Necropsy reports and anatomo-pathological observations from the archives of the Grand Ducal Medici family of Florence. Part II - The 17th and first half of the 18th century

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Abstract. During the Modern Age, dissection began to be practiced for medico-legal purposes, in order to investigate the causes of death. In particular, starting from the 15th century evidences of autopsies performed by doctors on their private patients emerge. These dissections were requested by those families who can afford the expenses, in order to search the possible presence of hereditary diseases and to predispose a prevention and cure. The extremely rich documentary archives of the Medici family, one of the most important family of the Italian Renaissance, report several description of necropsies carried out on the bodies of the members of the family. The analysis of these reports offers important direct information on the autopsy practices performed by court surgeons of the members of an aristocratic class in a period comprised between the 16th and the first half of the 18th century, and allows in some cases also to propose a retrospective diagnosis on the diseases that afflicted the Medici. Following a previous work that discussed the evidences dated back to the 16th century, this paper will be focused on the reports about autopsies carried out during the 17th and the first half of the 18th century. During this period, the reports became more accurate and detailed, reaching at the end of the period the characteristic of modern scientific autopsy notes. Therefore, in the majority of cases the lesions referred by the court physician provide sufficient element to propose a retrospective diagnosis based on the symptoms referred by the historical sources during the life of the patients and on the cadaveric examination.

Key words: 17th century, 18th century, Medici, autopsy, embalming, court surgeons

Introduction

The Medici were one of the most powerful families of the Italian Renaissance: starting from the 14th century, they ruled Florence and Tuscany for many generations thanks to their careful management of banking ventures and skilful political actions. Lovers of art and science, the Medici were patrons of famous artists and scientists, such as Michelangelo, Leonardo, Galileo and others, contributing to make Florence the intellectual centre of the Western world.

The extremely rich archival documents of the Medici family, whose corpses were submitted to au-

topsy after death, refer in several cases details about the clinical history of the main personages and the report of the necropsy performed by the court surgeons.

The majority of information about the Medici family deriving from archival documents and written sources are collected in the fundamental work of the Florentine physician and historian Gaetano Pieraccini (1864-1957) wrote in 1924 and reprint in 1986. These documents provide relevant information about the practice of autopsy carried out on the bodies of the Medici family for medico-legal purposes in a time range comprises between two centuries that is when the Medici sovereigns of Tuscany were nominated Grand Dukes. In a previous work the autopsy reports performed during the 16th century were analyzed; the present work is focused on the autopsy reports of the members of the family who lived within the 17th century and the first half of 18th century, when the dynasty extinguished because of the death without heirs of Giangastone, the last Grand Duke. For those members of noble family for whom no autopsy reports are mentioned will be excluded from our dissertation.

The skeletal remains of some personages included in this work were submitted to an anthropological and paleopathological study. In these cases, the results of the analysis of the autopsy registers will be compared with the information provided by the accurate examination of the skeletons, which revealed evident signs of autopsy practices such as horizontal and oblique craniotomies, longitudinal and transversal cuts of the sternum, and sectioning of the sternal extremities of the ribs (1).

Filippo (9 April 1598 - 3 April 1602)

Filippo was the sixth son of Ferdinando I and Cristina of Lorena. Very little is known about this child. The documents attest that on the same day of the death, April 3rd, the surgeons Pier Rossi, Fonseca and Turini autopsied the little corpse. They opened the thoracic and abdominal cavities and examined the internal organs. They reported that "We have been at Belvedere and we have opened don Filippo and [...] we found in the concavity of the thorax and in the lungs a quantity of rotten substance, large and thin. That was an astonishment, as it consisted in half a fiask of material, and furthermore among the intestine, in the abdominal cavity, abundance of this substance, thinner, came out [...]. The intestines were then all swollen, and full of wind; the other parts then, as the liver, the spleen, the kidneys and other parts were fine" (2).

The anatomo-pathological picture appears quite clear: Filippo presents a picture of acute suppurative bronchopneumonia, with pleuritic effusion, and suppurative peritonitis, thus suggesting a generalized acute septicemia.

Don Pietro (1554-1604)

Don Pietro, last son of Cosimo I and Eleonora, was ambassador for Florence in Spain. From the age of 24, he presented symptoms of a gastrointestinal disease. Court doctors described gastric bloating, fever, dark green vomit and several diarrhoeic episodes probably due to infectious enteritis treated with bloodletting and infusion of chamomile, rhubarb and barley. In the last 8 years of life, Don Pietro had severe relapsing fever, dark vomit and gastric pain, until he passed away at the age of 50. Chronicler Gomes de la Portilla wrote: "On Sunday 25 of April 1604 a surgeon performed the autopsy of the corpse; I was present too with the physicians Sepulveda, Real, the governor Silva and other noblemen. Opening the abdomen we heard a big noise of air and it seemed that a full bladder had broken out; we found the lungs grey in color, the heart healthy, the liver a little inflamed, the membrane very inflamed, the stomach with a quantity of melancholic humour and very little blood; all the rest was in quite good condition" (2).

