Brunel University (Uxbridge, UK), the free radical research pioneer who first identified trichloromethyl radical as the bioactivation metabolite of carbon tetrachloride capable of initiating toxic lipid peroxidation. After learning of a specific dialysable compound under investigation in Siena, it was T.F. Slater to suggest Mario Comporti to establish a collaboration with another NFCR scientist: the biochemist and aldehyde chemistry expert Hermann Esterbauer at the Karl Fraenzens University of Graz, Austria. It was thanks to that most fruitful collaboration that the main cytotoxic product of the phospholipid peroxidation occurring in cellular matter (microsomes) was finally identified as 4-hydroxynonenal (4HNE). That one indeed was the first demonstration that this fatty aldehyde – until then just known as a toxic/carcinogenic chemical deriving from the *in vitro* degradation of linoleic acid esters – was actually also forming as an endogenous product of lipid peroxidation in biological material. The seminal paper reporting those results *(Benedetti et al. 1980)* has received to date several hundreds of citations, and in years the finding originated a wealth of research studies in the most varied fields of human pathology as well as biomedical research in general.

Thus, at the beginning of 1980's, a core of experimental results in pathophysiology of lipid peroxidation was established, representing the conclusion of a first exciting phase in the scientific evolvement of Mario Comporti and his close co-workers. Time was then ripe for a second phase, in which Mario was to assume a role of supervisor for the novel perspectives stemming out from that original core – all of which variably related to redox equilibria and oxidative stress. By then the members of Mario's original team were ready to assume the responsibility of separate labs, each dealing with its own independent research line. Thus A. Benedetti, with younger co-worker R. Fulceri and their students, took the start from the effects of lipid peroxidation on cellular compartmentation of ionic calcium and moved on to investigate the minute details of IP3-mediated mechanisms at the endoplasmic reticulum level. M. Ferrali with L. Ciccoli focused on the roles played by redox-active iron in mediating oxidative reactions, with special reference to pathophysiology of erythrocytes. As a result of scientific collaboration with the neonatologists at the University of Siena, important studies were published on preterm infant anaemia. These were among the first investigations on oxidative stress in the newborn, a topic soon expanded by fruitful researches on neonatal brain damage. Research by A.F. Casini, with his students E. Maellaro and A. Pompella, was dedicated to the pathophysiology of cellular glutathione as well as characterization of glutathione-depending enzymes. Other research lines were centered on lung oxidative stress and fibrosis (G. Lungarella, C. Gardi), and lately on F_2-isoprostanes (C. Signorini). In most of the papers originating from the individual lines during this second phase Mario Comporti was continuously contributing his personal views as far as study design, discussion of results and preparation of manuscripts. The stringency, the absolute and tireless accuracy he would dedicate to these fundamental preparatory steps will represent a formidable example for a long time. His close co-workers will always preserve the memory of his office, his neatly ordered collection of reprints and photocopies, his working notes rigorously written with a pencil on half-folded sheets of paper in his peculiar angular, spiky – but anyhow fully legible handwriting.

At the turn of the 3rd millennium Mario was thus increasingly assuming the role of a senior mentor, peacefully intent to closely follow and enjoy the successes of his by then numerous followers. His inner good-natured, at times playful personality became gradually more apparent, more often than previously. Nevertheless his own personal impetus for active research was by no means dormant. Rather, with the help of younger co-workers, till the very last times before his retirement he could personally carry out experimental studies focused on pathophysiology of the newly described lipid

peroxidation products F_2-isoprostanes. The description of signalling pathways activated by these compounds in liver fibrosis was the subject of his own few last publications.

Mario Comporti was also a great poet, as it was mentioned on the occasion of a commemorative day in honour of the poet Mario Luzi. The two knew each other, and their love for poetry was so great that they became very good friends. Mention of the opinion of Mario Luzi about Mario Comporti's poetry is opportune: *'There is a preliminary choice, a deliberate and logical proposition of fidelity to consecrated and revered values in Comporti's writing. lt is nice to see how this choice is rewarded by the inner creation of the artist, how his secret creative impulse hovers and his thoughts search for their profundity. It is nice to see how such a liberal discipline is confirmed and improved by the perseverance of a vocation, besides the great technical skills. Therefore we must acknowledge and be proud of the value of his work. l am pleased to do it again.'* After *Deriva d'orizzonti* (1985), Mario's books of poems have been awarded several literary prizes, as proved by the shields that Mario proudly showed in his paternal house in Via di Città, its beloved house where everything had to remain in its place exactly as it was during his childhood. Among those, the literary prize he was awarded at Palazzo Vecchio in Florence by the International Academy 'Le Muse' is to be mentioned. At the National Library of Florence and at the 'Gabinetto Vieusseux' a few poems by Comporti were read before a distinguished audience. In order to understand how a man of science could combine his love for scientific research with poetry, we would better rely on his words. In the preface of his book on oxidative stress, Mario wrote: *'Research actually gives the possibility to create something and this means excitement to me. I decided to become a researcher to live this excitement, because it represents the only way I could get closer to the top of creativity. Research bewitches me, and makes me feel the same tension towards the absolute that can be reached by means of the most meaningful lyrical, pictorial and musical intuitions and inspirations.'* He was also the president of the *Sodalizio Amici della Chigiana*. It can be stated that Mario was a rare person, able to reach – at a high level – the so-called synthesis between classical and scientific culture.

Mario Comporti was not an unemotional researcher and a detached man of letters. He loved the *Palio* and did not disdain to follow the parade of the *Contrada della Giraffa* after its victory in August 1997. Since a log time, Mario Comporti was in the Board of the *Accademia dei Fisiocritici* and in 2007 he suggested the renewal of the ancient *Atti dell'Accademia dei Fisiocritici* – founded in 1761 – by introducing English language as in all other contemporary scientific journals. His proposal was accepted, and he became Editor in Chief of the new *Atti*; the first issue of the new publication, renamed *Journal of Siena Academy of Sciences*, was published in 2009. He was a fan of Siena Football Club when it was in *Serie A*, and he followed the championship competently. He was never superficial or sectarian, with his deep literary, historical, artistic and musical culture, with his jokes, impersonations, and by proposing absurd but subtle comparisons he could always create a peaceful atmosphere with his friends, who now miss him inconsolably. The loss of Mario Comporti has been tremendous not only for his pupils and friends, who understood and loved him, but also for the life itself of this Academy.

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DOI: 10.4081/jsas.2014.5814

IN SEARCH OF THE NEUROBIOLOGICAL BASIS OF DIVERGENT THINKING

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Abstract. Human mind can follow two opposite type of reasoning in everyday life as well as in science: convergent thinking, as the ability to get the unique solution to a problem, or divergent thinking, the ability to elaborate different answer to a question. The latter is usually considered as an essential feature of the "creative mind", together with Insight, an unpredictable and unexpected moment of exceptional thinking commonly reported as the "Eureka!" experience. During such processing, an unconscious reorganization process of previously unrelated problem elements is made and when the solution finally emerges to consciousness, the subject is not able to explain how he/she reached it. Because of its unpredictable and unconscious nature, as well as its connection with creativity and scientific discoveries, the definition and evaluation of insight is now one of the biggest challenges for modern cognitive neuroscience. Neurophysiological evidence begins to arise, making the enhancement of creativity thinking using non-invasive neuromodulation techniques a plausible future scenario.

Key words: convergent thinking; divergent thinking; insight; neuromodulation.

BACKGROUND

Divergent thinking is commonly regarded as the "creative thinking", since Guilford defined it as the ability to find unusual and original answers to an open-ended problem, where no specific correct answer is provide [1]. This type of thinking is based on cognitive and executive functions like flexibility and inhibition (of consolidated ideas) that help finding new and creative responses to a posed question. Differently, convergent thinking is described as the ability to find the unique correct solution to a specific problem or question [2], requiring a discrete capacity of deductive reasoning and working memory to integrate the provided elements in a defined but not explicit pattern. Scientists mostly agree in considering divergent thinking and insight as the fundamental events that can lead to a creative idea.

