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ORIGINAL ARTICLE

Absence of the spleen(s) in conjoined twins: a diagnostic clue of laterality defects? Radiological study of historical specimens

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Abstract
Background Laterality defects are quite common in thoracoileopagus and parapagus dicephalus but rare in other types of conjoined twins.
Objective To present the presumed laterality defects in cephalothoracoileopagus and prosopothoracoileopagus conjoined twins, based on the unilateral or bilateral absence or duplication of the spleen.
Materials and methods Three human anatomical specimens of craniothoracoileopagus (CTIP) twins and one of prosopothoracoileopagus (PTIP) twins were investigated. The specimens were part of the Museum Vrolik collection of the Department of Anatomy and Embryology of the Academic Medical Centre, University of Amsterdam, The Netherlands. The specimens were taken out of their jars and scanned with multidetector CT and volumetric T2-weighted MRI at 1.5 T.
Results The internal anatomy of the specimens was largely in accordance with previous reports. However, there was no recognisable spleen in the right twin in one CTIP specimen, in the left twin in one other CTIP specimen, and in both twins in the third CTIP specimen and in the PTIP specimen.
Conclusion Asplenia and polysplenia are considered reliable indicators of right and left isomerism, respectively. However, three of our four specimens had laterality patterns that did not correspond with those previously reported. Since no other parameters of laterality defects could be verified in these specimens, we concluded that asplenia was unlikely to be caused by laterality defects.

Keywords Conjoined twins · Laterality defects · Imaging · Historical specimen

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Introduction

Conjoined twinning is rare with an incidence of 1:200,000 live births and 1:200 monozygotic twins. Judging by the numerous tales, drawings and scientific notions, there has been interest in conjoined twins throughout the ages. Especially famous are Chang and Eng Bunker (1811–1874) from Thailand [1]. Chang and Eng were joined at the abdomen and travelled to England and the United States, where their appearance at exhibitions made sure they would be remembered as a constant source of curiosity [2]. Although being ethnic Chinese, their fame caused conjoined twins to become generally known as Siamese twins.

Despite the many hypotheses postulated during the past centuries, both the pathogenetic mechanism of conjoined twinning and the cause of monozygotic twinning itself are as yet unexplained. Some types of conjoined twining, but certainly not all, have a high frequency of laterality defects. We recently re-investigated anatomical specimens of conjoined twins in the Museum Vrolik collection in Amsterdam, The Netherlands, with CT and MRI. The external presentations of these specimens have been described previously [3]. We describe presumed laterality defects on imaging in a specific type of conjoined twinning in which these defects are considered uncommon. We discuss the occurrence of these defects in conjoined twinning and evaluate the anatomical markers that are used for their detection.

Materials and methods

We investigated three human anatomical specimens presenting with craniothoracoileopagus (CTIP) and one with prosopothoracoileopagus (PTIP). PTIP is a rarely reported conjunction type intermediate between CTIP and TIP [12]. These specimens are part of the Museum Vrolik collection of the Department of Anatomy and Embryology of the Academic Medical Centre, University of Amsterdam, The Netherlands. The collection, which was founded by Gerardus Vrolik (1775–1859) and his son Willem Vrolik (1801–1863), consists of more than 5,000 dried or fixed specimens of human and animal anatomy, embryology, pathology and congenital anomalies [3]. All three CTIP specimens had one fairly complete compound face and one hypoplastic face. The PTIP specimen had a broader compound thorax on one side compared with the other. Following Schwalbe [13], the side with the complete face and or broadest thorax was defined as the anterior side, with a right twin on the observer's left-hand side and vice versa.