The most mentioned symptom of Don Pietro, in addition to fever and abdominal pain, was the incoercible vomit of blood and dark material; the causes can be various but the most frequent are gastric tumor, esophageal varices caused by chyrrosis and peptic ulcer. Stomach cancer is excluded because the symptoms generally arise in advanced stage after which the death comes in few months, whereas the nobleman had a long time disease. Esophageal varices are most often a consequence of cirrhotic portal hypertension, and are present in almost half of patients at the time of diagnosis of cirrhosis whose estimated prevalence around the world is 100 (range 25 to 400) per 100,000 (3). Cirrhosis cause a marked anatomical alteration of the liver, but the autopsy of Don Pietro revealed only a little inflammation of the parenchyma, so this pathology can be ruled out.

The fact that the son of Cosimo suffered for gastric pain mainly in springtime and autumn suggest the diagnosis of peptic ulcer. This recurrent disease, whose etiology is multifactorial [*H. pylori* infection, stress, genetic factors (4)], typically appears with seasonal periodicity. A review of the literature conclude that peptic ulcer disease is lower during the summer than the other seasons of the year (5). The last acute stomach ache attack with fever and severe abdominal pain suggest the diagnosis of acute secondary peritonitis due to the perforation of the ulcer. The "very inflamed membrane" cited in the autopsy report would be the phlogistic peritoneum, while the "big noise of air" during the "opening of the abdomen" could indicate the wheezing spill of the free intra-abdominal gas which is a typical sign of a gastrointestinal tract perforation (6).

Instead, based on the anamnesis and clinical data, we believe that Don Pietro died because of an acute peritonitis due to a perforated gastric ulcer.

Ferdinando I (1549-1609)

Ferdinando I, son of Cosimo and Eleonora, was 3rd Grand Duke of Tuscany. His death was caused by heart failure accompanied by dropsy and intestinal occlusion at 60 years of age. He was submitted to autopsy and Roberto Lio, ambassador of the Republic of Venice in Florence, refers: "once opened the corpse, from the heart onward, which was beautiful, all the other parts were found damaged, as the liver was white, full of water and demonstrated a beginning of dropsy. The spleen was black and all the intestines damaged, he had no stone, but the disease was the windiness, that caused the aforesaid convulsion" (2). In the diary written by the chamber assistant Cesare Tinghi we read: "Once opened the corpse of His Majesty by Simone Cresci surgeon of His Majesty and with intervention of other physicians and found that the lungs were damaged and the liver, in the body [i.e. the abdomen] and in the intestines a large quantity of water was present; except for the heart, that was very beautiful, all was infected" (2).

The anatomo-pathological interpretation of this report suggests that Ferdinando was affected by abdominal occlusion with hepatic and intestinal edema and congestion of the spleen. Effects of occlusion could be hypothesized for the intestinal lesions and the intense meteorism; we think that they were not caused by cadaveric decay because it was February and the cold temperature should have prevented early putrefaction. Chronic intestinal obstruction was the hypothesis of the Court doctors too, since they specified that no stones (i.e. faecaloma) were found in the abdomen. The lungs were damaged and an abdominal edema is described; the expression that all was infected except for the heart could also indicate peritonitis.

The paleopathological examination of the skeletal remains of Ferdinando demonstrated the presence of the craniotomy, whereas no autopsy cuts on sternum and ribs were observed (1).

Francesco (1594-1614)

Don Francesco, 4th son of Ferdinando I and Cristina, died at 20 years of age of an acute intestinal disease, probably abdominal typhus. The death was dated May 17 at 17.45 and the corpse was submitted to autopsy on May 18, at 9.00 a.m. The report refers that "once opened the abdomen, the "hairnet" [mesentery] appeared worn and the intestine was pale and in some places red, mainly in the colon [...]. At the section the substance of the liver was yellow, the veins white without drops of blood inside. The colour of the spleen was livid, mainly the hollow part and similarly inside. The pancreas was dry, hard. In the stomach, a little liquor similar to broth was found. The intestine was full of liquor and wind similar to that found in the stomach. The duodenum in some parts was ulcerated. The jejune showed also a little ulceration. The colon downward was completely ulcerate, and with attached glandulae. The rectum was completely ulcerated, red. In the gallbladder [there were] bilious humor and ulcerations. The lungs of the right part were attached to the chest and the substance was white in some part and livid in some other, mixed. The little heart very exhausted, with a little fat. The bladder was ulcerated at the bottom, close to the rectum in two parts, which were livid. Once the cranium was cut, the beautiful natural brain appeared, without damage to the membranes and the substance, if not a little more white" (2).