Creativity is commonly considered the specific human ability to create something new, useful and generative [3] and it is regarded as the most important driving force of scientific, technological and artistic progress. While the identification of the neurobiological underpinning of fluid and crystallized intelligence is showing promising results thanks to straightforward testing tool for intelligence evaluation [4-7] creativity and insight still remain blurred concepts whose anatomical and functional definition still constitutes a challenge. Therefore, it is not surprising that research on creativity attracted many researchers but, giving the intrinsic difficulty on eliciting creative performance under controlled conditions, not much progress has been made so far [8].

Taken in account the little neurophysiological evidence about the underpinnings of divergent thinking, few experiments have been conducted with the non-invasive electrical stimulation in order to enhance individual performance on insight-related tasks. The possibility to modulate such an unexpected and unconscious generative event opens a new era of possibilities, not only restricted to neurophysiological research, but also of enormous importance to achieve a better understanding of the cognitive impairments accompanying several neurological and psychiatric disorders [9].

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INSIGHT: THEORY AND TASKS

As everyone knows, there were numerous cases of insight in scientific discovery, for instance Newton's finding about the law of gravitation [10], but the very first *insight* moment is classically attributed to Archimedes of Syracuse, who ran naked down the street shouting "*Eureka*!" after the discovery of the buoyancy's principle while taking a bath [11].

This episode provides a simple and clear characterization of *Aha* moments, which was defined for the first time by the Gestalt psychologists as an unconscious and unpredictable reorganization of the problem components, that involved the discovery of a new mental representation [12]. The insight problem solving, as we can see, is almost opposite to the classical "search" or "analytic problem solving strategy", which is voluntary and completely conscious, with the subject being able to explain all the passages applied to reach the solution [13].

During the last century various definitions of insight were proposed by researchers, with the last iteration proposed by Kounios and Beeman [14] postulating intuition/insight as including "*any sudden comprehension, realization, or problem solution that involves a reorganization of the elements of a person's mental representation of a stimulus, situation or event to yield a non obvious or non dominant interpretation*". Moreover, in a framework supported by many other researchers [15] the *Eureka* moment is not strictly related to the field of problem solving but it includes also other domains of cognition, like perception and language comprehension.

Because of the various fields where the insight-like process appears to take place (identification of ambiguous visual stimuli, comprehension of metaphors, resolution of scientific problem), Bowden and colleagues also speculate that all these different types of *Eureka* moments share a basic neural network and the same mental steps, whereas specific subcomponents allow to separate and identify the various "type" of insight and also to differentiate them from the analytical method [15].

As, intuition moment is considered a subcomponent of the creativity process, together with the divergent thinking and the artistic creativity [8]. However, the demarcation between creativity and these mental creativity elements are not so clear, despite many studies focused on them. *Insight* is often seen as the first step of the creative idea generation, since it happened in a lots of scientific discoveries, like the Newton episode with the apple fall from the tree and even the elaboration of relativity theory by Einstein. With these premises, we can understand the similarity of insight and creativity task using in literature to assess these two related pattern of thinking. RAT (Remote Associates Test) and the CRA (Compound remote associate task) tasks represent a classical example of such overlap. Created in the Sixties to evaluate the ability of identifying semantic distant association between provided words, RAT was used to assess the creativity and recently also for insight performance [16]. CRA were developed by Bowden in order to refine the RAT task, but with the aim of assessing the insight problem solving and not creativity in general. Indeed, CRA and RAT need to be solved with both divergent and convergent thinking: the former is aimed at exploring the words semantically related to the others provided, while the convergent component is leveraged to choose the unique solution. However, the most used task to assess creativity (Alternate Uses Task, AUT) is a pure divergent thinking task [17]. In our opinion, literature needs separate and different task to evaluate insight and creativity, because they are clearly not the same cognitive process, even if they seem to be really interconnected.

Finally, despite the fact that the *insight* is an unconscious and unpredictable process, Bowden and Beeman tried to propose a coherent sequence of events that could lead to intuition. First, they identify i) a strong conscious activation of information consolidated in the mental network of the subject accompanied by a weak and unconscious activation of information not directly related to the solutions in the initial subject's mental representation of the problem. Second, the activation of weak and secondary information conduct the subject to ii) a restructuration of the elements that allow the person to reach a new vision of the problem; finally, the appearance of the solution to consciousness elicits iii) a sense of enlightenment that was manifested with the typical *"Aha!"* exclamation [18].

The network that could support this process may be grounded in the hemispheric asymmetry: the initial weak sematic activation could take place in the right hemisphere, a process traditionally related to a general sematic coding process; on the contrary, it seems more likely that the dominant interpretation occurs the left hemisphere, which is involved in subtle sematic coding processes [15,18]. Given the recent evidence that relates the activation of right anterior superior temporal gyrus evaluate distant sematic relations between provided words [19] the restructuration process is considered to happen in this very cortical region.

As we can imagine, literature is just proposing the first evidence that could validate the last hypothesis on the neural substrates and functional steps for intuition. First of all, many researchers postulate that the main hemisphere where the insight events take place is the right because of its coarse semantic coding [15]. Moreover, Beeman and colleagues demonstrate specific activations of cortical regions during the resolution of CRA that support this process localization, specifically they revealed a primary activation in the right parietal lobe while the subject try to solve the task (and probably operate the reorganization of the problem's elements), followed by a shift of activation in the right temporal cortex when the solution emerges to the consciousness.

Giving thanks to recent development in electrophysiological and imaging techniques, identification the neural basis and the time series of insight events seems to be an imminent achievable goal.

MODULATION OF INSIGHT ABILITIES

Neuromodulation techniques are relatively recent non-invasive methods to interact with cognitive functions both in the healthy and pathological brain. They include transcranial electrical stimulation (tES) and transcranial magnetic stimulation (TMS). In the last 1985 TMS technique was used to evaluate the relevance of specific brain region in cognitive functions, pathophysiology of various neurologic and psychiatric disorders, leading to a consistent increase of clinical application field [20]. Transcranial electrical stimulation, developed more recently, was currently employed to explore the neural correlates of intelligence, executive functions and motor performance with first evidences of its utility in cognitive impairments [4].

tES allows using different type of electrical current delivered via electrode placed on the scalp, such as direct current in the case of tDCS (transcranial direct current stimulation, inducing either an excitatory or inhibitory effect), alternating current in tACS (transcranial alternating current stimulation), or random-noise in tRNS (transcranial random noise current stimulation). Despite the specific mechanism of every electrical stimulations, in all of them we couldn't determine a real fire of neurons under the electrode, but increment the probability that it could happen. In other words, we try to facilitate the activation of a selected cortex important for specific mental process, entering in communication with the brain region via its specific "language" (the electrical current). The TMS method is similar to tES, since it induces an electrical field on the cortex derived from the magnetic stimulation. The difference is that with this technique we can effectively induce a neuronal fire and that the stimulation site is more focal in the brain. TMS is now used to treat many neuropsychiatric illness such depression, bipolar disorder and Parkinson disease and the possibility of clinical applications is still increasing. Regarding the transcranial electrical stimulation studies, there are only three papers that used tDCS over the prefrontal cortex and two studies that stimulate the temporal cortex.

As for the temporal lobe, electrical stimulation (tDCS) was applied to the right anterior temporal lobe and lead to an increase in number of participants solving the task, in contrast to placebo stimulation (so called "sham") and stimulation of the left anterior temporal lobe. These findings are in agreement with the hypothesis that *insight-related processing* primarily involves the right hemisphere. However, there are limits for the reliability of this data because of the insight-task used, which was a single problem in the second study [21], and a very small set of problems of the same type in the first study [22]. Moving away from the temporal lobe, the first study applying tDCS over the prefrontal cortex was conducted by Cerruti [16], testing the effect of excitatory stimulation on the right and left dorsolateral prefrontal cortex. Results shown an improvement on the RAT score only for the stimulation conducted over left dorsolateral prefrontal cortex.

Afterwards, in Metuki *et al*. 2012 [23], excitatory stimulation of the left prefrontal cortex was shown to enhance the performance during the solution of CRA problems, selectively for the most difficult trials. Finally, Chrysikou *et al.* 2013 [24] tested inhibitory stimulation (*i.e*. catodal tDCS) over the right and left prefrontal cortex, during a uncommon uses generation task. Results demonstrated that only inhibitory stimulation on left prefrontal cortex enhance performance.

