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Pediatric medicolegal autopsy in France: A forensic histopathological approach

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ABSTRACT

The aim of postmortem medicolegal examination in pediatric death is primarily to establish the circumstances and causes of death and to exclude child abuse. In France, pediatric death is systematically documented by medicolegal or medical autopsy. In case of medicolegal autopsy, the complementary examinations, requested and financed by justice, are rarely limited to a histopathological examination. However in medical autopsies other tools are available to the pathologist as toxicology, biochemistry and molecular biology. The purpose of this article is to evaluate the efficacy of forensic histopathology in pediatric forensic autopsies. We analyze the main causes of pediatric death in a forensic context. Between 2004 and 2015, 157 infant deaths were identified in Marseille university hospital. The forensic histopathology and autopsy reports of all 157 cases were available for systematic review. Medical or surgical causes represented 41,3% of deaths in our center, accidental causes 8.1% and child abuse 28,8%. The definitive diagnosis was made at autopsy in 30% of cases and at histopathological examination in 70% highlighting that forensic histopathology is an indispensable tool in pediatric medicolegal autopsies. Significant histological abnormalities may be detected in selected organs such as the brain, lungs, heart, liver, adrenal glands and kidneys in spite of macroscopically normal appearances. This justifies systematic sampling of all organs. Despite the implementation of the French sudden infant death protocol which recommends medical autopsies, too many pediatric autopsies are carried out in a medicolegal context. 30% of the cases remain without diagnosis at the end of the autopsy and histological examination. This number could be reduced by the contribution of others laboratory investigation.

1. Introduction

In France and most European countries, deaths of children under one year of age passed below the threshold of 10 deaths per 1000 children around the year 1980.[1] Infant death has now become a rare and/or accidental phenomenon in all developed countries. According to INSEE (the French National Institute of Statistics and Economic Studies) the child mortality rate was 3.8 per 1000 live births in 2016. However, there are marked social and geographical inequalities in mortality at birth and during the first year of life in France.[2] The aim of postmortem medicolegal examination in pediatric death is primarily to establish the circumstances and causes of death and to exclude child maltreatment.[3,4]

In France, child death is systematically documented by autopsy. Since 2007, the recommendations of the French High Authority for Health[5] define the context in which autopsy should be performed: medicolegal autopsy or medical autopsy/hospital autopsy. The spectrum of pediatric diseases is wide, ranging from common to extremely rare diseases, and due to the absence of a history, most deaths remain suspicious and lead to forensic analysis.

Lesions occurring in the perinatal period and infancy encompass the entire field of pathology associating traumatic, inflammatory, vascular, neoplastic and metabolic conditions. Pediatric histopathology is a unique discipline and these lesions are often expressed differently from those of the same condition in adults. Comprehensive histopathological screening is important especially for investigating the mode and process of death, as well as contributory factors including predispositions and complications, rather than for determining the initiating cause of death. Lesions arising in the neonatal period or early childhood may go unnoticed during pediatric consultations and may be discovered later sometimes in the context of suspected child abuse or other circumstances of forensic importance.[6,7] Forensic pathologists need to be

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aware of these considerations so that proper interpretations can be made.

In France, in case of medicolegal autopsy, the complementary examinations are requested by the magistrate and financed by justice without forensic pathologist's discretion or suggestion. In this context, histopathological examination is often the only examination requested by the magistrate. Major laboratory sections including toxicology, biochemistry, microbiology and molecular biology are more rarely demanded by the courts. Although in medical autopsy, all of the laboratory exams are available to the pathologist.

The purpose of this article is to evaluate the efficacy of forensic histopathology in pediatric forensic autopsies, highlighting the histopathological lesions frequently observed. We analyze the main causes of pediatric death in a forensic context.

2. Materiel and methods

We conducted a retrospective review from January 1, 2004, to December 31, 2015. The eligible population included all infants and young children up to 2 years of age and underwent a forensic autopsy and pathological examination by our physicians, and whose histopathology and autopsy reports were available for systematic review. All cases were anonymized.