As for the anatomo-pathological considerations, the picture of ulcerations of small and large intestine supports the diagnosis of abdominal typhus, an infection caused by Gram-negative bacteria, the *Salmonella* species. Most infections are orofecal, i.e. caused by ingestion of food contaminated by animal or human feces. Ulcerative colitis (UC) is a chronic inflammatory condition of the gastrointestinal tract whose association with the Salmonella enterica serotypes (Typhi and Paratyphi A both) has been demonstrated (7). Possible or expected findings during autopsy are perforation with peritonitis, inflammation and ulceration of Peyer's plaque, intestinal hemorrhage and lymphadenitis. Differential diagnosis of the various clinical and macroscopic features of infectious gastroenteritis may be extremely difficult. Anyway, salmonella infections were a very widespread cause of death in antiquity and are still an important health problem nowadays. In Italy, for example, during the period 1982-1992 the percentages of Salmonella enteritidis isolations have increased from 2.4 to 57.1% from human beings and from 0.5 to 22.8% from food (8). In paleopathology, several studies, with the help of ancient DNA, have highlighted how many epidemics of the past, whose responsible was believed to be the plague, were due to a large contagion from Salmonella species (9, 10).

Don Giovanni (1567-1621)

The autopsy of Don Giovanni, illegitimate son of Cosimo, was performed two days after his death and do not reveal any specific alteration; in fact "the viscera of His Eminence were found very beautiful" (2).

Cosimo II (1590-1621)

Cosimo II, son of Ferdinando I and Cristina from Lorraine and 4th Grand Duke of Tuscany, had a poor health since he was a child. His condition was described as '*habitus tisicus*' (2) by the fact that tuberculosis weakened his body. He died at the age of 30 after eleven years of reign. "On the March 6th the necroscopy of the Granduke Cosimo II was performed. Once opened the body of His Majesty and puled out all the viscera and well considered all, they found the liver beautiful and without spot, the loins and the bladder beautiful and the heart good and hard, but the spleen little and little crumbled and the apices of the lungs a little ulcered and crumbled; in the abdomen the mesentery was little and the mesenteric veins narrow" (2).

This report proved indeed a pulmonary bilateral ulcerative lesion with retraction of the sclerotic pa-

renchyma certainly of tubercular origin. Curiously, no other signs of tuberculosis were detected during the autopsy.

Maria Maddalena of Austria (1589-1631)

Maria Maddalena of Austria, daughter of Carlo II and Maria Anna of Bavaria, was wife of Cosimo II: she suddenly died during a state trip in the direction of Vienna to meet his brother, Emperor Ferdinand II, after visiting the other brother Leopold in Innsbruck. The Court doctor, Ronconi, wrote in Latin the description of the evisceration of the body of the Archduchess. The organs were generally in very good conditions, except for the hearth and the lungs that were damaged. The hearth "was big, surrounded by a putrescent blood, and the fleshy substance [i.e. the myocardium], that is solid by nature, appeared flaccid" whereas the lungs "had copious humor from the apices" (2). This pathological picture has no character of specificity, so we can hypothesize a pulmonary infectious disease with cardiac involvement as a cause of death.

Maria (1575-1642)

Maria, 6th daughter of Francesco and Giovanna from Austria, was Queen of France and Navarra as second wife of Henry IV of France. On her death, alone and in exile in Cologne, there are few certain documents so that the causes of his demise remain obscure. However, it is well documented the fact that the sovereign suffered in the last years of life from 'dropsy' due to oliguria. The oedema of the legs was so severe that a phlyctena with superficial necrosis of the skin appeared. The necropsy report, written in French, affirmed that "the external exam of the corpse showed that the cancrene was generalized and from the right leg it had gained all the back. Large strips of epidermis come off and the rest of the skin was of a very bad color and intense yellow. The heart was about twice its volume; the abdominal cavity was full of a malodorous and purulent liquid. The intestines and the liver were in putrefaction; the same for the kidneys, which were atrophied, especially the right one; the pancreas and the mesentery equally in destruction. The ventricle [was] dilated and showed, inside, an excoriation similar to a sore" (2).

Excluding the organs with initial putrefactive phenomena (pancreas, intestines and liver), it is crucial to note the sclerosis of the kidneys and the marked cardiomegaly that must necessarily be related to the dropsy described by the Court doctors. In fact, we can hypothesize a pathology characterized by chronic kidney disease (CKD) (underlined by the poor diuresis reported by the chronicles) with intense oedema of the lower limbs and marked chronic heart failure (with the so-called 'bovine' heart) that may have led Maria to death. Actually over half of all heart failure patients may have moderate to severe chronic kidney disease (11). Over 80% heart failure patients are \geq 65 years and most of these patients suffer from one or more comorbidities like the obesity, and we know that there were both present in the Queen.

Unfortunately, in 1793, revolutionaries profaned the tomb of Maria in the church of Saint Denis and dispersed her remains.

