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PEDIATRIC

Whole-body post-mortem computed tomography compared with autopsy in the investigation of unexpected death in infants and children

Maïa Proisy · Antoine Jérôme Marchand · Philippe Loget · Renaud Bouvet · Michel Roussey · Fabienne Pelé · Céline Rozel · Catherine Treguier · Pierre Darnault · Bertrand Bruneau

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Abstract
Objectives To investigate the contribution of whole-body post-mortem computed tomography (PMCT) in sudden unexpected death in infants and children.
Methods Forty-seven cases of sudden unexpected death in children investigated with radiographic skeletal survey, whole-body PMCT and autopsy were enrolled. For imaging interpretation, non-specific post-mortem modifications and abnormal findings related to the presumed cause of death were considered separately. All findings were correlated with autopsy findings.
Results There were 31 boys and 16 girls. Of these, 44 children (93.6 %) were younger than 2 years. The cause of death was found at autopsy in 18 cases (38.3 %), with 4 confirmed as child abuse, 12 as infectious diseases, 1 as metabolic disease and 1 as bowel volvulus. PMCT results were in accordance with autopsy in all but three of these 18 cases. Death remains unexplained in 29 cases (61.7 %) and was correlated with no abnormal findings on PMCT in 27 cases. Major discrepancies between PMCT and autopsy findings concerned pulmonary analysis.
Conclusions Whole-body PMCT may detect relevant findings that can help to explain sudden unexpected death and is essential for detecting non-accidental injuries. We found broad concordance between autopsy and PMCT, except in a few cases of pneumonia. It is a non-invasive technique acceptable to relatives.
Key Points
- *Whole-body post-mortem computed tomography (PMCT) is an effective non-invasive method.*
- *Whole-body PMCT is essential for detecting child abuse in unexpected death.*
- *There is concordance on cause of death between PMCT and autopsy.*
- *Whole-body PMCT could improve autopsy through dissection and sampling guidance.*
- *PMCT shows findings that may be relevant when parents reject autopsy.*

Keywords Post-mortem diagnosis · Sudden death · Infant · Computed tomography · Autopsy

Abbreviations

CNS	central nervous system
CPA	cardiopulmonary arrest
CPR	cardiopulmonary resuscitation
GGO	ground glass opacity
IVG	intravascular gas
NAI	non-accidental injury

M. Proisy (✉) · A. J. Marchand · C. Rozel · C. Treguier · P. Darnault · B. Bruneau
Department of Radiology, Rennes University Hospital, CHU Hôpital Sud, Boulevard de Bulgarie, BP 90347, 35203 Rennes Cedex 2, France
e-mail: maia-proisy@orange.fr

P. Loget
Department of Pathology, University Hospital, Rennes, France

R. Bouvet
Department of Legal Medicine, University Hospital, Rennes, France

M. Roussey
Department of Paediatrics, University Hospital, Rennes, France

F. Pelé
Epidemiological and Public Health Service, University Hospital, Rennes, France

PMCT post-mortem computed tomography
SAH subarachnoid haemorrhage
SDH subdural haemorrhage
SUDI sudden unexpected death in infancy

Introduction

Sudden unexpected death in infancy (SUDI) is the commonest presentation of post-neonatal infant death. "SUDI" is a term used to refer to all cases of sudden and unexpected death in infancy [1]. In a proportion of SUDI cases, a post-mortem examination will reveal the cause of death ("explained" SUDI) [2]. However a large number of SUDI cases still remain unexplained and are too often not thoroughly investigated. The search for and identification of the cause of death are highly desirable, especially in order to exclude non-accidental trauma that may require provision of preventive care services [3].

Recommendations exist in France [4] and in other countries [5, 6] to provide guidelines for investigation of infant deaths. In France these investigations are conducted in SUDI referral centres. Radiographic skeletal surveys and cross-sectional brain imaging form part of the recommended imaging investigations. A systematic conventional autopsy, with macroscopic and histological investigation, is also advocated and systematically offered to parents. Except in the case of forensic investigation, written parental consent is required for autopsy in France. However parents may have emotional, cultural or religious reasons for refusing autopsy and a global trend of declining paediatric autopsy rates has been reported [7, 8].