All the autopsy were standardized according to the French protocol defined by the French High Authority for Health.[5] Specimens required for histology were fixed for at least 72–96 h in 10% buffered formalin before cutting. Hematoxylin, eosin and saffron (HES) staining was performed for all sections. Furthermore, other staining methods or immunochemistry was applied.

For the description of the most common pathological lesions, we excluded cases of abusive head trauma.

The following epidemiological data were collected: age, year of death, and gender. The principal macroscopic and microscopic lesions were also recorded, and the final diagnosis.

We differentiated the cases where the diagnosis could be made by autopsy alone from those requiring histopathological examination. The criteria for autopsy diagnosis of the cause of the death was for “infection” the presence of purulent secretion; for “surgical cause” any pathology that could have been treated by surgical procedure; for “prematurity” all postnatal complication related to birth before 37 weeks of amenorrhea, for “malformation” any congenital morphological alteration of an organ causing the death; for “fire” smoke soot covering the larynx, trachea and bronchi; for “drowning” the presence of fine white froth at the mouth, nose, air passage or lungs, voluminous water-logged lungs, the presence of water in the stomach; for “trauma” the presence of traumatic or hemorrhagic lesion causing the death; for “child abuse other than abusive head trauma” the presence of malnutrition, skin lesions or bones fractures of different age.

Simple statistical analyses were carried out in the form of percentages.

3. Results

Our institute has an average of 665 forensic autopsy cases per year, including 22 pediatric autopsies. We identified 215 infant and young children up to 2 years of age deaths from 2004 to 2015 who have undergone a forensic autopsy and histopathology: 55,3% of males, 43,7% of females, mean age: 9,2 months. Four primary causes of death were identified at the end of the autopsy and/or histopathological examination in this cohort (Table 1).

Fifty-eight (27%) of histopathological examinations related to abusive head trauma.

We retained 157 patients for descriptive histopathological analysis; 44.9% of girls and 55.1% of boys. The mean age was 11,2 months. The definitive diagnosis was made at autopsy in 30% of cases and at the histopathological examination in 70%. Isolated asphyxia and unknown causes of death were considered as uncertain cases.

Table 1
Causes of death.

Causes of death	Number (%)	Gender (Male/ Female)	Mean age (month)
Medical or surgical causes	89 (41,3%)	(47/42)	6,8
Infection	58 (27%)	(31/27)	12,8
Surgical cause	6 (2,7%)	(5/1)	12,1
Prematurity	16 (7,4%)	(6/10)	3,3
Malformation	6 (2,7%)	(3/3)	0,2
Metabolic disease	2 (1%)	(1/1)	2,6
Tumoral	1 (0,4%)	(1/0)	10,5
Accidental causes	16 (8.1%)	(10/6)	12,1
Fire	5 (2.7%)	(2/3)	13
Drowning	1 (0.4%)	(1/0)	8,6
Trauma (traffic accident, defenestration)	10 (4.6%)	(7/3)	13
Child abuse	62 (28,8%)	(39/29)	11,9
Child abuse other than abusive head trauma	4 (1,9%)	(2/2)	20
Abusive head trauma	58 (27%)	(33/25)	3,8
Uncertain causes	48 (22,3%)	(21/20)	6
Unknown	17 (7.9%)	(8/9)	5,5
Isolated asphyxia	31 (14,4%)	(18/13)	6,6

Centre nervous system examination

The brain was examined in 147 children (93.6%). A neurological cause explained 6% of deaths; the cause of death was made:

- purely on macroscopic examination in 4,7% of the deaths (acute meningitis, traumatic brain injury, leukemia, hemorrhagic or ischemic prenatal condition).
- purely on histology: none.

Macroscopic examination was normal in 49.6% of cases. The principal macroscopic lesions were edema, arachnoid anomaly (purulence, focal hemorrhage), ventricular dilatation, cystic destruction, traumatic lesions and neoplastic lesions (corpus callosum lipoma, choroid plexus papilloma).