As it is clearly visible, there are just a handful of studies assessing the possibility to modulate insight abilities in humans, mostly focusing on the prefrontal and temporal lobe by only using direct current stimulation protocols. Most importantly, results seem concordant only for stimulation over the temporal lobe, while positive effects are present both for excitatory and inhibitory stimulation. Overall, the left prefrontal cortex seems to be more implicated in the insight process than the right prefrontal cortex.

For what concerned TMS, only one study about the perception of degraded images is available to date. Results shown that right and left prefrontal TMS reduced the performance of healthy subjects, with results being in contrast with previously cited experiments using tDCS on the prefrontal cortex, even though the task were different.

CONCLUSIONS

Research on *insight* is really fascinating thanks to its characteristic unpredictability and unconscious nature. Despite the scientific interest on this mental process is constantly increasing we are still facing strong challenges in its definition, measurement and potentially, enhancement. Latest development in imaging techniques and electrophysiological investigations makes feasible to enlight the neural mechanism of insight, with benefits spanning from the study of developmental disorders to ageing processes. Moreover, the promising results of recent neuromodulation protocols open new questions about the possible use of electrical and magnetic stimulation to enhance problems solving ability in pathological conditions and to boost the physiological cognitive limits of healthy subjects, with strong ethical issues to be considered.

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DOI: 10.4081/jsas.2014.5816

PRENATAL DIAGNOSIS AND SURGICAL INNOVATIONS IN CONGENITAL DIAPHRAGMATIC HERNIA: EVALUATION OF PRE- AND POST-OPERATIVE MANAGEMENT

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Abstract. Introduction. Congenital diaphragmatic hernia (CDH) is still today considered a challenge from surgeons. Considerable progress in prenatal diagnosis, intensive care unit of neonates and surgical techniques, with the possibility to perform minimally access surgery, widely increased survival rates. The aim of this study is to analyze our series about long and short-term outcomes, also considering the progress made by minimally invasive techniques. **Methods.** The study was performed at Pediatric Surgery of Siena. It is a retrospective study that analyzed all patients with CDH (Bochdalek) treated in the last 14 years, from 2000 to 2013. Sex, side of the defect, presence of prenatal diagnosis, age of onset and symptoms, associate malformation, herniated organs, surgical technique and site of surgery, complications, recurrences, survival and follow-up were analyzed. **Results.** We included 23 patients. Five of them, were ruled out because of affected by diaphragmatic eventration or acquired diaphragmatic hernia. Forteen patients (77%) presented left CDH and 4 patients (23%) a right one. The male female ratio were 14:4. Prenatal diagnosis was performed in 5 patients (27,5%) at a mean gestational age of 29 weeks. Forteen patients (77%) had an early onset of symptoms (first day of life). Most common symptoms were respiratory distress and cyanosis; 4 patients (23%) had a late onset of symptoms, at a mean age of 9 months, and most common symptoms were failure to thrive and vomiting. Seven patients (39%) had associated malformation: common mesenterium (5 pts-71%). The colon was the most commonly herniated organ, present in 15 patients (83%), followed by small intestine in 13 patients (72%), stomach in 11 patients (61%), spleen in 9 patients (50%) and liver in 4 patients (23%). Seventeen patients (94,5%) underwent open surgery: 10 of them (59%) underwent a subcostal laparotomy approach, 7 of them (41%) underwent a supra-umbelical laparotomy approach; 1 patient (5%) underwent minimally access surgery with thoracoscopy access. We performed performed surgery in the intensive care unit in 3 patients (16,5%). Six patients (33%) developed minor postoperatory complications. No patient had recurrence. Four patients died so we report a mortality rate of 23%. A follow-up investigation, with an average duration of 87 months, it is still going on in 5 patients (27,5%). **Conclusions.** The our survival rate was 77% and it reflects the encouraging reported data in the recent literature. These results are due to the reliability of the new resuscitation strategies, such as high-frequency oscillatory ventilation and the use of NO, the ability to perform surgery in the neonatal intensive care unit and, especially, to successfully perform minimally invasive surgery in newborn. The improvement of the survival showed the increasing of long-term morbidity end the requirement of a multidisciplinary follow-up. For these reasons, a multidisciplinary pathway for the management of young patients has been created, to follow them in a standardized way as early as the prenatal diagnosis.

Key words: Congenital diaphragmatic hernia (CDH), child, Minimally invasive surgery.

INTRODUCTION

Congenital diaphragmatic hernia (CDH) is one of the most common major congenital anomalies, with an incidence of 1 in 3000 live births worldwide [1].

Over the last years, improvement in prenatal diagnosis and new therapeutic approaches, as high-frequency oscillatory ventilation, inhaled nitric oxide, permissive hypercapnia, have been used for the management of these new-borns [2].

Today, surgery is therefore considered the least controversial part of the treatment of CDH. Minimally invasive surgery (MIS) for infants and children continues to grow and appears to be gaining added acceptance for CDH repair [3].

Average survival for CDH has improved from 50% to 70-80% and even up to 90% in some institutions [1].

We evaluate the influence of the progress of prenatal diagnosis, of the management in the neonatal intensive care unit (NICU) and of MIS CDH repair on patient's short- and long-term outcomes.

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MATERIALS AND METHODS

This is a retrospective study that was carried out in the Clinic of Paediatric Surgery of Siena (Italy). We identified patients from a prospectively kept database. We included all patients with CDH (Bockdalek) who were treated at our Institution between January 2000 and December 2013. Five patients were excluded because of affected by diaphragm event ratio or acquired diaphragmatic hernia. We analysed these patient's characteristics: demographics data, prenatal diagnosis (ultrasound foetal MRI and VR-Render), gestational age, delivery and birth weight, side of the defect, associated anomalies, symptoms and age of onset, postnatal management, surgical aspects (timing, location, technique and operative approach, herniated organs, using of a patch) short- and long-term outcomes. For the purpose of this study we defined emergency surgery when it was performed without reaching hemodynamic stabilization and deferred emergency surgery when it was performed after achievement of hemodynamic stability.

Statistical analysis were conducted to evaluate the correlation between prenatal diagnosis/method of delivery and type of ventilation strategy/surgery timing, and also to evaluate the possible association between complications and demographic data, associated malformations, side of CDH, ventilation strategies, surgical location and timing of surgical repair.

We statistically analysed the correlation between mortality and demographic data, associated malformations, side of CDH, herniated organs, ventilation strategy, timing of surgical repair and surgical location.

We used Fisher exact test and we considered statistical significance as $P<0.05$.

RESULTS

Eighteen patients were included: 14 (78.5%) male and 4 (21.5%) females.

Five patients (27.5%) presented at our observation with a prenatal diagnosis of CDH: in 4 cases (80%), it was performed only by ultrasound detection and 1 patient (20%) required foetal MRI to confirm the diagnosis. In this case we took advantage of a three-dimensional reconstruction technique called VR-Render. Prenatal diagnosis was performed at a mean gestational age of 29 weeks (range: 18-37 weeks).

Four patients (22%) were born preterm (32-36 weeks) with Low Birth Weight (LBW, range: 1890-2100 g). Ten patients (55.5%) carried out a caesarean delivery. Fourteen patients (78%) had a left sided CDH, 4 (22%) had a right sided defect. Nine (50%) babies showed associated anomalies (Figure 1).

Fourteen patients (78%) had an early onset of symptoms: all of them had respiratory distress and cyanosis, 3 patients (21.5%) showed additionally interstitial emphysema, hypotonia, haematological disorders.

The statistical analysis showed a significant association between the presence of a prenatal diagnosis and mode of delivery with a P-value of 0.035 (Table 1).

Four patients (22%) had a late onset of symptoms with vomiting, crying spells and growth retardation at a mean age of detection of 9.5 months (3 -16 months).

Table 1. Correlation between prenatal diagnosis and method of delivery.