"Virtual autopsy" is an increasingly widespread non-invasive method referring to post-mortem imaging, using mainly computed tomography (CT) or magnetic resonance imaging (MRI). For several years virtual autopsy has sometimes been offered as a concomitant method or as an alternative to conventional autopsy. Several studies have reported the use of post-mortem imaging in adult deaths [9–14]. However there has been little focus on post-mortem imaging specifically for paediatric populations, and only one study [15] has focused on PMCT for detecting causes of sudden death in infants and children (15 patients, and an autopsy was conducted on 2). In addition to being a non-invasive method of investigation, virtual autopsy has several other advantages, which include the opportunity to analyse organs in situ, the possibility of storing images, visualisation of non-dissected organs, and the possibility of repetition and reviewing if necessary [16].

In our institution we have performed post-mortem computed tomography (PMCT) of the brain for many years [17], and since 2005 whole-body PMCT has been systematically performed in addition to radiographic skeletal survey in all cases of sudden unexpected death in infants and children.

The aim of this study was to investigate the contribution of whole-body PMCT in cases of sudden unexpected death in children and in particular SUDI.

Materials and methods

Study group

Between March 2005 and May 2011, 52 sudden unexpected deaths of infants and children with no known pre-existing disease were investigated at our institution. We excluded 5 cases due to parents' refusal to permit autopsy. Finally 47 underwent radiographic skeletal survey, whole-body PMCT and autopsy and were subsequently included in this study (Fig. 1).

The study was approved by the local ethics committee and did not require informed consent from the relatives of the deceased to perform imaging examinations.

Image acquisition

All CT examinations were performed using 16-slice multidetector CT (Philips Brilliance, Cleveland, Ohio, USA) with the same protocol. The imaging parameters used were as follows: 120 kV, 300 mAs, collimation 16×0.75, pitch 0.688, rotation time 0.5 s, slice thickness 2 mm, increment 1 mm. The cadavers were imaged in the supine position, with arms adjacent to the body. Volumetric CT data were acquired from the vertex to the feet. No contrast material was administered.

The radiographic skeletal survey consisted of anterior and lateral skull views, an anteroposterior rib radiograph, and anterior and lateral views of the spine and limbs.

Image interpretation

Two paediatric radiologists experienced in post-mortem imaging interpreted the whole-body PMCT and skeletal radiographs. The circumstances of death and autopsy findings were unknown at the time of image interpretation. The radiologists used a standardised and exhaustive checklist. Images were reviewed on a Philips workstation (Philips Medical Systems, Cleveland, Ohio, USA) with two-dimensional transverse, coronal, sagittal and oblique data sets, and three-dimensional volume-rendered images. Final image interpretation was reached in consensus. The presumed cause of death was established when abnormal findings were seen on the whole-body PMCT images. A diagnosis of unexplained death, with no cause of death apparent on imaging, was established when there were only isolated non-specific post-mortem modifications.