The specimens were taken out of their jars and scanned by CT and MRI. CT was performed on a 16-slice Philips scanner (MX8000, Philips Medical Systems, Best, The Netherlands). A slice thickness of 1 mm with three-dimensional (3D) reconstructions of the skeleton was possible (120 kV, 200 mAs). MRI was performed on a 1.5-T GE scanner (Genesis Signa, general electric healthcare, Chalfont St. Giles, United Kingdom). Sequences consisted of 3D T2-weighted series with reconstructions in three perpendicular planes (TR/TE, 2,500/68 ms; flip angle, 90°; slice thickness, 3 mm). T1-weighted series were acquired but did not add to visualisation of the specimen and were therefore not used for the anatomical evaluation.

Results

In accordance with the default internal anatomy of CTIP and PTIP [14], we found neo-axially oriented compound thymuses, sternums and livers (Fig. 1), shared or compound viscerocraniums (i.e. craniofacial), pharynges, tracheas and hearts, shared oesophagus (Fig. 2), shared or separate stomach(s) and separate neurocraniums, spinal cords, lower intestinal tracts and urogenital organs. One of the CTIP specimens had a diaphragmatic hernia. Detailed investigation of the organs was impossible due to maceration and fixation artefacts. CT images were only useful in detecting bony conjunctions and this even proved to be difficult, since the specimens' skin had hardened with age. When viewed by CT, the skin appeared to have attained a density similar to that of bone, which made 3D reconstructions difficult to obtain. This probably resulted from skeletal minerals that were washed out by acidified fixatives and precipitated in the skin. The skeleton could be visualised and showed in all cases fusion of parts of the skull and chest (Fig. 3). In none of our cases was a fusion of the pelvic bones seen.

In contrast to other reports, we noticed absence of a recognisable spleen in the right twin in one CTIP specimen,

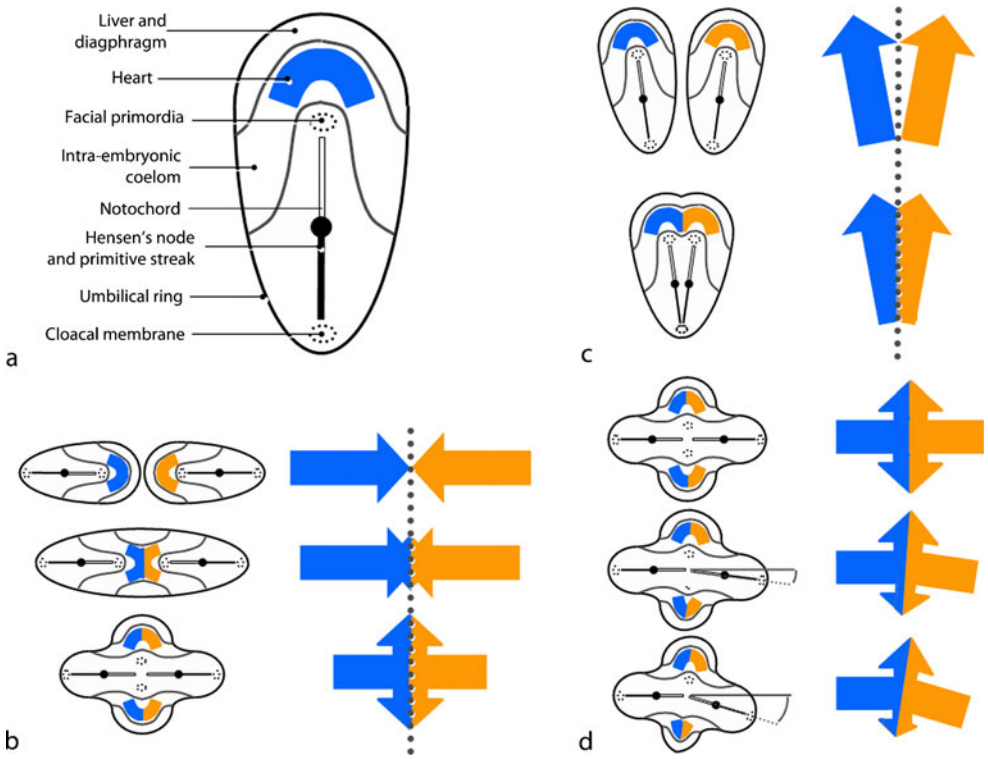

Fig. 1 Schematic representation of the embryonic disc and possible interactions in conjoined twins. **a** The embryonic disc at late gastrulation. **b** Principle of neo-axial orientation (shown in thoracoileopagus and cephalothoracoileopagus). **c** Principle of interaction aplasia (shown in dicephalus). **d** Principle of oblique conjunction (shown in cephalothoracoileopagus) with combined neo-axial orientation and interaction aplasia