P=0.035	Spontaneous	Cesarean	Total
Prenatal diagnosis +	0	5	5
Prenatal diagnosis -	8	5	13
Total	8	10	18

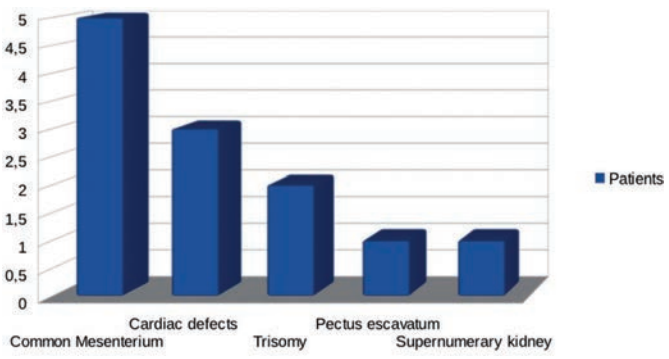

Figure 1. Associated malformation distribution in our series.

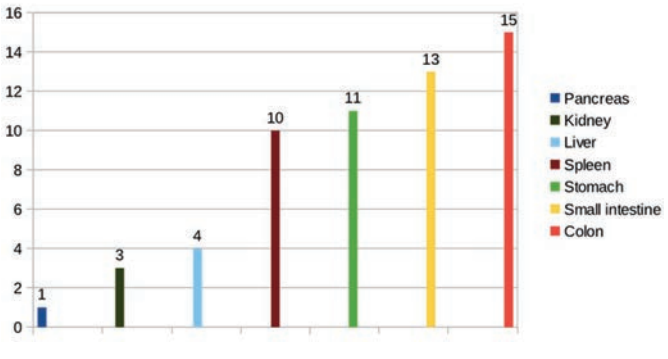

Figure 2. Herniated organs distribution in our series.

All patients (100%) underwent a preoperative chest-abdomen x-ray.

A gastric tube was placed in all patients and they were intubated.

Nine patients (50%) were ventilated with conventional strategy, (VCM) and 9 (50%) patients underwent High Frequency Oscillatory Ventilation (HFOV).

Six (33%) babies underwent surgery in emergency mode. Twelve (67%) babies underwent surgery in deferred emergency mode.

The correlation between ventilation strategy and surgery timing did not show a statistically significant difference, with a P-value of 0.62.

Fifteen patients (83.5%) underwent surgery in the operating room, 3 patients (26.5%) in NICU.

Seventeen (94.5%) patients underwent open surgery, 10 (59%) of them by a subcostal approach, 6 (35%) by sovraombellicale transverse approach, and 1 patient (6%) with a right thoracic approach. One patient (5.5%), underwent MIS with a thoracic approach.

Herniated organs are showed in Figure 2.

All patients underwent primary closure. No patch was placed.

Six patients (33%) developed postoperative complications: 4 of them (67%) developed bowel adhesions, 2 (33%) pneumothorax, 1 (17%) bilateral renal failure and 1 patient (17%) pneumonia associated with atelectasis. All complications were resolved, except for the patient with severe bilateral renal failure who died in the following days.

The statistical analysis showed that there was no statistically association between complications and demographic data, associated malformations, side of CDH, ventilatory strategies, timing of surgery and surgical location.

There were no recurrence in our series.

Death occurred in 4 patients (22%), respectively, for a marked pre-existing pulmonary hypertension, for severe malformations, due to the onset of a serious Multi Organ Failure (MOF) and severe acidosis followed by cardiac arrest.

The statistical analysis has shown that patients with low birth weight and premature infants are statistically associated with a worse prognosis in term of mortality with a P-value of 0.003 (Table 2). There was no correlation between mortality and associate malformations, side of the defect and herniation of stomach and liver. However our patient with trisomy showed higher mortality (P-value 0.08), such as patients who underwent HFOV and surgery in emergency mode (Tables 3-5).

There was no differences in mortality, instead, between patients underwent surgery in NICU and those underwent surgery in operating room (P=1.0).

Five patients (28%) were included in a follow-up program. The mean follow-up to date is of 87 months (62-112). All of them have regular values of weight and height during percentile, and a normal result of control x-ray. One patient (20%) repeated echocardiography and follow-up cardiology at 3 months due to associated cardiac malformations with normal results. One patient (20%) underwent an upper digestive system x-ray, due to a gastric volvulus with normal results.

DISCUSSION

The knowledge about the CDH are still evolving. Prenatal diagnosis has brought a great help, allowing to plan a caesarean birth in a tertiary centre, to perform surgery in the uterus in cases of severe pulmonary

Table 2. Correlation between mortality and weigh and gestational age at birth.

P=0.003	Deceased	Survivors	Total
LBW + preterm	4	0	4
ABW + term	0	14	14
Total	4	14	18

Table 3. Correlation between mortality an trisomy.

P=0.08	Deceased	Survivors	Total
Trisomy +	2	0	2
Trisomy -	1	6	7
Total	3	6	9

Table 4. Correlation between ventilation strategy and mortality.

P=0.08	Deceased	Survivors	Total
VCM	0	9	9
HFO	4	5	9
Total	4	14	18

Table 5. Correlation between mortality and timing of surgery.

P=0.08	Deceased	Survivors	Total
Emergency	3	3	6
Deferred emergency	1	11	12
Total	4	14	18

hypoplasia, or to terminate the pregnancy [4]. With its improvement the diagnosis can and should be made automatically in almost all cases [5]. It is interesting to note that in our series, 4 (80%) of the 5 cases with prenatal diagnosis are dated in the period between 2010 and 2013. In the light of these considerations, 4 of 7 patients, from 2010 to 2013, corresponding to 58%, have a prenatal diagnosis, highlighting an improvement, over time, of ultrasound detection. Similar to Literature, our study underlined the main role of prenatal ultrasound in providing a definitive diagnosis. We also confirmed that foetal MRI may help in case of difficult diagnosis, and we also benefit from a three-dimensional reconstruction technique as VR-Render (Figure 3). It is an interactive system for volume visualization which enables practitioners to quickly explore and analyse 3D medical or scientific data on a standard PC.

Optimizing ventilation strategy in patients with CDH may help to prevent chronic respiratory diseases. However evidence-based standardized treatment protocols are leaking in the field of this pathology. Consequently, ventilation strategies may differ between centres and ventilatory support is often based upon expert opinion [6]. To date, conventional ventilation is the most widely used , while in many institutions HFOV is used as rescue therapy. In some centres however, HFOV is used as the initial ventilation mode [7]. From our results HFOV seems to be associated with a higher mortality; however patients undergoing HFOV were the most uncompromising and probably this has affected the outcome of the statistical analysis. We think that this strategy may improve gas exchange, reduce barotrauma and decrease the presence of inflammatory mediators, reason why it has been used with a higher frequency in the last years.

Early CDH repair was thought to improve ventilation by reducing intrathoracic pressure after reduction of herniated viscera. However this strategy led to emergent procedures often performed on unstable infants. Reports started appearing in the mid-1980s suggesting that survival may be improved if surgery was delayed until preoperative stabilization was achieved, recognizing the impact of persistent pulmonary hypertension on survival [8]. In our opinion and due to our results, according to CDH EURO Consortium [9], even though there are no scientific evidence in favour of delayed surgery, we prefer reaching a preoperative hemodynamic stabilization.

Perform surgery in NICU carries on potential disadvantages including the risk of infection, inadequate lighting and delayed discharge. Lago *et al*. have argued, to now, the only study that analyses the outcome of the patients in the operating room than those operated in NICU [10]. They demonstrated that patients in the ICU have been shown to have a prevalence of: positive blood cultures (11 *vs* 0%), bronchial aspirate positive (16 *vs* 0%), postoperative mortality (33 *vs* 7%) and a longer hospital stay (26 *vs* 13%) [10].

However our results are comforting: there are no significant differences between the patients operated on in the operating room and in NICU in terms of postoperative complications and mortality: this leads us to think that the intervention in the NICU can be a viable alternative in all critically ill patients, in which transport to operating room may worsen their condition.