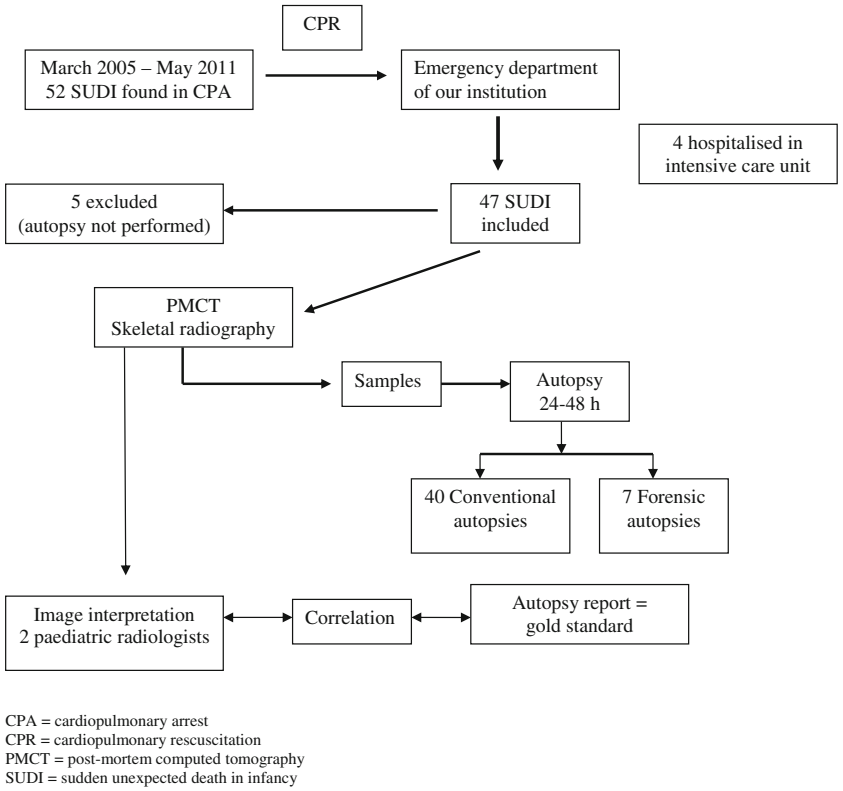

Fig. 1 Study protocol. *CPA* cardiopulmonary arrest, *CPR* cardiopulmonary resuscitation, *PMCT* post-mortem computed tomography, *SUDI* sudden unexpected death in infancy

Autopsy technique

Autopsy was systematically performed within 24–72 h of death by a board-certified paediatric pathologist or a forensic pathologist according to a standardised protocol [18], including macroscopic and histological examination and biological investigations. Histological samples were not obtained by an image-guided procedure. At the time of autopsy, the pathologist was blinded to the findings of the PMCT.

Statistical analysis

The study population, imaging results and autopsy finding variables were represented as numbers plus or minus a percentage for qualitative variables. Quantitative variables were described by a mean±standard deviation or median (range).

The Spearman correlation test was used to compare two quantitative variables and Student's test to compare means. The kappa coefficient was calculated to measure the concordance between whole-body PMCT and autopsy.

Results

Study group description

Forty-seven children underwent both whole-body PMCT and autopsy (Fig. 1). The group included 44 children younger than 2 years (mean age, 6.2±5.9 months). Three children were older than 2 years (4, 5 and 8 years). There were 31 boys and 16 girls. All patients underwent cardiopulmonary resuscitation (CPR). Four children were resuscitated and admitted to the intensive care unit, dying shortly after admission.

In 7 cases a forensic investigation was needed: 4 suspected child abuse cases and the 3 children over 2 years who were not considered as having SUDI because of their age. Before sample collection and autopsy all children underwent radiographic skeletal survey and whole-body PMCT. Post-mortem imaging was performed rapidly after arrival of the body at the emergency room. The median interval between certification of death and PMCT acquisition was 2 h 01 min (range, 20 min to 5 h 13 min).

Post-mortem examination was a conventional autopsy (n=40) or a forensic autopsy (n=7).

Cause of death

Autopsy revealed an identifiable cause of death in 18 cases (38.3 %). The causes of death at autopsy were found to be child abuse (n=4), pneumonia (n=10), pneumonia and gastroenteritis (n=1), parvovirus B19 pancarditis (n=1), metabolic disease (n=1) and bowel volvulus (n=1). In our study the whole-body PMCT revealed an identifiable cause of death in accordance with the autopsy cause of death in 15 of these 18 cases (Table 1). Autopsy did not find any

Table 1 Autopsy cause of death and correlation with consensual whole-body PMCT radiological cause of death

		Autopsy		
		+	−	
PMCT	+	15	2	17 (36.2 %)
	−	3	27	30 (63.8 %)
		18 (38.3 %)	29 (61.7 %)	47 (100 %)

PMCT Post-mortem computed tomography, + a cause of death was found, − no cause of death was found

macroscopically or histologically detectable cause of death in 29 cases (61.7 %): there was concordance with whole-body PMCT in 27 of these 29 cases (Table 1). There were 2 false positive cases on PMCT arising from the conclusion of abnormal findings with a cause of death (pneumonia), whereas autopsy did not find any cause of death and the conclusion was unexplained death. There were 3 false negative PMCT cases: PMCT led to the conclusion of no abnormal findings and no cause of death, whereas autopsy found a cause of death (pneumonia) in these 3 cases.

The kappa coefficient was good (κ=0.79).

Finally PMCT was diagnostic (cause of death) in 15/18 cases (83.3 %) with autopsy correlation and 15/47 (31.2 %) of all cases in this patient population.