Leopoldo (1617-1675)

Cardinal Leopoldo, last son of Cosimo II and Maria Maddalena of Austria, showed one of longest autopsy report of the Medici family. The body was opened the day after the death and "the thorax was both externally and internally with a natural color without any humor. The substance of the lungs in the dorsal part of the extremities of the lobes, right and left, was inflamed for an extension of four fingers [...] the remaining part was natural. The pericardium was not wet and the hearth was brown, with a proportionate size and a flaccid consistency rather than compact, with the ventricles empty; in the right part was found a bloody polyp, soft and a span long. [...] The stomach had a normal size and shape, but the external color was not normal since it clearly appeared very inflamed, with the veins very swollen and full of dark blood. In the inner part, the inflammation was even more evident not only in all of the veins but also in the whole part [...]. The intestines, externally and internally, had normal color and no other substance was found except the one that should be present normally. The extremity of the rectum had a livid color for a height of two fingers, where we found three small wrinkles with a size of a lens and fistulous for a length of a finger, from which came out a rotten material with a good color and in a quantity of a spoon. The peritoneum, the mesentery, the liver, the spleen, the pancreas and the urinary bladder were all in an excellent state of preservation. The liver however was larger than the normal size [...]. The two kidneys were quite small, with natural color, soft consistency and with some cysts full of water on the outer surface [...]. Opened the cranium, from the inner cavity a portion of bloody serum overflew and the *dura madre* appeared in a reddish color [...], the pia madre appeared inflamed and almost black with enlarged black veins even though the brain was not mutated in color and condition [...]".

No severe conditions were noticed sufficient to find the cause of death even if the necropsy report appeared very detailed and 'modern' in the way the organs are analyzed and dissected. Except for a chronic rectal fistula with abscess, other descriptions could be related to thanatological phenomena (e.g. the inflamed aspect of the lungs and the red color of the meninges). It is possible therefore that the Cardinal died for an acute disease that did not entail evident changes of the inner organs.

Vittoria della Rovere (1622-1694)

Vittoria della Rovere, daughter of the last Duke of Urbino, Federico Ubaldo Della Rovere, married Ferdinando II in 1634. We have extensive documentation on the state of health of the noblewoman since its birth, who as a child never suffered from serious illnesses, with the exception of sporadic and minor ailments (colds, fever, and toothache). However, during the pregnancy at the age of 17, he contracted the smallpox that caused the loss of his son, born premature. Over of the years Maria Vittoria adopted a sedentary lifestyle not disposed to physical activity, which led her to suffer from the consequences of mild obesity, such as oedema of the lower limbs and subsequently heart failure. After her death, occurred at the age of 72, the autopsy and subsequent embalming were complicated by the imposing mass of the woman who spent in bed most of the last year of her life. The diary of Tinghi refers: "Twelve hours after the death of the Grand Dukess her corpse was opened and it appeared of very big size to the surrounding people, as each tight had the circumference of one arm and two third. The color of the skin in all the hypogastric region [was] very polished almost similar to that of the gangrene, and in the posterior part of the right knee a sore with loss of the skin was found started, as well as in the buttocks, being the sore large like a half plate. They therefore opened the corpse... and taken out the intestines, and a large quantity of fat, they embalmed the body... From the inspection of the corpse it was observed that the origin of the death... it seemed that had depended from the not total suppression, but largely for the urine for the time of two months done in this princess, not by fault of the urinary canals, which were found pure and innocent, but for defect of separation". This description suggest that the there was an altered function of the kidneys. In the "Information of the death and funerals of the Grand Dukess Vittoria della Rovere (2)" the necropsy is so summarized: "In the corpse water was found everywhere".

The circumferences of the thighs (97 cm) and the numerous bedsores are also cited, especially at the sacral area and behind the knees. The autopsy report shows in particular the large quantity of liquids of which the organs were soaked. This confirms that the cause of death should be sought in generalized edema due to congestive heart failure.

Ferdinando (1663-1713)

Prince Ferdinando, first son of Cosimo III and Margherita Luisa of Orléans, died before his father and never became Grand Duke. In 1689, he married Violante Beatrice, daughter of an imperial elector Ferdinand of Bavaria and Adelaide of Savoy. However, from the last trip to Venice in 1696, on the occasion of the Carnival, Ferdinand returned suffering from syphilis that inexorably led him first to mental illness and then to death in 1713. The neurological involvement also manifested in form of paralysis, convulsions and unconsciousness in the last 4 years of his life. He was treated with mercury pills, but was intoxicated by his physician, the English Dr. Maundy, with exaggerated doses, which certainly aggravated the neuropathies. The corpse was analyzed by the barber-surgeon Grassi in presence of various professors, "who recognized that the viscera were healthy without defect, except for a lung, which was dry, for the lack of blood, of humid and of sera". In another report it is referred that the corpse "was found missing at all of humid and blood, and with all the viscera very beautiful, and every other part of the brain intact and healthy" (2).

All agreed on the physiological aspect of all organs, but with excessive state of dehydration and poor presence of blood. The report is excessively concise and, although they knew the cerebral syphilis, the analysis of the brain is hasty since there was not reported any alteration. In that time, the alterations caused by syphilis to the nervous system were not recognized; only the lesion to the lung, which can be interpreted as a pulmonary sclerosis of syphilitic nature, was observed.