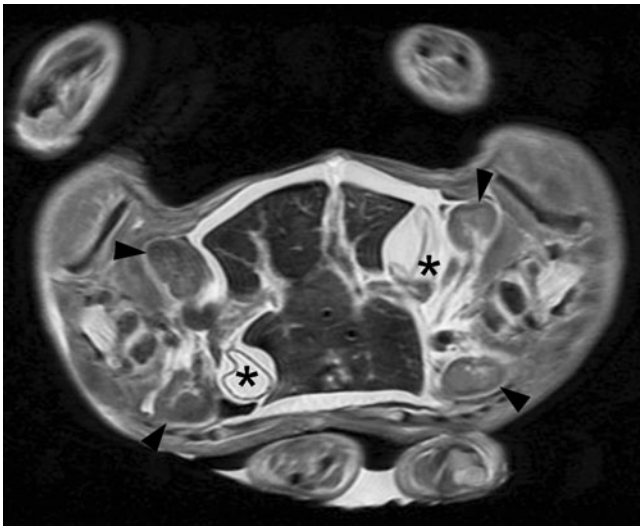

Fig. 2 Axial T2-weighted image (TR/TE, 2,500/68 ms; flip angle, 90°; slice thickness, 3 mm) of a cephalothoracoileopagus specimen with two neo-axially oriented compound livers. There are four normal kidneys (*arrowheads*) and two stomachs (*asterisks*)

in the left twin in one other CTIP specimen (Fig. 4), and in both twins in the third CTIP specimen and in the PTIP specimen. No ectopic splenic tissue was seen in the asplenic specimens, neither in the abdomen nor thorax.

Discussion

According to the site and degree of conjunction, conjoined twins can be grouped into ventral, lateral, caudal and neural types. Ventral conjoined twins are joined at the periumbilical regions and, with increasing degrees of conjunction, also at the thorax, neck, face and head. Caudal conjoined twins are joined at the periumbilical as well as the pelvic region. Lateral conjoined twins have a single lower body half and with increasing degrees of conjunction, also a single thorax, neck, head and face. In ventral and caudal conjoined twins, all structures involved in the conjunction, except for the umbilicus, are duplicated but have an altered topography (i.e. neo-axial orientation). In lateral conjoined twins, however, structures involved in the conjunction are not formed at all (i.e. interaction aplasia). Most conjoined twins can be categorised either within one of these groups or present with a combined ventral-lateral or caudal-lateral conjunction pattern. Neural conjoined twins are joined at the cranial, spinal and/or sacro-coccygeal region. They form the rarest group and, in contrast to the other types, they always have two umbilical cords. The nomenclature of the various conjoined twin types seems rather complex but is in fact merely a designation of the areas of conjunction (Table 1). In current medical literature 'ileo' is often left out of the nomenclature.

Despite the enigmatic pathogenesis of conjoined twins, most of their morphological characteristics and peculiarities