Non-specific post-mortem imaging modifications compared with autopsy

Vascular post-mortem modifications

The effect of blood sedimentation after death causes dependent vessel hyperdensity (hypostasis). We found a significant (P<0.001) correlation between the density measured in the posterior sagittal sinus (mean, 55 HU±9.5 HU) and the density measured in the dependent part of the heart (mean, 53.4 HU±9.4 HU). Intravascular clotting was already frequently seen in the cardiac cavity and major vessels (hepatic portal vein, aorta, etc.). Hyperattenuating aortic wall was a common finding (n=47, 100 %).

Intravascular gas (IVG) bubbles were seen in 24 subjects (51 %). For all subjects with IVG detected in the brain (n=14, 29.7 %), the liver (n=17, 36.1 %) or the abdomen (n=10, 21.2 %) IVG was also seen in the cardiac cavity (n=24, 51.0 %). In our study, there was no correlation between the presence of IVG and CPR time. Median CPR time was 30 min (range, 15–60 min) in the group with presence of IVG and 32 min (range, 10–60 min) in the group without IVG. Nor was there any correlation between the presence of IVG and PMCT imaging time.

Abdominal post-mortem modifications

Excess gas in bowels and stomach distension (Fig. 2) were frequently seen (n=31), and sometimes even periportal oedema (n=36).

Pulmonary post-mortem modifications

Ground glass opacity (GGO) was observed in 41 subjects (87.2 %): mild (n=16), moderate (n=21) or severe (n=4). In 14 cases there was no other pulmonary finding. Isolated mild or moderate GGO in these 14 cases was considered a non-specific post-mortem finding and was correlated with non-specific pulmonary oedema at histology in 12 cases (Fig. 3a, b). In 2 cases autopsy revealed pneumonia at histology.

In 10 cases we found mild bilateral consolidation that was also considered a non-specific finding, which correlated with non-specific pulmonary oedema at histology in 9 cases (pneumonia in one case at autopsy).

Endotracheal or endobronchial air defect with material in the larynx (n=8), trachea (n=20), main bronchi and small bronchi (n=28) was not always correlated with autopsy findings.

Iatrogenic post-mortem modifications

Twelve (25.5 %) children had infiltration of the legs with the presence of gas bubbles on PMCT, due to intraosseous adrenaline treatment during CPR.

Post-mortem pathological imaging findings compared with autopsy

Imaging of the head

Diffuse cerebral ischaemic injuries (Fig. 4) were found in 5 cases at PMCT and at autopsy (Table 2). Four were children hospitalised in the intensive care unit including 2 shaken baby syndrome cases. Bilateral subdural haemorrhage (SDH) associated with subarachnoid haemorrhage (SAH) was found in 3 cases of shaken baby syndrome (Figs. 4 and 5). Two children had skull fractures (Fig. 5), including 1 infant who had 2 fractures detected at PMCT associated with haemorrhage, and one other who had an isolated skull fracture without intracranial bleeding. An 8-year-old boy had brain calcifications attributable to an occult pre-existing metabolic disorder. No ventricular dilation or congenital brain malformation was detected.

Extracranial bone imaging

One child who presented with SDH had a callus on 2 metacarpal bones seen on radiographs and PMCT images (Fig. 4). No rib fractures or skeletal dysplasia were observed on the radiographs, PMCT images or at autopsy.