However, microscopic examination can refine the diagnosis or understand the physiopathological mechanism at death. Meningitis was associated with cortical vein and sagittal sinus thrombosis in half of the case.

Non-specific microscopic lesions were found in 87% of cases and are summarized in Fig. 1.

The peri-ventricular area was the principal localization of chronic anoxia ischemia. Secondary lesions to prenatal ischemic or hemorrhagic conditions were ventricular dilatation with periventricular gliosis, leukomalacia, and cystic destruction of white matter.

The eyes were examined in 33 children and were all devoid of microscopic abnormality.

No cervical spinal cord examination was performed.

Heart examination

The heart was examined in 153 children (96.2%). Macroscopic and microscopic examination was normal, respectively, in 84.9% and 60% of cases. A cardiac pathology accounted for 7.4% of deaths: the cause of death was made:

- purely on macroscopic examination in 2,6% of deaths (cardiac malformation: valvulopathy, intra-ventricular communication);
-purely on histology in 1,9% of deaths (myocarditis: acute, chronic and eosinophilic inflammation, associated with myocardic necrosis).

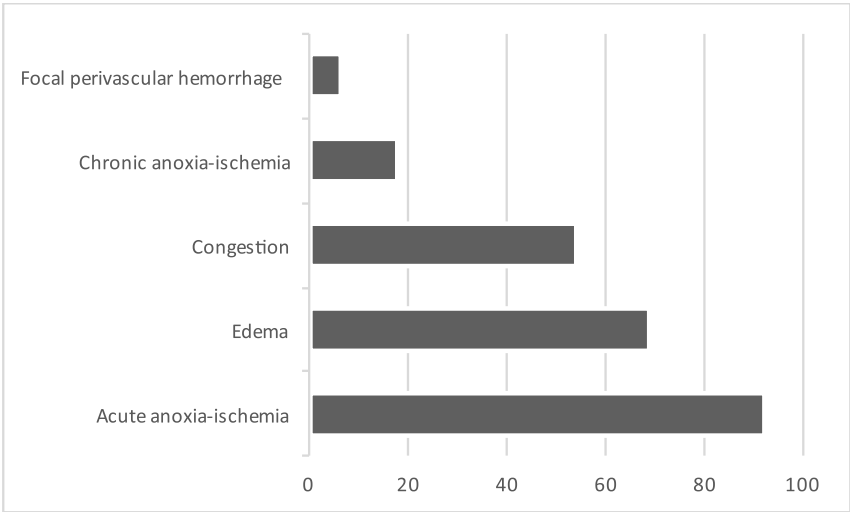

Fig. 1. Nonspecific pathological changes observed in the brain.

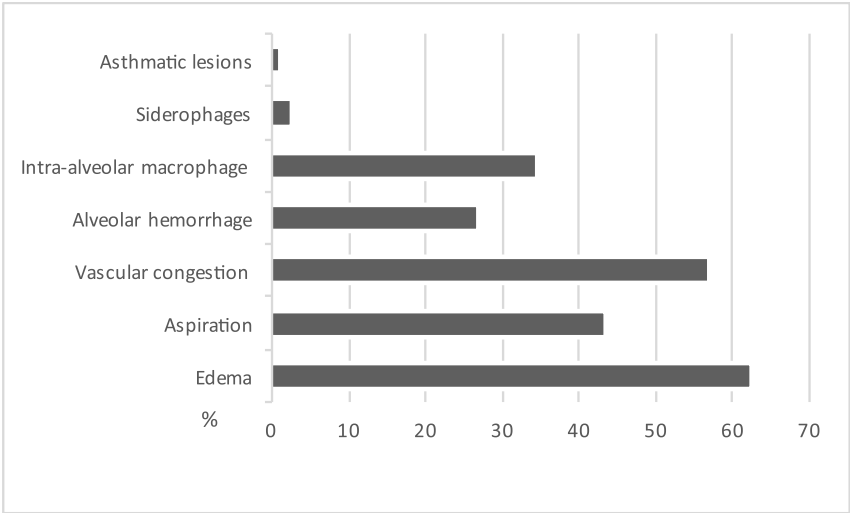

Fig. 2. Pathological changes observed in the lung.