Margherita Luisa of Orléans (1645-1721)

Margherita Luisa of Orléans, daughter of the Duke Gaston of Orléans and Margherita of Lorraine, had a turbulent marriage with Cosimo III until she get the separation and the authorization to return to France, her homeland, where she died at the age of 76. Among the information about her health that are reported in detail by the doctors of the Court, there is a very interesting episode occurred on the evening of July 16, 1712. The Grand Duchess suddenly lost the motility of her left arm and leg, twisted her mouth on one side and was seized by aphasia. In the following days Margherita partially recovered her mobility and returned to talk, but a new apoplectic episode occurred in December 1713 caused the definitive decay of the noblewoman's clinical conditions. These symptoms are clearly compatible with an ischemic stroke localized in the right hemisphere of the brain. It is difficult to identify the etiology of this disease for the Duchess since many may be the causes, including atherosclerosis, diabetes, cardiac diseases and high blood pressure.

The last year of her life is studded with episodes of severe gastrointestinal disorders associated with fe-

ver alternated with cough and phlegm. The doctors also question the mental lucidity of the woman as she started to laugh for no reason, was no longer able to look after herself and stutter incomprehensible words. Finally, after the doctor found her dead on September 17, the autopsy and embalming was arranged in Paris. The necropsy report was drafted in French and is an interesting document for the history of medicine since it demonstrates the high quality and the great modernity of French physicians of that era. Here the translation: "this 18, at 10h we undersigned assembled in the Hotel of S.A.R Royal square... have proceeded to open the body of Her Royal Highness dead the day before about 10h in the morning, after 6 months of languor and 9 years of paralysis. Having started with the head we had found the brain of a natural color and consistence, the dura and the pia much more dense and bloaten of blood than these membranes normally are, being in some part dry and unequal for the obstruction of their glandes, which naturally imperceptible, after the superior sinus of the falx, granular and rough under the fingers like the sand grains. All the ventricles of the brain were strongly dilated for a great abundance of turbid serum of which they are full, to which the lethargy of 24h, which has preceded the death, can be attributed. The chest had anything unnatural, if not the heart which was very fat and of flaccid consistency and soft which rip under the fingers, particularly the left ventricle. In the lower abdomen, we found the intestines which navigated in a purulent material without being altered neither the stomach. The gallbladder filled with a stone of the dimensions of the gallbladder itself, and above the coating of the liver in the concave part, an abscess that has to be considered the cause of fevers, irregular thrills, disgust, want to vomit, vomits themselves and other accidents which supervened to the paralysis after 5 or 6 months. The stone of the gallbladder could cause this abscess for its size and solidity compressing the neighboring vessels. We also remarked that of the two ovaries, the right one was perfectly bright of the shape and hardness of a chestnut. The left one much bigger than the natural state of an oblong shape and of a consistency so hard that the chisel could not penetrate it, all the vesicles, which are called eggs were small bone lamellae applied one over the other" (2).

This report reveal a great deal of precision and a methodological approach not dissimilar to that of modern pathologists. All the anatomical alterations (like the meningeal thickening, the hypertrophy of the Pacchionian granulation etc.) are minutely described, and the clinic-epicritic reconstruction is in detail. For example, doctors recognized a purulent peritonitis secondary to liver abscess, correlating the symptomatology described by Margherita in the last years of his life. The study of the brain demonstrates the dilatation of the ventricles, which is in accordance with the severe cognitive decay of the sovereign. It is very interesting to note the meticulous description of the female genital organs that represents a unicum among the reports of the Medici family. Both ovaries appeared calcific and almost impossible to cut; also, within the ovary minute 'eggs' that are referable to the involution of the ovarian follicle are described. Calcifications may be associated with neoplastic disease, either benign (teratoma, mucinous cystadenoma, thecoma) or malignant (serous carcinoma), or with endometriosis (12). In non-neoplastic elderly ovaries, bilateral calcifications are also associated with corpora albicantia, which are the regressed form of a corpus luteum (i.e. an endocrine structure that develops from an ovarian follicle). Most corpora albicantia are resorpted in premenopausal women, but they may persist in the ovaries of postmenopausal women (13). In the absence of a symptomatology and macroscopic alterations referable to a malignant neoplastic disease, we believe that the appearance of the ovaries of Margherita is due to regression phenomena related to its advanced age or possibly to a benign neoplasm such as a fibroma or thecoma.