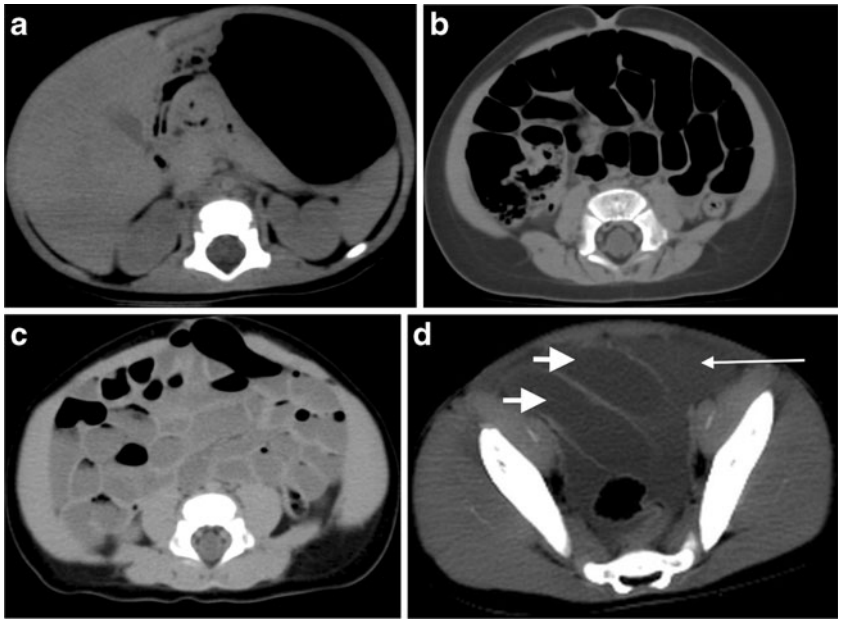

Fig. 2 Findings on abdominal transverse PMCT images. **a** Non-specific gaseous gastric distension corresponding to non-specific PMCT findings. **b** Non-specific gaseous bowel distension corresponding to non-specific PMCT findings. **c** Pathological fluid-filled bowel distension. The cause of death at autopsy was pneumonia and signs of dehydration due to gastroenteritis a few days before death. Samples were positive for rotavirus. **d** Fluid-filled pelvic bowel distension (*short arrows*) and peritoneal effusion (*long arrow*). The cause of death at autopsy was septic shock due to bowel necrosis secondary to volvulus

Cardio-thoracic imaging

Two infants had cardiomegaly on PMCT confirmed at autopsy with a heart weight higher than normal for their age. The cause of death was parvovirus B19 pancarditis in one case and pneumonia in the other. Coronary artery origin visualisation was only possible in 15 subjects (31.9 %) and correlated with age ($P<0.05$). Coronary artery origins