The principal causes of death were cardiac malformation, hypertrophic heart disease and myocarditis. Hypertrophic heart disease was mentioned during the autopsy, and was confirmed in microscopy for 17 cases with hypertrophic myocardial cells for all the case, necrosis in 35% of cases and with fibrosis in 29.4%. The main pathological changes are summarized in Fig. 2. The children with persistent patent foramen ovale were all aged less than 6 months and represented 21% of our cohort. Non lethal cardiac malformations were observed in 4.9% of the cases. Low flow myocardial necrosis of was observed in 8% of the cases.

Upper airway examination

The lungs were examined in 100% of cases. The most frequent pathological changes are described in Fig. 2. Pulmonary causes accounted for almost half of deaths (Table 2). The cause of death was made purely on macroscopic examination only in 10% of deaths (major acute pneumonia, fire).

Asphyxia was diagnosed according to the histologic description proposed by Dettmeyer[8] and Meyer[9] such as alveolar overdistension with alveolar rupture, intra-alveolar hemorrhage with alveolar edema, vascular congestion, swelling pneumocytes, dystelectasis, lymphangiectasis, micro-thrombi.

Intra-alveolar siderophages were observed in 4 cases with no cardiac anomaly. Asthmatic lesions were not linked with the death mechanism.

Table 2
Lung-related causes of death.

Lung-related causes of death	Percentage
Inhalation	33
Asphyxia	26.5
Viral pneumonia	17
Acute bacterial broncho-pneumonia	8
Acute respiratory distress syndrome	5.1
Drowning	3.2
Fire (sout)	3.0
Pulmonary immaturity	1.2
Pulmonary arterial hypertension	1.2

The larynx and trachea were examined in 116 children. Macroscopic and microscopic examination was normal in 84% and 54.4% of cases, respectively. The most frequent pathological changes were acute and chronic inflammation (both 24% of the pathological sample).

Three deaths were attributed to a post-operative complication (tonsillectomy) and were described during the autopsy examination.

Digestive tract examination

A digestive pathology accounted for 4.6% of deaths; all were secondary to a colon or small intestine pathology. The cause of death was made purely on macroscopic examination in 4% of the deaths (surgical

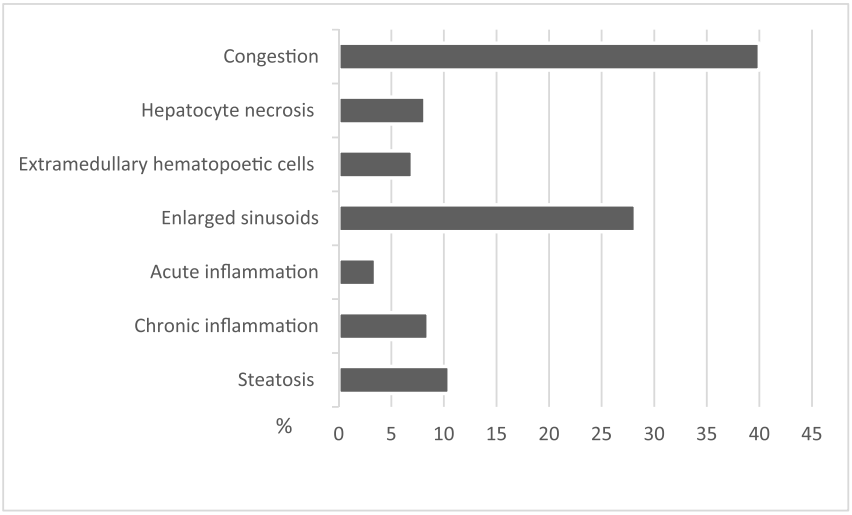

Fig. 3. Pathological changes observed in the liver.

cause: acute intestinal intussusceptions, ulcer, postoperative complication, traumatic injury). The diagnosis was made on microscopic examination in two cases of acute enteritis and candidiasis leading to necrotizing enterocolitis.