The proliferation of minimally invasive surgery (MIS) in paediatric surgery has allowed for the laparoscopic and thoracoscopic repairs of neonatal CDH to become routine in some institutions. The use of MIS approaches have been suggested to be advantageous over traditional open surgery, including less pain and incisional complications, avoidance of thoracotomy-related sequelae, as well as reduction of surgical stress [11]. Despite the wide-spread application of MIS, comparative outcomes remain elusive. Current evidence has been limited to case

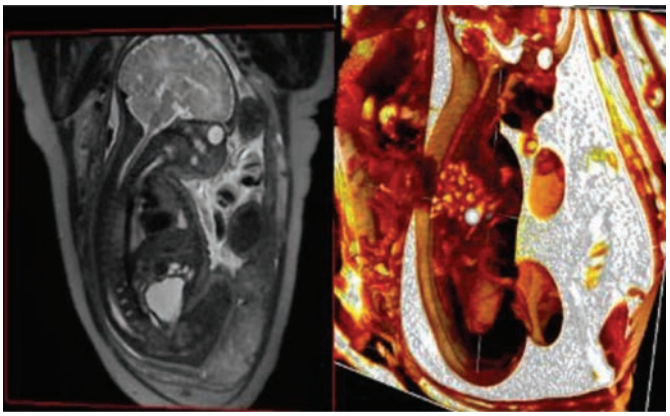

Figure 3. Fetal MRI and its 3-dimensional reconstruction by VR-Render.

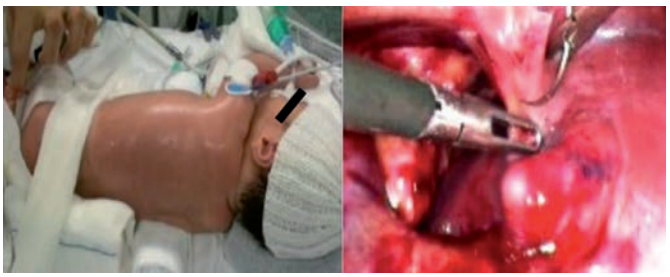

Figure 4. Positioning of the patient in the operating room and intraoperative corresponding image.

series and meta-analysis [12]. Our case had excellent results: the baby was discharged in day 9 postoperative and shows no recurrence, no complications neither long terms sequelae (Figure 4). It demonstrate that all cases with no compromises ventilatory parameters, pulmonary hypertension easily controlled with good prognosis can be successfully treated with minimally invasive techniques.

Several centres have shown that survival of patients with CDH is directly correlate with severity of pulmonary hypertension. Many studies have demonstrated that persistent sustained severe pulmonary hypertension is associated with significant worse survival [1]. Actually our study demonstrated the same results: our mortality is strictly correlated with premature and LBW infants who did never reach preoperative stabilization and underwent surgery in emergency mode. However our series reached 78% of survival, which is a very satisfactory result.

CONCLUSIONS

The interdisciplinary counselling between paediatric surgeon and neonatologist is crucial for the survival of the child: the CDH is a resuscitation emergency not surgical, therefore, the stabilization of the patients remain a key element.

Surgery is almost everywhere deferred to allow a better ventilatory and hemodynamic balance.

In addition our study underline that NICU, as a surgery location, can be a valid alternative to operatory room, showing no significant differences either in terms of postoperative complications, either in terms of mortality. In conclusion a multidisciplinary long-term follow-up is needed for this patients as it is showed from our study.

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DOI: 10.4081/jsas.2014.4844

A CASE REPORT OF GIANT GENITAL WARTS

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Abstract. Giant genital warts (GGW) represent a rare form of sexually transmitted disease caused by the human papillomavirus, arising more frequently in the vulvar and perianal regions as large exophytic cauliflower-like mass. Estimated rate of recurrence is 60 to 66%, while malignant transformation is possible and it has been reported in 30 to 56% of cases. A 45-years-old woman was admitted to our Structure of Plastic and Reconstructive Surgery, Siena, Italy with an extensive cauliflower-like masses diffused on vulvar and perianal region. The patient was treated in general anaesthesia, with a wide en bloc excision up to free clinical edges and immediate reconstruction of the vulvar continuity. Buschke Lowenstein tumour or giant genital warts is a sporadic tumour with an elevate local recurrence rate. In some cases, surgery can be very difficult and it must be associated to other strategies. An accurate follow-up is always necessary.

Key words: Giant genital warts, acuminatum condyloma, Buschke-Lowenstein tumor.

INTRODUCTION

Giant genital warts (GGW) represent a rare form of sexually transmitted disease caused by the human papillomavirus (HPV), arising more frequently in the vulvar and perianal regions as large exophytic cauliflower-like mass. HPV serotypes 6 and 11 are the pathogens responsible of this disease. Buschke and Lowenstein described giant genital warts in 1925 [1]. This tumour shows high growth speed and a high recurrence after treatment, so wide wounds with clear margins are often necessary for a complete surgical excision [2]. Buschke-Lowenstein tumour (BLT) shows an incidence of 0.1%, has an invasive growth and high recurrence after treatment. Estimated rate of recurrence is 60 to 66% [3] while malignant transformation is possible and it has been reported in 30 to 56% of cases [4,5].

CASE REPORT

A 45-years-old heterosexual woman was admitted to the Structure of Plastic and Reconstructive Surgery of University of Siena (Italy) in October 2013, complaining of genital discomfort. Three years before, the patient had noticed the evidence of little papillary lesions in the perivulvar region, which became progressively more numerous and voluminous, extending to the perianal region as giant, irregularly ovular masses. A clinical examination revealed extensive cauliflower-like masses diffused on vulvar and perianal region, irregular borders, colour ranging from purple to pink (Figure 1).

There was no propagation into the anal canal or into the vagina. The lesions caused difficulty in sitting and compromised the patient's sexual activity. There wasn't clinical lymphadenopathy; past medical history was negative for other sex transmitted diseases and immunosuppression. The patient was treated in general anaesthesia, with a wide *en bloc* excision up to free clinical edges and immediate reconstruction of the vulvar continuity. The surgical cutting of the skin was made with a scalpel, while cutting and coagulation of the dermis and subcutaneous tissues was performed with an electric scalpel. The large wounds were closed by suturing the external portion of the labia minora with the medial aspect of the labia majora and it was not necessary to resort to surgical flaps. In order to minimize the risk of faecal contamination of the wound, a stoma was harvested and maintained for one month (Figure 2).

The patient underwent periodical checks to reveal any local recurrence (Figure 3).

Histopathological examination reveals an epidermal hyperplasia with para and hyperkeratosis. A lymphoistiocytic inflammatory infiltrate was present, with spikes produced by papillae rich koilocytes.

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DISCUSSION

In 1925 a lesion locally invasive, with rapid growing was first described by Abraham Buschke and Ludwig Lowenstein as "carcinoma-like condylomata acuminate" now Buschke-Lowenstein tumour (BLT). BLT is a rare sexually transmitted disease with an incidence of 0.1%. It is characterized by invasive growth and high recurrence after treatment. Estimated risk of recurrence is 60 to 66%. In some cases malignant transformation is possible and it has been reported in 30 to 56% of cases [4]. The lesions are triggered by HPV, in particular genotypes 6 and 11 are involved. HPV types 16, 18, 31 and 33 are often found in lesion with neoplastic transformation [6,7]. Occasionally types 16 and 18 are involved too [6,8]. Some authors consider poor hygiene and sexual promiscuity some risk factor for the disease. The mean age of patients with giant genital warts is 43 years. The anatomical region most affected by the lesions in the female is the vulva in 90%. Anorectal location is less frequent and sovrapubic localization is rare [9,10]. The lesions appear histologically as exophytic mass with epidermal hyperplasia, hyperkeratosis and parakeratosis, without basement membrane disruption but with compression of deep dermis. Immunosuppression can promote the tumour's growth, so every patient with this condition must be checked for HIV, hepatitis virus and syphilis. The patient examined in this work wasn't immunosuppressed Some authors consider giant genital warts (GGW) as precancerous lesions [11] and in any case a correlation between these lesions and verrucous carcinoma is shown, thus making an early radical treatment advisable.

Verrucous carcinoma was first described by Vackerman in 1948; it is a low grade squamous cell carcinoma with slow and progressive growth, minimal dysplasia and low incidence of metastases. Mortality is estimate about in 20% of patients [12]. The diagnoses can be difficult due to cytological characteristics [12]. Unlike the Buschke Lowenstein tumour, the verrucous carcinoma shows exophytic and endophytic growth: well-differentiated squamous cells penetrate the underling tissue across a papillomatous surface. These cellular elements are organized in sinuses and crypts stuffed by keratotic debris [13].