Cosimo III (1642-1723)

Cosimo III, son of Ferdinando II and Vittoria della Rovere, is a key figure in the history of the Medici family because his reign is the longest in the history of Tuscany, and his political and economic choices resulted in a worsening of the decline of the kingdom, which in fact ceased with the death of his son, Giangastone. At the age of 81 the Grand Duke died because of a gradual decay of the general conditions lasted 53 days (14). The necropsy was carried out by Giuseppe del Papa, lecturer of medicine in Pisa, who refers: "All the corpse seen and observed externally did not demonstrate any particular defect, but instead a solemn universal emaciation of the limbs and especially of the thighs and legs, and of the arms, which appeared as bones of skeleton dressed with a dry skin; the rib cage was fleshless for the extreme thinness of its integuments, but the cage did not little appearance for its natural breadth, and also the lower abdomen, although dressed by very thin teguments, did its appearance of sufficient elevation to contain a liver of no little size, as the not little mesentery. Only exteriorly it could be observed a long strip of skin very livid in the right part of the thorax and in the flank, where the H[is] R[oyal] H[ighness] rested always with the weight of all the body, that it is possible that in the last moments of his life had produced this external and superficial skin bruise. Once opened the lower abdomen the very large size of the liver was immediately visible and of good consistency and of excellent color with its gallbladder without any trace, as also the spleen both in size and in substance, was not blameworthy. Not so can be said the ventricle, which was observed very vitiated, not only for its dark and denigrated color, and in particular in the left part around the superior orifice, but also as the ventricle had its tunics thin and consumpted, so that for any little force applied to them they broke, so there was no wonder in knowing that HRH from several and several years had very scarce appetite and from any little quantity of food received always boredom and trouble, and never he could had food with some activity and especially those acid, bitter, salty, aromatic, and until the hot and cold of the food caused him immediate harassment. The intestines were filled in all their long tract of gas with very big excrement inside the last and big intestines, and all together had their tunics very thin and fleshless without any blame. The major defects were observed in the urinary canals and instruments, and firstly the left kidney was in the pelvis dilated and swollen for the abundant urine which contained, and more dilated was all its annexed ureter to be still swollen and filled with urine for all its length until its last approach to the bowel, where inside the ureter itself a stone stably fixed and imbed of the dimensions of a little date pit, which prevented the course and descent of the urine. The right kidney

had its natural consistency, as well as its annexed ureter was free and open and therefore all the urine descended; but it is true that in both the abovementioned kidneys several little stones and more than a little sand were found. The urinary bladder appeared between all other viscera the most broken down and vicious, for the fact that all its internal surface was plagued by a livid and dark sore deriving from a mortification or gangrene, and this dark color was communicated for all the substance of the tunics of the bladder and was diffuse also at the urethra itself for half of its length. Outside the bladder it is worthy of being observed that both the glandulate bodies called prostate were big of a size very unnatural. Inside the thorax no defect was observed which deserves to be described, for the fact that a certain dark and obscure color which was seen in some place of the lungs is in effect usual in all corpses produced by the stagnation of the blood occurring in the last of the life, and in particular in the corpses of old men who suffered the affliction of a long infirmity, and lastly a long agony. The heart then in the advanced age was observed of bog size and robust fibers and without any astonishment neither internal nor external. Finally inside the skull anything worth to be mentioned was observed, whereas all the substance of the brain together its membranes appeared of natural color without extravagant oppression of sera, and also the skull bones appeared good for their size and robusticity more than usual and natural" (2).

The autopsy is extraordinarily detailed and precise, from the careful external examination of the body to the evisceration and the analysis of the different organs. No district is overlooked and every detail is investigated, such as the gallbladder content, the appearance of the mesentery and the mediastinum. The genitourinary district is investigated and described with greater precision. Correctly, the doctors dwell on its pathological aspects because the renal and urinary diseases were responsible for the death of Cosimo. The left ureter appeared completely obstructed by a stone, while the right kidney contained numerous small stones and gravel. The bladder and ureter had an internal ulcerated surface with black color and flaccid consistency, and contained dark liquid. Finally, the pronounced hypertrophy of the prostate lobes with the consequent obstruction of the urine outflow was reported. With this description, we can easily formulate an epicrisis to clarify the cause of death of the Grand Duke. The subject was of an advantage age and suffered from benign prostatic hyperplasia, a very common condition in adults and elderly (15). This led to a urinary stasis with renal suffering and especially with a severe bladder infection, probably bacterial (hemorrhagic cystitis) that irreparably compromise the health of the monarch.

Giangastone (1671-1737), the last Medici

Son of Cosimo III and Margherita Luisa of Orléans, Giangastone was the last Grand Duke of the Medici dynasty, ruling from 1723 to 1737. In the last years, he became obese and very weak, consumed by a dissolute and lecherous lifestyle.