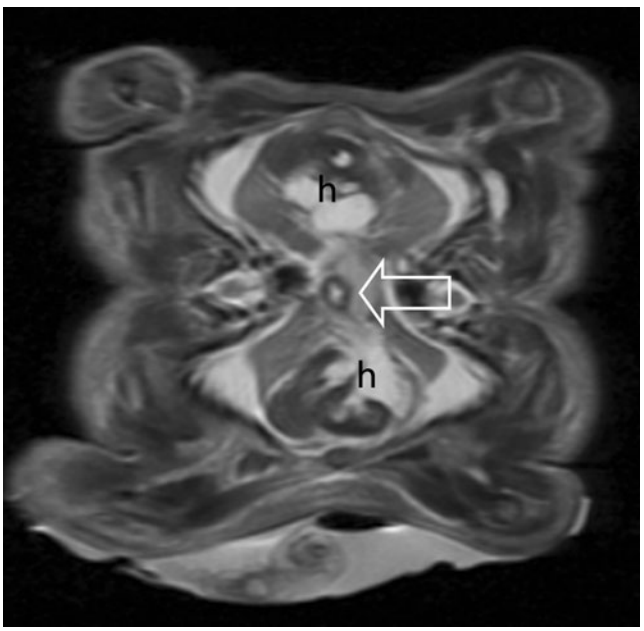

Fig. 3 Axial T2-weighted image (TR/TE, 2,500/68 ms; flip angle, 90°; slice thickness, 3 mm) of a cephalothoracoileopagus specimen with a shared oesophagus (*arrow*) and two well developed compound hearts (*h*)

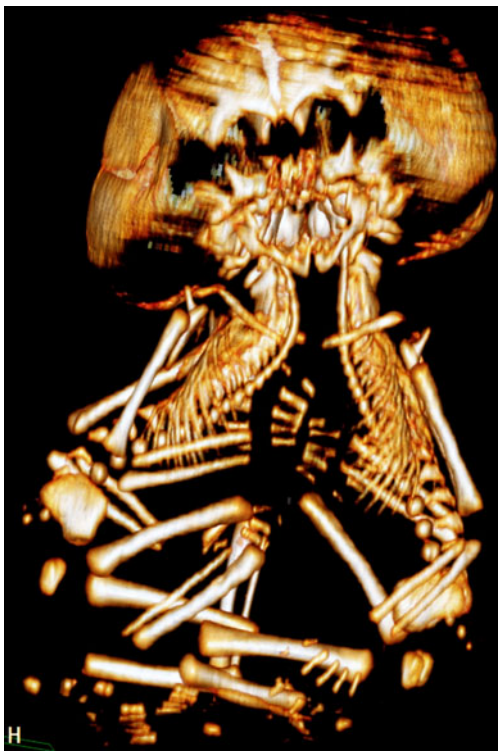

Fig. 4 Surface-shaded rendering of a cephalothoracoileopagus specimen. The compound skull is clearly demonstrated

Table 1 Nomenclature of conjoined twins

Name	Joined at
Ventral types	
Omphalopagus (OP)	Abdomen
Thoraco[ileo]pagus (TIP)	Abdomen and thorax
Prosopothoraco[ileo]pagus (PTIP)	Abdomen, thorax and neck/face
Cephalothoraco[ileo]pagus (CTIP)	Abdomen, thorax and head
Caudal types	
[Ileo]ischiopagus (IIP)	Abdomen and pelvis
Lateral types	
[Parapagus] dicephalus (PDC)	Lower (and upper) body, 2 heads
[Parapagus] diprosopus (PDP)	Whole body, 1 head, 2 faces
Neural types	
Craniopagus (CP)	Skull
Rachipagus (RP)	Vertebral column
Pygopagus (PP)	Sacrococcygeal region

can readily be concluded from the presence of two, instead of one, embryonic primordia on the surface of the spherical blastula with their initial reciprocal distance and position determining the site and degree of conjunction. Proceeding growth results in secondary fusion of these primordia [1, 4], which is accompanied by neoaxial orientation and interaction aplasia [5, 6]. Neo-axial orientation, as seen in ventral and caudal conjoined twins, refers to the mechanism by which compound organs and structures are formed by equal contribution of both embryos and located in a plane perpendicular to the original. Interaction aplasia, which is characteristic for lateral conjoined twins, refers to suppression of formation of organs and structures in the conjunction area. Quite often, ventral conjoined twins also show some interaction aplasia since they almost always face each other at an angle (Fig. 5).