Surgery is one of most relevant option to eradicate

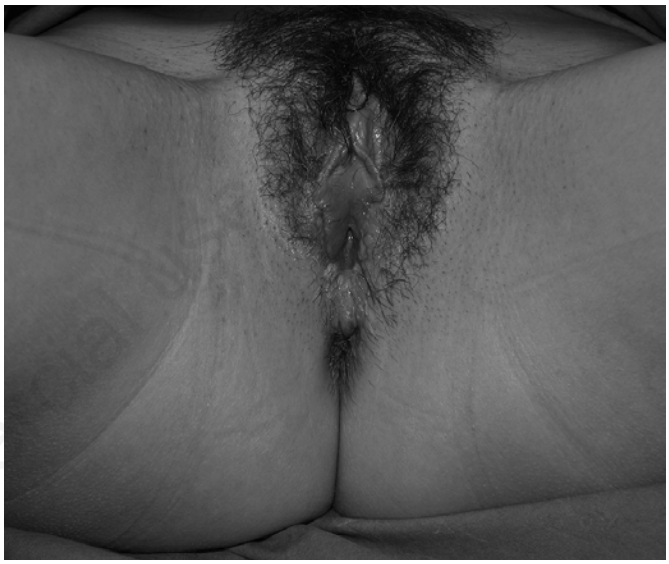

Figure 2. Immediate post-operative photo.

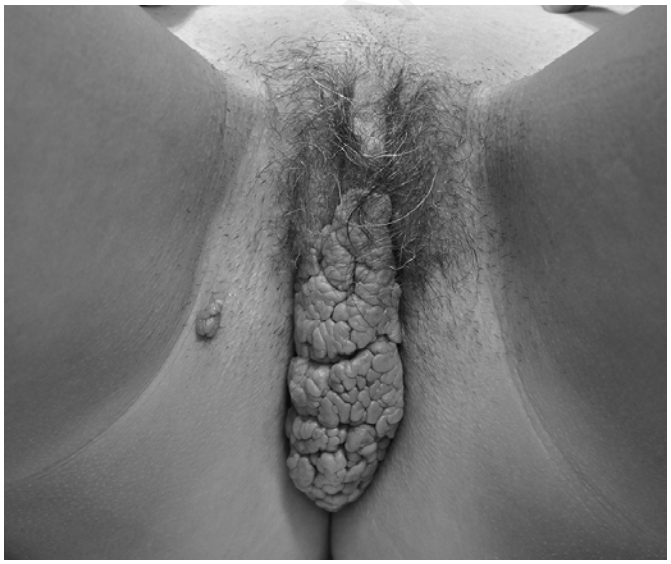

Figure 1. Examination shows cauliflower-like masses diffused on vulvar and perianal region.

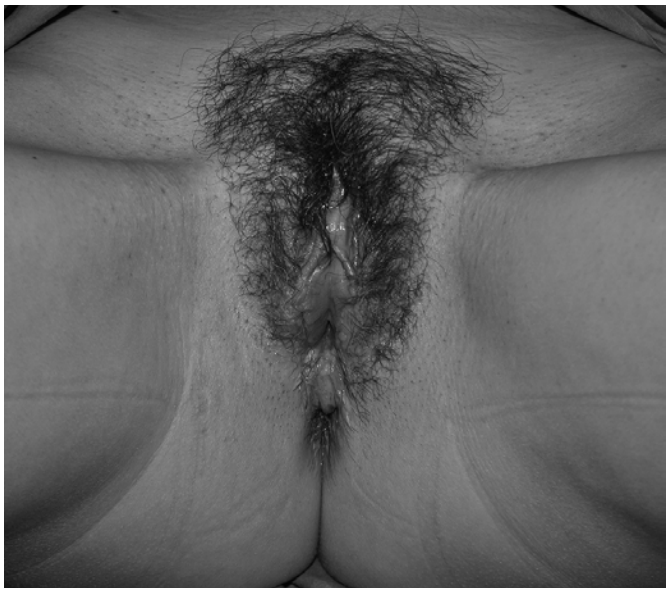

Figure 3. Photo taken after three months.

a giant genital warts, but particularly for extensive lesions, other therapies such as chemoradiation, topical and intralesional drugs, carbon dioxide laser therapy (etc.) can be used alone or in association to reduce the risk of recurrence [7]. Some authors prefers other treatment such as solution with podofilox solution [14]. Some authors do not prefer harvesting a stoma in these patients, but only prescribing low fibre diet, loperamide and bowel cleansing in post-operative period [15,16].

CONCLUSIONS

Buschke Lowenstein tumour (BLT) or giant genital warts (GGW) is a sporadic tumour with elevate local recurrence rate. It has a stronger and documented correlation with verrucous carcinoma, so diagnosis and therapy must be accurate and complete. Surgical complete excision remain the main treatment although there are several alternative treatments that, used with surgery, can increase radical rate reducing the risk of recurrence. In some cases, surgery can be very difficult and it must be associated to other strategies. An accurate follow-up is always necessary.

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DOI: 10.4081/jsas.2014.4852

BREAST IMPLANT RUPTURE AS A COMPLICATION OF HEART SURGERY IN MEDIAN STERNOTOMY

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Abstract. The authors report a case of a woman who underwent heart surgery in median sternotomy after breast reconstruction using prosthesis in 1984. After this open heart surgery in 2008, she developed an injury at right breast implant with intra and extra capsular silicone gel spread out the prosthesis.

Key words: Breast implant; median sternotomy; breast reconstruction; breast augmentation.

CASE REPORT

A 64 years old women suffered from breast implant rupture after cardiac surgery in full median sternotomy.

She underwent right madden mastectomy in 1981; three years later she received a secondary reconstruction using prosthesis.

In 2001 a stenting of right coronary artery was performed for an inferior myocardial infarction; in 2008 for heart valves incompetence a mitral and tricuspid valve anuloplasty were performed in full longitudinal median sternotomy.

Few weeks later she start complain about a flogistic process at the right breast and, subsequently, she noticed a right paramedian region swelling but no further clinical investigation was made.

In April 2009, she was admitted in hospital with severe pyrexia associated to an important nodular inflammatory process, a cutaneous presternal fistula with mixed jelly and pus like secretion with oedema of implanted region (Figure 1); marked sign of periferical legs stasis was present as well.

In emergency she removed injuried right breast implant and intra and extra capsular silicone gel spread out the prosthesis (Figure 2).

Histology revealed granuloma-like chronic inflammation; this process developed around a fatty paraffinoma-like secretion and, for *Staphilococcus aureus* positivity of this material, Teicoplanin 400 mg, Ampicillin/Sulbactam 3 g and Ciprofloxacin 200 mg was started.

At post operative day 8 (POD) she was discharged with no fever, with twice weekly wound control follow up and the decision to use VAC therapy to improve healing process.

Despite re-ephitalization at POD 50, general clinical condition worsening in terms of dyspnoea and heart failure.

Again at POD 65 scar dehiscence and a percutaneous fistula producing jelly and pus-like material was present.

Critical general condition discouraged any treatment more than daily wound medication. Three weeks later patients died for severe unresponsive heart failure.

DISCUSSION

In 2011, more than 85,000 breast implant procedures were performed in Italy, including breast reconstruction, augmentation mammoplasty and men pectoral implants. The safety of breast implants has been highlighted by numerous studies in both reconstructive and aesthetic surgery. However specific issues such as implant risks and follow up after cardiac surgery in full median sternotomy are not well established.

Taupmann *et al.* describe the presence of silicon in the chest cavity due to iatrogenic breast implant rupture [1].

Rice *et al.* report the treatment of a post-traumatic migration of silicon into the pleural space in a patient who underwent breast augmentation ten years before [2].