The esophagus was examined in 35 children. Macroscopic and microscopic examination was normal in 4 and 27 children, respectively, while 22.8% presented inflammation (associated with pulmonary, otorhinolaryngeal or acute digestive infectious diseases). One case presented with focal esophageal candidiasis.

The colon and small intestine were examined in 97 children. Macroscopic (excluding autolysis) and microscopic examination was normal in 95% and 64.9% of cases, respectively.

The most frequent pathological changes were inflammation (58.9%) and ischemia (20.5%).

The liver was examined in 146 children. Macroscopic and microscopic examination was normal in 78.8% and 41.7% of cases, respectively. No liver disease was responsible for death. The most frequent pathological changes are described in Fig. 3.

Steatosis was associated with infectious disease in 22% of cases, a metabolic disease in 11% and was isolated in 77%. Hepatocyte necrosis was associated with infectious disease, cardiac failure and prematurity.

Lymphoid tissue examination

The thymus was examined in 116 children. Macroscopic and microscopic examination was normal in 95.6% and 50% of cases, respectively, while 46% showed anoxia patterns (starry sky macrophages in the thymus). Seven cases showed macroscopically petechial hemorrhage. All were confirmed under the microscope.

The spleen was examined in 118 children. Macroscopic and microscopic examination was normal in 55 children. Vascular congestion was seen in 25.4% of cases. Lymphocytic depopulation was observed in 9.3% of cases (only cases of prolonged cardiovascular failure). Germinal hyperplasia was observed in 19.4% of the cases (in 4 cases of uncertain death and 19 cases of infectious disease). No deaths were related to lymphoid tissue disorders.

Endocrine tissue examination

No deaths were related to endocrine tissue pathology.

The thyroid was examined in 24 children. Macroscopic and microscopic examination was normal in 23, while a single case had microcalcifications.

The pancreas was examined in 100 children. Macroscopic (excluding autolysis) and microscopic examination was normal in 100% and 73% of cases, respectively. The most frequent pathological changes were enlarged islet cells (15%), congestion (6%) and thick mucus (1%).

The adrenal gland was examined in 75 children. Macroscopic and microscopic examination was normal in 66.6% and 56% of cases, respectively. Hemorrhage was observed in 33.3% of cases, while only one newborn showed bilateral hemorrhage (massive meconium inhalation). Hemorrhage was associated with acute respiratory distress (80%), asphyxic lesions of the lung (60%), sepsis (9.3%) and cardiac circulatory failure (6.2%). One case of inhalation pneumonia presented medullary necrosis. Isolated cases showed medullary calcification, siderophages and fibrosis, and medullary hyperplasia.

Kidney examination

The kidney was examined in 140 children. Macroscopic and microscopic examination was normal in 95% and 49.2% of cases, respectively. No deaths were attributable to renal disease. The main renal pathologies were traumatic injury, acute pyelonephritis, and tubulopathy associated with metabolic disease. The most frequent non-specific pathological changes were congestion (45%), endovascular clot and calcification. Acute tubular stress and acute tubular necrosis, observed in 6.4% of cases, were associated with prolonged cardiovascular failure, sepsis and dehydration.