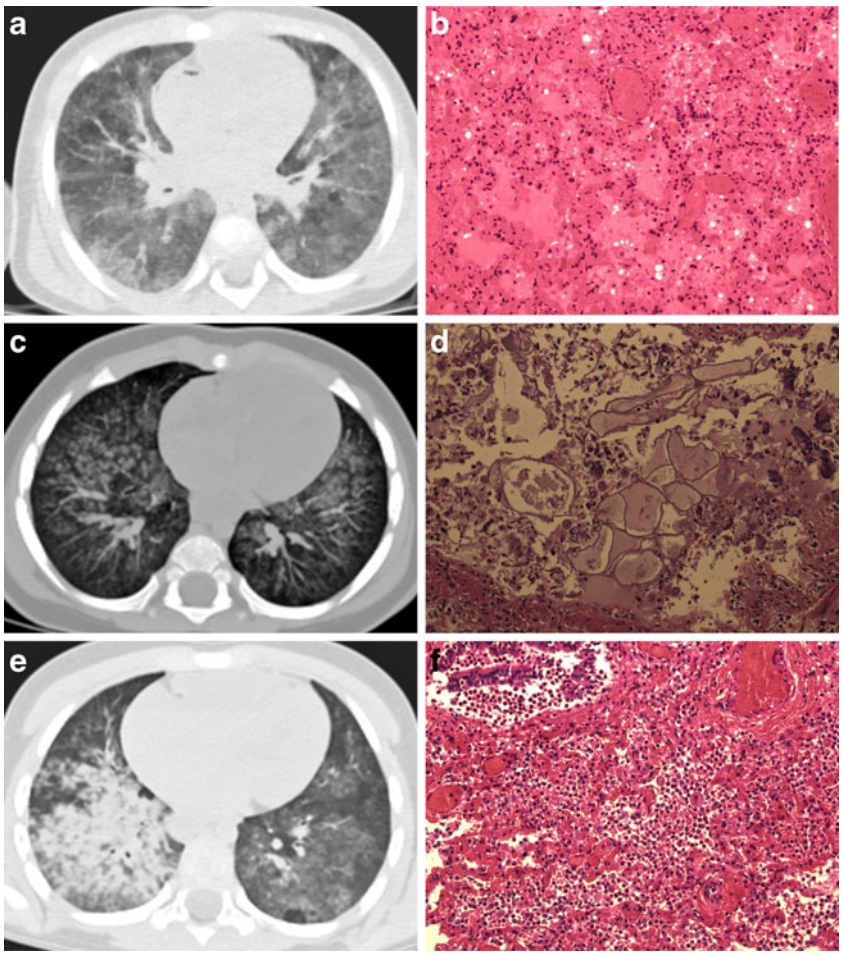

Fig. 3 Pulmonary PMCT findings correlated with autopsy histological findings. Transverse PMCT image shows non-specific bilateral and symmetrical pulmonary ground glass opacity (**a**) correlated at autopsy with minor histological abnormalities such as pulmonary congestion (**b**) not directly relevant to the cause of death. Transverse PMCT of the chest shows bilateral centrilobular nodules with a tree-in-bud pattern (**c**). Microscopically the alveoli are filled with gastric matter (**d**) corresponding to aspiration. Transverse PMCT of the lung window setting shows severe asymmetrical consolidation, associated with centrilobular nodules and GGO (**e**). Microscopically consolidations correspond to pneumonia. The alveoli are filled with polymorphonuclear leucocytes (**f**)

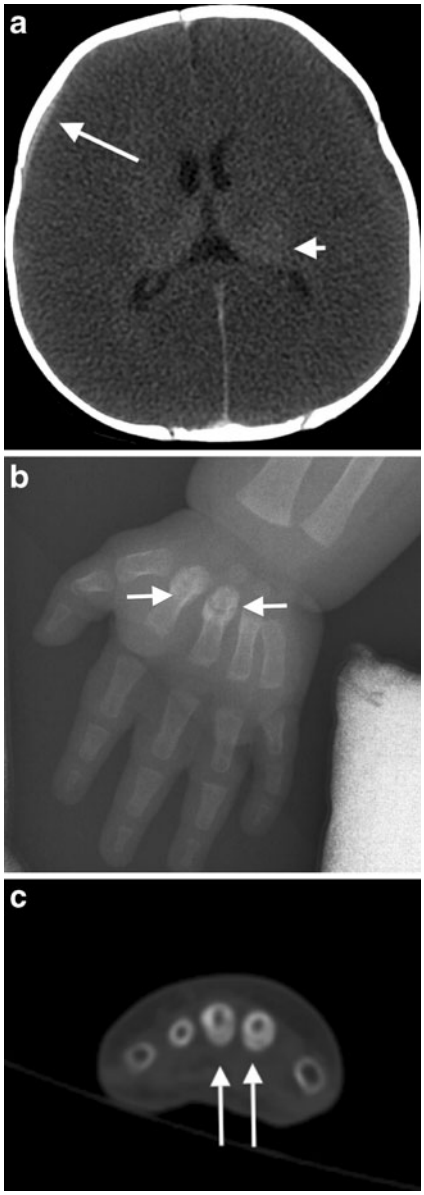

Fig. 4 A 6-month-old-infant resuscitated after CPR and who died after a short stay in the intensive care unit. **a** Axial PMCT image reveals hyperdense subdural haemorrhage (*long arrow*) and diffuse ischaemic cerebral injuries with loss of corticomedullary differentiation, sparing the thalami (*short arrow*). Right-hand radiograph (**b**) and transverse PMCT (**c**) show healing of two metacarpal fractures (*arrows*)

were seen on PMCT in 16 % (6/37) of subjects younger than 12 months and 90 % (9/10) of children older than 12 months of age. There were a few discrepancies between minor abnormal cardiac findings seen at autopsy and not observed on PMCT. These findings were a small ostium secundum atrial septal defect in 3 cases and dysplasia of the mitral valve in 1 case. These minor histological abnormalities were not relevant to the cause of death.

Pulmonary modifications found were GGO, consolidation and centrilobular nodules (Fig. 3). Small centrilobular nodules were visible in 11 subjects and they always had a

Table 2 Pathological findings on whole-body PMCT scan

	Number (*n*)
Bilateral subdural haematoma	3
Subarachnoid haemorrhage	3
Ischemic brain injuries	5
Skull fracture	2
Fracture healing of metacarpal bones	1
Brain calcifications	1
Cardiomegaly	2
Centrilobular nodules with tree-in-bud pattern	10
Pulmonary parenchymal consolidations (moderate and severe)	12
Pleural effusion	4
Fluid-filled bowel distension	2
Peritoneal effusion	4
Hepatic steatosis	1