Chen *et al.* describe a prosthesis in the chest as a complication of breast augmentation [3]. Levine *et al.* report intrathoracic silicone associated to bilateral implant rup-

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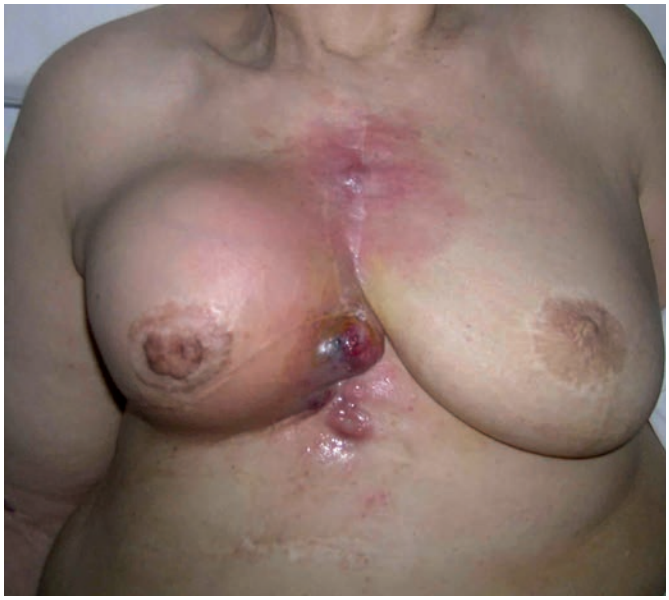

Figure 1. The important nodular inflammatory process associated to a cutaneous presternal fistula with mixed jelly and pus like secretion with oedema of implanted region.

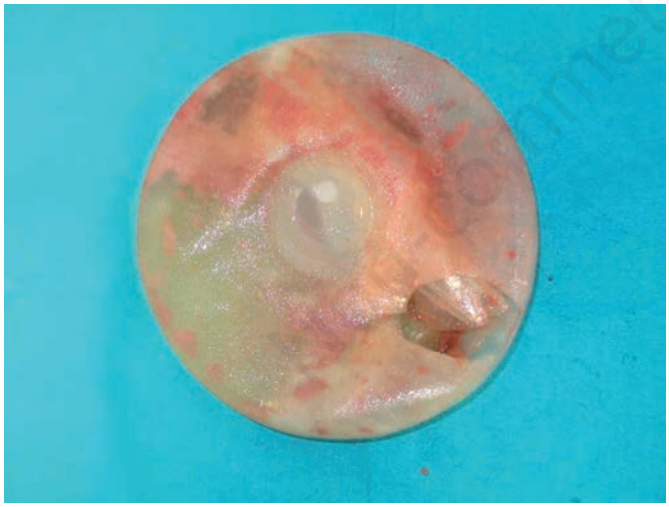

Figure 2. Right breast implant presented an intra and extra capsular rupture.

ture one year after atrial septal closure surgery after previous radical mastectomy and breast reconstruction [4].

Mehta *et al.* described the migration of a intact breast implant inside the chest cavity after thoracotomy surgery [5].

In our case a twenty years old breast prosthesis has been damaged during open heart surgical procedure.

Management of this kind of complications is one of the most difficult problems in secondary procedures, due to the characteristics of silicon and its reaction with the surrounding tissues.

Although a clear causal link between the patient's general condition and the implant rupture is not well established, surgical options were clearly limited by systemic clinical condition. Perhaps, early diagnosis would have changed the course of events.

Growing practice in utilizing breast implants is increasing the possibilities years later, of surgical procedures years later that increase risk of complications. A correct early diagnosis through both the exactly understandings of clinical signs and the use of imaging techniques, would reduce this kind of complications.

CONCLUSIONS

In conclusion, it could be important proper updates training for cardiac surgeons in perioperative management of this kind of patients as well as a dedicated chapter in informed consent for breast implanted subjects underline particular surgical risks.

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DOI: 10.4081/jsas.2014.5176

SQUAMOUS CELL CARCINOMA OF THE EYELID DEVELOPING ON A CUTANEOUS LICHEN PLANUS LESION

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Abstract. Squamous cell carcinoma is the second most common malignant tumor of skin. We present a case of a 67 years-old patient with a squamous cell carcinoma developing on a cutaneous lichen planus lesion, located on his right upper eyelid.

Key words: Carcinoma, Squamous Cell, Eyelid Neoplasms, Lichen Planus.

CASE REPORT

Squamous cell carcinoma (SCC) is the second most common malignant tumor of skin [1]. Approximately, 5% of skin tumors occur in the eyelids. The incidence of the disease is higher in men over 40 years of age, basal cell carcinoma being observed more frequently than the squamous cell type. The incidence of eyelid skin tumors is mostly a result of environmental factors including sunlight and ultra violet exposure and genetic factors including skin pigmentation. The different incidence of eyelid cancers among countries may be because of variations in skin types, geographical latitudes and health behaviour [2]. Clinically neglected, advanced SCC of the eyelid can have devastating outcome [3].

We present a case of a 67 years-old patient with a tumor, located on his right upper eyelid (Figure 1). He also had two suspicious growths on his front and scalp. The protrusion of the eyelid's tumor prevented the perfect closing of the eyelids. This lesion has been present for about six months, at the time of the first visit.

The patient had no history of immunosuppression. The patient's medical history includes the removal of other 3 squamous cell carcinomas localized to the head, the chest and the shoulder, over the past 13 years. He also reported, as a risk factor, prolonged sun exposure during 40-year employment as construction worker. Cancer of the right upper eyelid was excised, along with two suspicious growths of the head, during the same operation. The eyelid's epithelium was immediately reconstructed using auto transplantation with autologous retroauricular graft.

Other surgical wounds were closed with simple advancement flaps. The final clinical result was satisfactory (Figure 2).

Histological diagnosis of the tumor localized to the eyelid (Figure 3) was acantholytic squamous cell carcinoma infiltrating the reticular dermis, on the background of lichen planus (LP), while the histological report of the other two growths in front and scalp was actinic keratosis lichenoides. To the best of our knowledge, this is the first case of squamous cell carcinoma of the eyelid insurgent on lichen planus.

The patient's history was silent with regard to the presence of lichen planus in himself or his family. Physical examination showed no presence of lichenoid lesions on the skin nor in the oral cavity nor on the scalp.

The patient had a postoperative course without complications or recurrences. After two months of follow up, the patient was very pleased with the result.

Malignant transformation of LP is a controversial subject with much conflicting evidence. Clinically, hypertrophic lichen planus can mimic squamous cell carcinoma [4]; infiltration into deep dermis and invasion of blood vessels and nerves, are features more suggestive of SCC. Sometimes, direct immunofluorescence may help in the differential diagnosis.

Studies suggest an estimated 0.3-3% risk of malignancy in patients with oral lichen planus; squamous cell carcinoma can also arise on cicatricial alopecia due to lichen planopilaris [5]. However, cutaneous lichen planus does not carry an increased risk of malignant degeneration.

In our patient, SCC aroused on a LP skin lesion. Few studies have described the occurrence of squamous cell carcinomas from longstanding, non-healing, lesions of cutaneous lichen planus [6].

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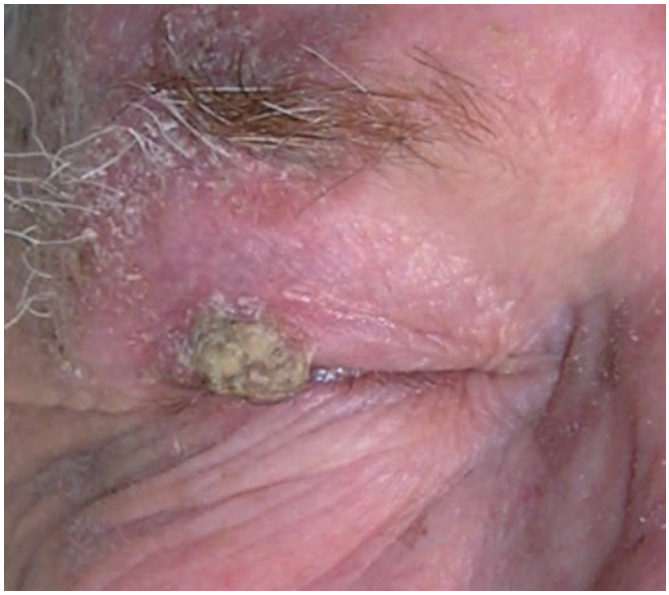

Figure 1. Eyelid squamous cell carcinoma on lichen planus.