The above model also provides insight in the high incidence of laterality defects in specific conjoined twin types. Disorders of the normal left-right body plan (situs solitus) include complete mirror image (situs inversus), partial mirror image (situs ambiguus or heterotaxia), double left-side morphology (left isomerism) and double right-side morphology (right isomerism). During gastrulation, left-right asymmetry is established by a cascade of genetic signals and cilia-mediated preferential flow at the site of Hensen's node that culminate in the exclusively left-side expression of the *NODAL* gene in the lateral plate mesoderm (LPM) [7]. Normally, the left-side LPM is at an adequate distance from the right-side LPM and the notochord will act as a natural watershed between sides, thus preventing Nodal protein diffusion from the left to the right side. In certain types of conjoined twins, however, the left-side LPM of one twin may come in direct contact with the right-side LPM of the other twin when the embryonic primordia secondarily fuse, thereby disrupting the normal left-right patterning in at least one of the twins [8]. Laterality defects have been reported in about 50% of thoracoileopagus (TIP) and parapagus dicephalus (PDC) types of conjoined twins [8–11]. In all other types of conjoined twins, laterality defects are considered to be rare.

Laterality defects in singletons are readily diagnosed by the position and number of the internal organs and

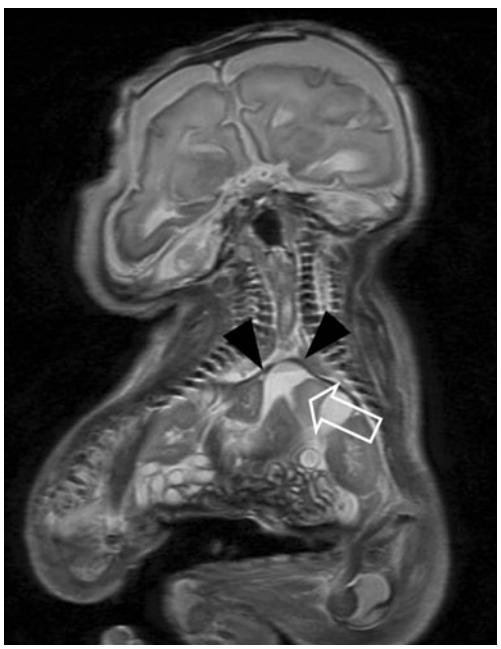

Fig. 5 Sagittal T2-weighed image (TR/TE, 2,500/68 ms; flip angle, 90°; slice thickness, 3 mm) of a cephalothoracoileopagus specimen. A unilateral spleen is seen (*arrow*). In the sagittal plane the continuous shared diaphragm is clearly visible (*arrowheads*)

structures, most of which have a specific left- or right-side topography or morphology (Table 2). In conjoined twins, however, nearly all these structures can be subjected to neo-axial orientation and/or interaction aplasia, which may profoundly hamper the detection of laterality defects. In ventral conjoined twins, the lungs and the spleen—thanks to their topographic position—are usually not involved in the conjunction process, but lung lobulation may be difficult to assess with certainty on MRI and the position of the spleen may be altered due to diaphragmatic hernia or malrotation. Nevertheless, asplenia and polysplenia are generally considered reliable indicators of right and left isomerism respectively.

From studies of laterality defects in TIP and PDC, in conjoined twins it can be concluded that if these defects are present, they only affect one of the twins and that the conjoined sides of PDC, if not situs solitus, show homonymous sidedness (i.e. left-left or right-right) [8–11]. This results in the four patterns of distorted laterality found in PDC conjoined twins: situs inversus or left isomerism in the left twin (RL-LR or LL-LR), and situs inversus or right isomerism in the right twin (LR-RL or LR-RR). Interestingly, the same patterns are found in TIP [8, 10]. The occurrence of laterality defects in PDC can be assumed to result from the fusion of (parts of) the LPM of both twins in the plane of conjunction (Fig. 6) but the laterality defects found in TIP twins are less readily explained, considering their bilateral opposing LPMs [8]. However, since ventral conjoined twins almost always face each other at an angle, thereby creating an anterior and a posterior aspect, it is conceivable that the LPMs of both twins come into contact exclusively at the posterior aspect. Indeed, this could explain the laterality patterns found in TIP [6].