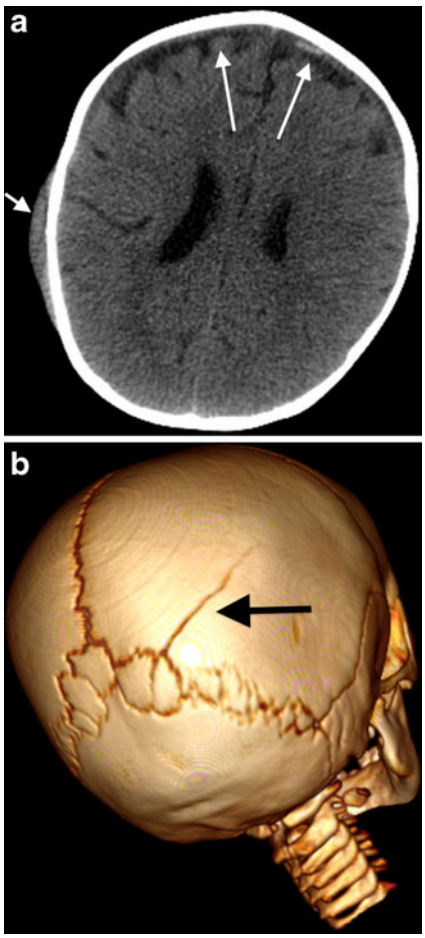

Fig. 5 A 9-month-old boy found in CPA in his cot. **a** Axial brain PMCT shows bilateral subdural haemorrhage with hyperdensity suggestive of recent bleeding (*long arrows*). Haematoma in front of a parietal skull fracture (*short arrow*). **b** High-resolution PMCT 3D projection showing a parietal skull fracture

tree-in-bud pattern. They were always associated with endobronchial air defects. These imaging findings were correlated with terminal bronchiole filling at autopsy. The material was gastric contents due to aspiration in 6 cases and infectious material in 5 cases of pneumonia.

Significant parenchymal consolidations were seen in 12 cases (25.5 %), and were either moderate (n=6) or severe (n=6). In 4 cases, consolidations were not considered as infectious diseases on PMCT (correlated with autopsy): 2 children hospitalised in the intensive care unit and 2 children with consolidation in a dependent distribution. In 8 of these 12 cases, pneumonia was suspected on the basis of the PMCT findings. These findings were confirmed at histology in 6 cases (moderate consolidations n=2, severe consolidations n=4) and not correlated with pneumonia at autopsy in 2 cases (moderate consolidations n=1, severe consolidations n=1).

Pleural effusion was seen in 4 cases including 1 child hospitalised in the intensive care unit, 2 children with infectious pneumonia, and 1 boy who had heart failure due to bowel volvulus.

Abdominal/pelvic imaging

Bowel distension with fluid build-up was detected in 2 cases (Fig. 2): 1 case of intestinal obstruction due to volvulus in a 4-year-old-boy and 1 case of gastroenteritis. Significant peritoneal effusion was detected in 5 subjects including 3 subjects hospitalised in the intensive care unit before death, 1 case of bowel volvulus and 1 case of parvovirus B19 pancarditis. Hepatic steatosis (mean liver density=22 HU), confirmed at autopsy, was diagnosed in one child who had parvovirus B19 hepatitis. Mean liver density was 49 HU in other cases (range, 38–63 HU) and mean spleen density was 43 HU (range, 33–56 HU).

Discussion

With the development of post-mortem imaging, radiologists should become more familiar with non-specific post-mortem modifications in order to distinguish them from specific signs that can explain death [19]. In our study we found the same post-mortem modifications as in adults, such as hyperattenuating aortic wall [20], hypostasis [21], and clotting in the heart and major vessels [22]. IVG is also a common finding but its origin remains unclear [23–25]; two main theories have been put forward: CPR and putrefaction. Our study showed no significant correlation with either the duration of CPR or the timing of PMCT.

In our study the autopsy revealed an identifiable cause of death in 38.3 % of cases, consistent with data in the literature [26].