"On the morning of 10 [June], it was judged necessary to open the body of the Royal corpse, which was done at 3 p.m. by five surgeons who were his chamber assistants, with the presence of Dr. Niccolò Gualtieri, physician of His Royal Majesty [...] and the following things were observed: all the integuments and all the viscera contained in the thorax and in the lower abdomen were generally seen occupied by a perfect fatness, which does not astound, especially those who know with how little food the Grand Duke has been nourished, in particular in the last five weeks of his life. Once opened the skull, the brain, and the cerebellum were seen without lesions, with abundant humidity, and all of excellent color and of excellent substance. The lung, particularly in the right lobe, had in the surface, and much more in its substance, a color not only different from the natural with some portion of extravasated lymph, and a part of bad color so that it was similar to rotten, but this change must be considered occurred in the last days of the disease, and in the long and painful agony suffered by His Royal Highness; therefore, his breathing has always been very natural and equally natural has been the decubitus, and similarly the pulse was observed without that alteration which generally accompanies the long diseases of the lungs. The heart was of considerable size, but had a languid and limp fibers, and in its two ventricles, as it is observed most of the time in the cadavers, two long and thin polyps, but resistant to cut, were observed. The liver in all the substance was of not bad constitution, except the gallbladder that was empty, and without a drop of bile. In the ventricle the tunics were seen infinitely thinned, weakened and limp, so that as soon as it was possible to seen it, nevertheless the great diligence of the surgeons, the simple contact with their hands very easily lacerated it. At its bottom a little portion of fat, smelly and dark substance floated. The pancreas, the spleen, the mesentery and all the intestines were in their natural state, and of a fibrous and galliard consistence, but the intestines were empty, as the arteries and the veins still contained little quantities of blood, and much lower than the quantity of its temperament. In the opening of the kidneys, which were very large and robust, some little calculi were observed which were about to move to the pelvis, and other [calculi] held in the ureters, and a few were fallen in the bladder, and in total they were 18 in number of different dimensions and colors. However, in the right ureter four fingers far from the entrance of the bladder one was found, which properly was attributed the definition of stone, as it reached the weight of 5 deniers, and 11 grains. This one, being of very strong substance, smooth and formed by very thin layers, with great violence kept the ureter outstretched, and as it caused a very great pain to the Royal Sick, and a great violent effort in the act of urinate, thus it is highly believable that, united to the miserable weakness and inability of the ventricle could have been one of the fatal causes, for which we had lost our very clement Sovereign. Once finished the section, the Royal Body was diligently joined and embalmed with different precious aromas."

The observations of the court physicians allow supposing that Giangastone was obese and that he was affected by terminal bronchopneumonia of the right lung; as for the heart, a cardiomegaly with whitening due to congestive heart failure and two intravetricular myxomas could be suspected. In the stomach an atrophic gastritis seems to be described, whereas, the strangury was caused evidently by the well described renal, ureteral and bladder calculosis with cystitis. The death occurred probably for heart failure.

At the paleopathological examination, the skull showed the sign of a craniotomy. His corpse appeared wrapped in a large quantity of clothes, which prevented recovery and observation of the postcranial skeleton (1).

Discussion

The period under consideration is that in which Théophile Bonet of Geneva (1620–89) reported the observations made in 3,000 autopsies in his *Sepulchretum* first published in 1679. Nevertheless, the practical origins of the modern autopsy lie in the following century with anatomist Giovanni Battista Morgagni (1682-1771), professor at the University of Padua. He produced the first major work on the subject, *De sedibus et causis morborum per anatomen indagates*, in 1761, where he describes nearly 700 autopsies correlating the symptoms presented by the patients during life with the lesions observed in the cadavers. With Morgagni the humoral pathology, which had dominated the medicine for century was finally abandoned in favour of a modern pathology of organ.

As for the Medici, at the beginning of the 17th century the descriptions are still oriented to the quantifications of liquids, or humors, according to the theories of Hippocrates and Galen. This is valid also outside the boundaries of Italy, judging from the investigation of the corpse of Don Pietro, which took place in Spain and whose necropsy description, written in Spanish, demonstrates the same cultural background of Italy.

Later in the 17th century, the trend toward brief autopsy descriptions observed in the previous century was abandoned in favour of more accurate human dissection. Reports describe in detail the processes of the examination and the appearances of the organs observed during the autopsies.

We must dwell on what is handed down to us on the study of the corpse of Maria (death in 1642) and Margherita Luisa of Orleans (1645-1721) because, despite having been executed in two distinctly different epochs, both were performed in France. In both cases, the high value of the French medicine of that time is shown because the autopsy is performed with modern criteria. All the organs are analysed and dissected with precision and method, the colours of the organs and their characteristics are described and all the alterations are put in connection in order to formulate a complete epicrisis in which the sequence of the initial, intermediate and final death causes are listed.

In Italy, the full maturity in the necropsy study takes place at the end of the 17^{th} century and is well

demonstrated by the descriptions of the body of Cardinal Leopoldo and Ferdinando II. Indeed the approach to the corpse is modern so that the doctors linger on the external inspection of the corpse with the complete evaluation of the skin and of any external pathological phenomena. All the alterations are then put in relation to each other and with the symptomatology that the subject manifested in life. The interest towards 'the humors' seems to be set aside for a more modern and 'scientific' approach.