Laterality defects appear to be uncommon in CTIP. We reviewed 46 case reports of human CTIP published in the English, German and French literature between 1980 and 2010, of which 23 were informative with respect to splenic morphology (details and references are available on request). The presence of a single spleen, in addition to other signs suggestive of a laterality disorder, was reported in only one case. In this case there was situs solitus in the left twin and right isomerism in the right twin [15], which fits with one of the patterns described above (LR-RR). Apparently, the LPMs of CTIP twins are subjected to neo-axial orientation before they come into contact with each other, even if the conjunction is markedly oblique (Fig. 5). A single spleen without any signs of laterality defects was found in one other case [16]. In PTIP, absence of a spleen seems slightly more common. In the 18 reports published in the past 100 years, a single spleen was found in four out of 13 informative cases (details and references are available on request). Considering their intermediate state between CTIP and TIP, one would expect the incidence of laterality defects in PTIP to be higher than in CTIP, especially in those cases with an internal morphology comparable with TIP. Indeed, three of the four cases with an absent spleen had a shared heart, which is in accordance with the default anatomy of TIP [8]. However, no other signs suggestive of laterality defects were mentioned in any of the PTIP case reports.

Based on our findings, we were inclined to assume the presence of laterality defects in all four specimens. The theoretical and reported rarity of laterality defects in CTIP and probably also in PTIP forced us to reconsider this diagnosis in our cases and to question the reliability of the spleen as a diagnostic marker. Moreover, three of our cases presented with laterality patterns that do not correspond with the ones mentioned above, being the specimen with asplenia in the left twin (RR-LR) and the two with asplenia in both twins (RR-RR). Since no other parameters of laterality defects could be verified in these specimens, we concluded

Table 2 Position and morphology of some asymmetrical organs and structures in laterality defects

	Situs solitus	Situs inversus	Left isomerism	Right isomerism
Heart				
Left auricle and pulmonary veins	L	R	L and R	Absent
Right auricle and superior vena cava	R	L	Absent/aberrant drainage	L and R
Lungs				
Left lung and bronchus	L	R	L and R	Absent
Right lung and bronchus	R	L	Absent	L and R
Liver	R	L	M	M
Stomach				
Greater curvature	L	R	L or R	L or R
Spleen	L	R	Multiple	Absent