One of the main purposes of post-mortem investigation in SUDI, and particularly post-mortem imaging, is to identify findings related to child abuse. In our study, whole-body PMCT detected 4 non-accidental deaths. In 2 cases there was a clinical suspicion of non-accidental injury (NAI) due to haematoma on the skin (face or chest) and in the other 2 cases there was no clinical suspicion of NAI. Three children had bilateral SDH associated with SAH. Parenchymal brain lesions in child abuse are mainly shear injuries [27]. These injuries are more visible with MRI in living children, particularly with diffusion-weighted MRI at an early stage [28]. In our study, 2 cases of child abuse were reported with diffuse ischaemic parenchymal brain lesions. However they were also hospitalised in the intensive care unit before dying. It was therefore difficult to attribute lesions to abuse rather than initial cardiopulmonary arrest. In one case of child abuse with CNS injury, 2 healing metacarpal metaphyseal fractures were found on both radiography and PMCT. They were undoubtedly more apparent on plain radiography. Imaging is superior to autopsy in detecting fractures, as conventional autopsy does not routinely examine the whole skeleton. No rib fractures were detected on either imaging or autopsy, consistent with the fact that rib fracture due to CPR is uncommon in children [27].

In 14 cases of explained SUDI, a final non-traumatic cause of death was found at autopsy, which correlated with imaging findings in 11 cases. Within the explained death group, 66.6 % (n=12) of cases were due to infections, most commonly pneumonia. Consolidation and GGO were frequently observed in our study. Broad concordance was found between consolidation severity and evidence of pneumonia at autopsy. Yet there were some discrepancies between the PMCT and autopsy findings. The most common sources of discrepancy arose from the final diagnosis of pneumonia, which was missed or over-attributed on imaging. The interpretation of non-traumatic post-mortem findings of the lung is challenging because some modifications may be influenced by several post-mortem changes which depend on how long after death PMCT is performed [29, 30]. Autopsy was used as the gold standard for the diagnosis of pneumonia. However pneumonia may demonstrate patchy organ involvement and one histological lung section from each lung lobe may involve healthy parenchyma. In this case PMCT could improve autopsy quality by helping to perform sampling under CT guidance [31]. Small centrilobular nodules with a tree-in-bud pattern [32] always correlated with terminal bronchiole filling. Histological findings related to material in the airways concerned gastric content aspiration or endogenous infectious material. Pleural effusion and peritoneal effusion were found in cases of explained death. We therefore considered them to be one of the specific PMCT findings suggesting the cause of death, in accordance with the literature [29], except in cases of children hospitalised in the intensive care unit. Unlike diffuse gaseous dilation, which was a non-specific post-

mortem modification, fluid-filled bowel dilation was suggestive of the cause of death in one case of bowel obstruction and another of gastroenteritis.

Twenty-nine SUDI cases remained unexplained after extensive investigations. For these cases, autopsy found no detectable cause of death, and there was broad concordance with PMCT, except in 2 false positive cases of pneumonia at PMCT. Non-specific pulmonary modifications were frequent such as mild GGO and mild consolidations, which commonly correlated at autopsy with minor histological abnormalities not directly relevant to the cause of death, such as intra-alveolar haemorrhage, haemosiderin-laden macrophages, pulmonary congestion or pulmonary oedema [33]. In some cases, an endotracheal or endobronchial air defect was observed, which could be explained by aspiration before death or by CPR. According to Filograna's study [34], PMCT imaging of airways and lungs alone does not provide sufficient data for identifying the aspirated material or differentiating between pre- and post-mortem aspiration.

One limitation of PMCT is poor resolution of cardiac structure. Post-mortem clotting, intra-cardiac gas, absence of contrast agent and collapsed cavities limit the detection of cardiac abnormality. Only one cardiac-related cause of death was found in our study and was not missed on PMCT owing to the finding of cardiomegaly. The accuracy of post-mortem MRI should be evaluated in SUDI to detect myocardial infarction or cardiomyopathy, which may be detected in adult deaths [35]. Post-mortem angiographic techniques are being developed for adult populations [36], particularly coronary angiography [37, 38], and should be investigated in children to detect congenital coronary heart disease.

In conclusion, we found broad concordance between PMCT and autopsy findings. Whole-body PMCT is highly concordant, helpful and essential for detecting NAI. There are some discrepancies with autopsy particularly in cases of pneumonia. This is due to the difficulty involved in post-mortem analysis of the pulmonary parenchyma. Another limitation of PMCT is cardiac analysis and post-mortem MRI could be evaluated for this purpose. Whole-body PMCT could improve autopsy by providing guidance for dissection and sampling, and it is an efficient method concomitant with autopsy. Whole-body PMCT is a feasible, fast and non-invasive technique for detecting the cause of sudden unexpected death in infants and children. Moreover it is an investigation method that is acceptable to relatives and can yield essential findings that may be particularly relevant when parents reject autopsy.

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