4. Discussion

Autopsy, although often considered the gold standard in the determination of the causes of death, is often inadequate and allowed a definitive diagnosis in only 30% of the case in pediatric death. As we observed in our study, forensic histopathology yielded a diagnosis in 70% of cases. A complement of research by radiology, toxicology, molecular biology, biochemistry must be necessary to refine these results. These researches, in French forensic context are asked in a very inconstant way by the magistrate except for histopathology. Despite the implementation of the French SIDS protocol which recommends medical autopsies, too many pediatric autopsies are carried out in a medicolegal context. Thanks to this protocol, the French Ministry of Health is committed to funding all major laboratory sections including toxicology, biochemistry, molecular biology and radiology. This observation highlights a real loss for establishing a complete diagnosis of the cause of death in pediatric forensic autopsy. This should emphasize the importance, when the context is favorable, to choose the path of medical autopsy in the event of a pediatric death.

Accidental deaths (drowning, trauma, fire) accounted for 8.1% of autopsy deaths. Child abuse was diagnosed in 28,8% of cases.

We found a high rate of anoxic-ischemic neuronal lesions. These are particularly frequent in sudden unexplained deaths in children.[10] Histological changes are generally considered to occur about 6 or more hours after an ischemic or hypoxic episode.[7] In some circumstances, acute anoxic-ischemic changes can occur in neurons as rapidly as half an hour, particularly in previously healthy individuals, as in suicidal or accidental hanging, acute cardiac arrest or anesthetic accident.[11] Purkinje cells can show acute anoxic-ischemic changes more rapidly than elsewhere, especially in perinatal hypoxia.[7,12] Dating of the onset of acute anoxic-ischemic lesions should not be proposed. In the immature infant, the sites of vulnerability to anoxic-ischemic episodes are the brain stem, central gray nuclei and peri-ventricular white matter.[7] The brain of an infant responds differently to hypoxia and ischemia: white matter is more often affected than the gray substance. Periventricular or intraventricular hemorrhage is found in 40–45% of premature infants.[13] We found these lesions in 13 premature infants (8.1% of the population) which are well below the expected level.

The incidental discovery of intracranial neoplasia is not uncommon. In most cases, these tumors were glial tumors.[14] Tumors of the central nervous system are the most common solid tumors of the child. This is the second cancer (20%) after leukemias (30%).[15] Often, there are no preceding symptoms.[14,16]

Meningitis is an extremely serious condition with a high mortality rate that may approach 100% in bacterial meningitis. Viral (lymphocytic) meningitis typically does not cause sudden death, especially in the absence of severe inflammation in the brain or other organs.[17] Bacterial meningitis was the cause of 5 deaths in our study population.

We found no microscopic or macroscopic anomaly of the eyes. Periorbital/conjunctival hemorrhages have been described in pediatric drowning victims.[18] The eyes were not examined in any of our cases of drowning. Like Maxeiner et al.,[19] we found no hemorrhages secondary to resuscitation maneuvers.

Apart from autopsies in cases of suspected child abuse and or shaking, cervical spinal cord examination is a rare autopsy technique applied in forensic autopsies.

Like Ohya et al., pulmonary edema and hemorrhage were the pathological changes most frequently observed.[20] Most cases of accidental mechanical asphyxia occurred in the first year of life (20%) or between the ages of 1 and 2 years (13%).[9] Meyer et al.[9] showed that strangulation (in the home environment) explained 46% of deaths, positional asphyxia (with chest compression) 31%, and aspiration (mainly of foreign bodies) 23%. In our study, asphyxia was observed in 26% of cases. The presence of pulmonary intra-alveolar siderophages has long been considered as characteristic of suffocation. However, Krous et al. have shown that the number of siderophages varies considerably between deaths due to sudden infant death syndrome (SIDS) and cases of accidental or inflicted choking.[21] Hemosiderin is indicative of previous hemorrhage in the lungs (at least 2 days earlier) or aspiration of blood with subsequent breakdown of hemoglobin and, as such, is non-specific.[22] The mere presence of food material such as milk in the bronchi or bronchioles without any tissue reaction is not necessarily evidence of aspiration. Agonal aspiration of gastric contents may occur in the perimortem period or during resuscitative efforts.[4]

Postoperative hemorrhage is a frequent complication of tonsillectomy,[23] with rare cases leading to death.