In 1723, the autopsy on Cosimo III is extraordinarily detailed and precise, from the careful external examination of the body to the evisceration. Giuseppe Del Papa, Master of Anatomy at the University of Pisa, performed the procedure that was one of the most important university town in Italy. The city had a long tradition of anatomic studies since also the autopsy on Don Francesco (death about a hundred years before Cosimo III in 1614) was led by the Master of Anatomy of Pisa with the help of seven assistant doctors. With the study of the body of Cosimo III also the evisceration technique changes, as it is performed, like nowadays, starting from the thorax and then analysing the abdomen and the pelvic organs. It almost seems to read a modern report, in fact it is first described the corpse externally and then the dissection is performed.

Finally, Niccolò Gualtieri, Royal Court Doctor, carried out the autopsy of the last Medici, Giangastone, who died in 1737, with other five surgeons and several assistants. The report seems almost to anticipate the novelties that will be introduced by Morgagni a few years later; in fact, the approach is fully scientific and every single organ is cut, described and related to the medical records of the Sovereign. For example, the brain is not treated as a single entity, but is divided into its individual parts, such as the cerebellum. In conclusion, despite being in the first half of the 18th century, we find in this report the same terms and techniques that will come substantially unchanged until the post Second World War period when, with the advent of new discoveries and new imaging techniques, there is the birth of modern medicine.

The analysis of the documents relating to the autopsy investigations proves to be of great interest and importance. These archives are in fact a very valuable source of information about the state of health of past populations and reveal which diseases were present and how they were treated. It is possible to understand how the influence of new theories and new scholars is reflected in the practice of autopsies learned in the great university centres of the time.

Moreover, comparing the detailed nosographic descriptions of the court doctors with the skeletal material of the great Medici family is fundamental to better understand the evolution of the pathological anatomy and of the legal medicine and provides an indispensable contribution to the history of medicine.

References

- Giuffra V, Fornaciari A, Minozzi S, Vitiello A, Fornaciari G. Autoptic practices in 16th-18th century Florence: skeletal evidences from the Medici family. International Journal of Paleopathology 15, 2016, pp.21-30.
- 2. Pieraccini G. La stirpe dei Medici di Cafaggiolo, vol. 2. Firenze: Nardini Editore, 1986.
- La Vecchia C, Levi F, Lucchini F, et al. Worldwide patterns and trends in mortality from liver cirrhosis, 1955 to 1990. Ann Epidemiol. 1994;4:480-486.
- Vergara M, Catalan M, Gisbert JP, Calvet X. Meta-analysis: role of Helicobacter pylori eradication in the prevention of peptic ulcer in NSAID users. Aliment Pharmacol Ther. 2005 Jun 15. 21(12):1411-8.
- Gibinski K. A review of seasonal periodicity in peptic ulcer disease. Chronobiol Int. 1987;4(1):91-9.
- Coppolino FF, Gatta G, Di Grezia G, Reginelli A, Iacobellis F, Vallone G, Giganti M, Genovese EA. Gastrointestinal perforation: ultrasonographic diagnosis. Crit Ultrasound J. 2013; 5(Suppl 1): S4.
- Tripathi MK, Pratap CB, Dixit VK, Singh TB, Shukla SK, Jain AK, Nath G. Ulcerative Colitis and Its Association with Salmonella Species. Interdiscip Perspect Infect Dis. 2016;2016:5854285.

- Fantasia M, Filetici E. Salmonella enteritidis in Italy. International Journal of Food Microbiology. Volume 21, Issues 1–2, January 1994, Pages 7-13.
- Papagrigorakis MJ, Yapijakis C, Synodinos PN, Baziotopoulou-Valavani E. DNA examination of ancient dental pulp incriminates typhoid fever as probable cause of the Plague of Athens. Int J Infect Dis. 2006 May;10(3):206-14.
- 10. Vågene ÅJ, Herbig A, Campana MG, Robles García NM, Warinner C, Sabin S, Spyrou MA, Andrades Valtueña A, Huson D, Tuross N, Bos KI, Krause J. Salmonella enterica genomes from victims of a major sixteenth-century epidemic in Mexico. Nat Ecol Evol. 2018 Mar;2(3):520-528.
- Ahmed A, Campbell RC. Epidemiology of Chronic Kidney Disease in Heart Failure. Heart failure clinics. 2008;4(4):387-399.
- Lanzafame S, Nicolosi AG, Caltabiano R. Bilateral massive osseous metaplasia in ovaries: "ovarian stones". Gynecological Surgery. September 2007, Volume 4, Issue 3, pp 191–193.
- Brown DL, Hirsch MS, Muto MG and Laing FC. Unresorbed Corpora Albicantia Mimicking a Sonographically Solid Ovarian Mass in a Postmenopausal Woman. Journal of Ultrasound in Medicine. 2004; 23: 1523-1526.
- Relazione dell'ultima malattia, morte, processione, e sepoltura dell'Altezza Reale del serenissimo Cosimo III Granduca di Toscana. Stamperia di S.A.R. per Tartini e Franchi. Firenze, 1723.
- Barry M, Roehrborn C. Management of benign prostatic hyperplasia. Annu Rev Med. 1997;48:177-89.

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