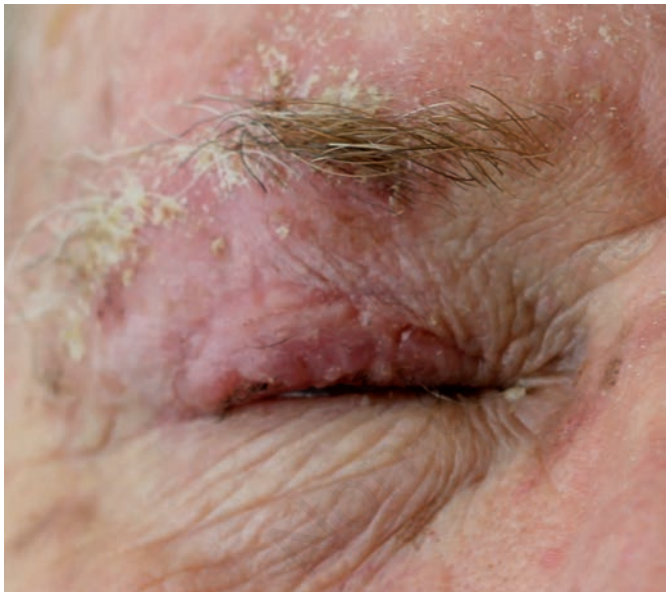

Figure 2. This picture was made 18 days after surgical resection and simultaneous reconstruction with retroauricular graft.

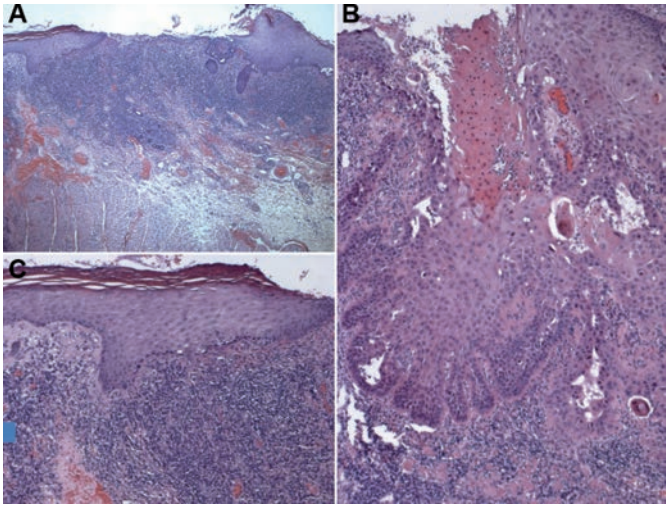

Figure 3. At scanning power, an ulcerate; microinvasive squamous cell carcinoma is observable nearby a lichenoid dermatitis (A). In another area, the SCC infiltrates the reticular dermis (B). At higher power, features of a lichen planus are evident (ortokeratotic, hyperkeratosis, hypergranulosis, band-like, subepidermal inflammatory infiltrate) (C). Hematoxylin & Eosin, Original Magnification: A) 25×; B) 25×; C) 50×.

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Annual scientific meeting July 9 2014

A case of appendix carcinoid in a pediatric patient. A subtle clinical presentation

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Introduction
The appendix carcinoid, although rare (with an incidence of 0,08%), is the more frequent gastrointestinal tumor in children and teen. In most cases these tumors cannot be diagnosed or they can be incidentally found during a surgical exploration for acute abdomen. Only in few cases there are symptoms of a carcinoid's syndrome (flushing, diarrhea and wheezing). In this work we present the manegement of a patient with an appendix carcinoid revealed during an appendicectomy performed for a peritonitis caused by a perforated appendicitis, underlining the importance of diagnosis and long term follow-up.

Case report
A 13-years girl came to our attention with an history of ten days abdominal pain localized in the right iliac fossa. The clinical valutation, blood tests and abdominal ultrasound were suggestive of abdominal abscess and the patient undergone to surgical intervention. An appendicectomy was performed and the histological examination revealed the presence of a carcinoid localized on the top of the appendix. Actually, the patient is free from disease in a ten months follow-up.

Conclusions
Given occasional diagnosis and paucity of works in literature about the course of this kind of tumors in childhood, it would be preferable a conservative surgical treatment and a close long term follow-up.

Management and outcome of Herlyn-Werner-Wunderlich syndrome: conservative treatment in pediatric age

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Introduction
Herlyn–Werner–Wunderlich syndrome (HWWS) is a rare congenital mullerian anomaly consisting of uterus didelphys, hemivaginal septum, and unilateral renal agenesis. Reported data in pediatric age are rare. We report our case of HWWS.

Case report
A 4-years-old girl came to our department with diagnosis of pelvic mass associated with lower abdominal pain since 1 year, that had worsened in the last 5 months. On physical examination the mass was palpated in the right lower abdomen. The external genitalia were normal. Abdominal ultrasound (US) showed a mass in the pelvic cavity associated with normal uterus and agenesis of right kidney. MRI with contrast confirmed all of those data and showed a transverse vaginal septum. Examination under anesthesia, cystoscopy and vaginoscopy were planned and done. Trans Hymenal resection of vaginal septum was performed. Postoperative course was normal. At last follow up (1 years after surgery) patient was in healthy.

Discussion and Conclusions
This syndrome is a rare anomaly in the spectrum of mullerian ducts diseases. Patients with HWWS usually are aymptomatic until adolescent age, but the onset can be earlier, as in our case. The suspicion must be considered in all females with renal agenesia. A correct diagnosis and management, indeed, ensure a good long term outcome without any problems in term of fertility and sexual aspects.

The human rachis: can it be considered a shock absorber (that was produced by exaptation) rather than a column?

M. Tanga, F. Ghelli, G. Gelati

Corpus (International Group for the Cultural Studies of the body)

Our paper is focused on two fundamental points: the first one is a terminological proposal and the second one is a question. Obviously these two things are strictly related one another.
The terminological proposal is aimed to name "vertebral shock absorber" the human rachis (globally considered, when it is in physiological conditions) in its most typical function: to sustain static/dynamic stresses, that moreover are directed according to its axial direction, obviously when this coincides with gravitational line. This aspects can be studied by modal analysis and by the model of *Eigenvectors* and *Eigenvalues*. According to our opinion, the mechanical feature must be considered as prevalent if compared with the structural one. Following it human rachis is usually named "column".
This mechanic sustain is distributed on three lines that are summarily parallel and are linked one another (by isthmuses and vertebral arches to build an horizontal ring) so they can be considered a unique compact viscous-elastic system. Each one of these three vertical sub-structure is built as a stacking of metameric elements (modules) along a continuous line.
This spatial linear disposition is regarding: vertebral bodies (that are alternated with inter-vertebral discs and are placed on the median line) and articular processes of vertebras (two symmetric lines posterior to vertebral bodies).
In chordates' notochord, in fishes' rachis and in the vertebral "beam" of tetrapods the solicitations are transversal and trend to disaggregate the vertebral chain. Instead, in human pilaster the main static solicitation, the gravitational charge, trends to make it collapse: the reciprocal pressure pushes the vertebras one against the others. Sagittal physiological curves seem a partial retreat under the gravitational charge, a beginning breaking of vertebral instable balance. Maybe it is so, but the sinuous shape of human rachis makes it much more resistant to further charges, both static (to lift something) and dynamic (falling down after an elevation jump). The curves elastically become more/less empathized and so they make the human rachis a very efficient shock absorber.
The related question is if we can define "exaptations" evolutionary jumps of rachis: from central axis of first fishes living in water to beam of terrestrial tetrapods, to shelf in first bipeds, to column or, as we propose, vertical shock absorber in human beings. In both cases, of a positive or of a negative answer, it could be opportune to establish criteria and limits to define an evolutionary transformation as "exaptation" or "not-exaptation".
The transformation of the function of the exoskeleton of arthropods (from protective shell in many water species to locomotion sustain in terrestrial species), of the feathers (from thermal defense in Dinosauria to aerodynamic structures in Birds) and of the appendixes of vertebrates (from fins in water species to paws in terrestrial tetrapods) have been considered exaptations. Similarly we propose of considering exaptation the change of mechanical function of human rachis.
Anyway every transformation is a change of function and/or of structure, but it could be heuristically interesting to have criteria and limits available to classify each case.

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