Our findings on deaths from cardiac causes are consistent with those in the literature. Congenital heart malformation and myocarditis were the most frequent cardiac causes of death.[24] One case of idiopathic eosinophilic endomyocarditis has been described,[25] but our case was less severe than that described, so we could not conclude on this diagnosis. Cardiomyopathies or endocardial fibroelastosis were also observed, all of which could explain sudden death.[8] When anatomical closure does not occur, the foramen ovale remains patent, as found in up to 34.3% of subjects during the first three decades of life.[26] We found 21% of patent foramen ovale in our series.

In the larynx and trachea, inflammation was the most frequent finding. The frequency of such inflammation is therefore not specific for sudden unexpected death in infancy (SUDI), and seems to reflect the high incidence of upper respiratory tract infections in this age group.[27]

Infection has been found to be associated with starry sky macrophages in the thymus, with calcification, or with debris in the Hassal's corpuscles.[28] In our study, none was associated with infection. In our experience, they are related to past or subacute anoxia. Petechial hemorrhages are seen in sudden unexplained deaths and after cardiopulmonary resuscitation.[8]

Gastroesophageal reflux has been discussed with regard to findings in cases of suspected SUDI but we observed no focal cortical defects or unexplained inflammation.

Malformation of the digestive tract has been found to concern 4.8% of stillborn and live-born children.[29] We expected signs suggesting gastroesophageal reflux to be more frequent. The number of diffuse extramedullary hematopoetic cells was higher in SIDS than in non-SIDS cases.[8] Intestinal obstruction may be due to a variety of causes, including intussusception, volvulus, and bowel atresia. We observed two cases of lymphoid hyperplasia of the ileal wall, probably associated with a recent episode of gastroenteritis, causing acute intestinal intussusception.

Examinations of the pancreas and pancreatic islets in cases of suspected SIDS yielded no specific histopathological findings according to Dettmeyer.[8]

No specific change was found on kidney examination. A variety of non-specific changes can occur in the kidneys in systemic diseases, including multisystem disorders, hypertension and diabetes.[30] Kidney failure is a common occurrence in severely ill patients. Pyelonephritis can lead to sepsis and death. Kidney malignancies (Wilms tumor) can cause death. These circumstances are rare in children.

Germinal hyperplasia in the spleen is secondary to antigenic stimulation.[31]

Necrosis or extensive hemorrhage of the adrenal glands are not seen in SUDI.[8] On the other hand, necrosis and hemorrhage have been described in acute infectious disease[32] and asphyxia.[33]

The first step in forensic pathology analysis is gross examination, complementing autopsy description, obtaining adequate samples for histology. Some authors[31,34] declare that systematic microscopic examination of numerous organs is often useless and should be limited to cases of adults with no anatomic cause of death. This opinion is rejected by the majority of the scientific community[28,33] who emphasize that “histological analysis had a major impact on previously performed gross diagnosis at necropsy, especially in the lungs, liver, and kidneys”. In pediatrics, even if macroscopic examination is normal, systematic specimens (brain, heart, lungs, kidneys, liver) can be used to identify the exact cause of death.[34] Other organs (thymus, adrenal gland, pancreas), although not necessarily useful for the final diagnosis, can however show the presence of an earlier pathological condition which may have contributed to death, so we consider they too should be examined.

5. Conclusion

Despite the implementation of the French SIDS protocol which recommends medical autopsies, too many pediatric autopsies are carried out in a medicolegal context. Accidental and child abuse deaths represented less than 40% of the medicolegal autopsies performed in our center. Forensic histopathology is an indispensable tool in pediatric medicolegal autopsy. It is twice as efficient as autopsy alone to achieve a precise etiological diagnosis. Significant histological abnormalities may be detected in selected organs such as the brain, lungs, heart, liver, adrenal glands and kidneys with macroscopically normal appearances. This justifies systematic sampling of all organs.

Conflicts of interest

None. This study received no specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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