L left-side, *R* right-side, *M* median

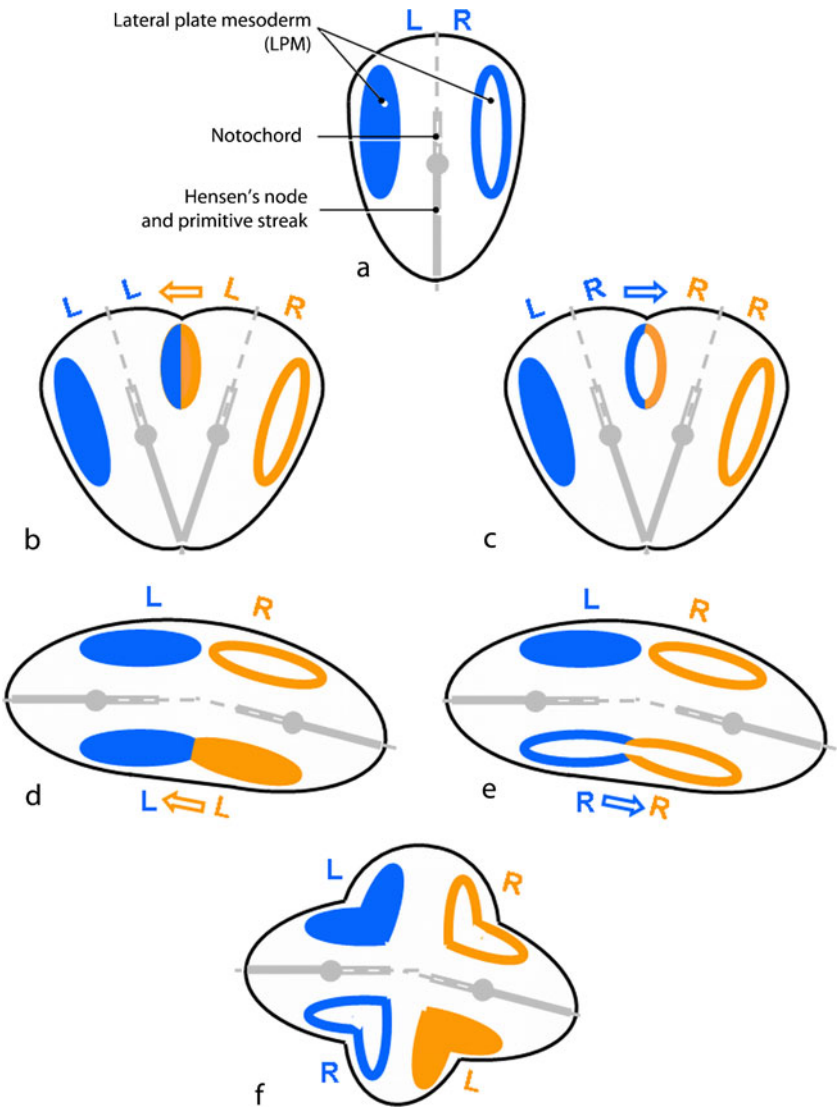

Fig. 6 The embryonic disc at early gastrulation seen from the amniotic side. **a** Normal singleton disc. **b** Parapagus dicephalus with the left lateral plate mesoderm (LPM) of the right twin disturbing the left-right patterning in the left twin. **c** Parapagus dicephalus with the right LPM of the left twin disturbing the left-right patterning in the right twin. **d** Thoracoileopagus (obliquely oriented) with the left LPM of the right twin disturbing the left-right patterning in the left twin. **e** Thoracoileopagus (obliquely oriented) with the right LPM of the left twin disturbing the left-right patterning in the right twin. **f** Cephalothoracoileopagus without LPM contact between the twins

that the absence of a spleen was unlikely to be caused by right isomerism. During normal embryology, the spleen develops in the dorsal mesogastrium after the greater curvature of the stomach, to which it is attached, and starts rotating to the left [17]. The possible causes of an absent spleen in postmortem imaging of conjoined twins are listed in Table 3. Theoretically, an absent spleen could represent congenital isolated asplenia, but this condition is exceedingly rare [18]. It is possible that postmortem maceration is responsible for the (pseudo) absence of a spleen in one or more of our cases. Alternatively, it may be correlated to the development of the (usually) shared stomach in CTIP and PTIP, in particular with its two dorsal mesogastria, but the precise mechanism is as yet elusive.

A collection of conjoined twins, like that kept at the Museum Vrolik, is becoming, from a scientific point of view, increasingly valuable with time. With the advance of prenatal diagnosis congenital anomalies are discovered in an early stage of pregnancy, providing the parents with a choice of termination. As a result, full-grown conjoined twins are, therefore, rarely born in developed countries, adding value to the opportunities the Vrolik collection offers in terms of examining fully developed congenital anomalies. Similar collections are fairly rare; Grassi et al. [19] performed a study similar to ours with specimens from the Museum of Anatomy of the Second University of Naples. Additional information about the whole spectrum of conjoined twin types might be obtained by collaboration between anatomical museums.

Table 3 Possible causes of an absent spleen in postmortem imaging of conjoined twins

Right isomerism
Lateral or extremely angulated conjunction
Congenital isolated asplenia
Pseudo-absence (thoracic location caused by diaphragmatic hernia)
Postmortem artifact (maceration)

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