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Paleopathological analysis of a probable case of Jarcho-Levin syndrome from the 18th century Northern Italy

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Abstract. This case report examines the differential diagnosis of an unusually fused chest belonging to a perinatal human remain retrieved in the crypt of Roccapelago (Italy). This specimen, which dated back to the final 18th century, showed a severe synostosis of the costovertebral articulations and posterior arches. The specimen was examined macroscopically and radiologically for the purpose of identify differences in mineral density. It also underwent computed tomography scan in order to create a 3D digital model and virtually reposition in anatomical position. The radiological trophism, size, and osteological maturity of the specimen are compatible with a perinate. The chest structure shows a characteristic crab like morphology, with the costovertebral articulations and some posterior arches completely fused. Accordingly, a diagnosis of Jarcho-Levin Syndrome has been suggested. This case appears to be the first report, to the knowledge of the authors, of a probable Jarcho-Levin syndrome, which dated before Jarcho and Levin codified this pathology in the scientific literature.

Key words: spondylocostal dysplasia syndrome, Jarcho-Levin syndrome, paleopathology

Introduction

Jarcho-Levin Syndrome is an autosomal-recessive disorder characterized by multiple vertebral and costal anomalies presenting at different levels of the vertebral column. This syndrome was first described by Saul Jarcho and Paul M. Levin in 1938 (1), when they studied the case of two Puerto Rican siblings affected by a shortened trunk, abnormal vertebral segmentation and irregularly aligned ribs. Since then, this pathology was named after its discoverers, and this term has been used for a variety of clinical cases showing chest anomalies (2). More recently, this nosological entity has been divided in two sub-categories, which have different survival rates, anomalies and inheritance mode (3):

- spondylocostal dysplasia (SCD) is characterized by the presence of a "crab-like" or "fan-like" rib pattern, due to the decrease in number of the ribs, and to their posterior fusion. It has a high mortality rate and its exact prevalence is unknown;
- spondylothoracic dysplasia (STD) is not characterized by the presence of the "crab-like" rib configuration; instead, it shows an abnormal orientation of the ribs with irregularities in shape and size, bifurcation, broadening and fusion. The survival rate is higher than in SCD (about 50%); its affecting approximately one in 12,000 people (4).

Up to now, numerous cases of Jarcho-Levin Syndrome have been reported in the medical literature

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(4–6) but, to the best of our knowledge, there are no published palaeopathological findings of this condition (7) .

Here we present what could be the first case report which dates back to the 18th century.

Historical and archaeological context

During the excavation campaign into the Church of the Conversion of San Paul, in Roccapelago (Modena, Northern Italy) (Fig. 1), a hidden crypt which contained a large skeletal assemblage was discovered. The archaeological excavation was conducted between 2009 and 2011 (8), and yielded the remains of more than 400 individuals. This crypt was used as a cemetery by the inhabitants of the small village of Roccapelago between the 16th and the 18th centuries. This large amount of human remains mostly consisted of commingled and completely skeletonized human remains, with a few corpses, especially among the most recent SU (i.e. SU23), that have undergone a different process of decomposition. In fact, thanks to the presence of two small windows that contributed to maintain the environment dry and ventilated (9), some partially mummified remains, still in anatomical connection, were retrieved. The study of the textiles suggested that the bodies were dressed in tunics and socks, and were wrapped in shrouds. The age range of this skeletal assemblage is very wide, as hundreds of non-adults skeletal remains were also retrieved (9, 10).

Here, we study a probable case of Jarcho-Levin Syndrome in a perinate retrieved from the crypt of Roccapelago (Modena, Italy).

Materials and Methods

The subject of this study is a perinatal partially fused chest (RP34). These remains were retrieved from SU34, dated to the final 18th century based on stratigraphy and archaeological findings (11-14). All the skeletons of SU34 were disarticulated, preventing the association of single bone elements to single infants; for this reason, it was not possible to retrieve additional bone elements that could safely be attributed to RP34. SU34 is placed on the south side of the crypt, which was indicated in the parish records as "grave of the angels" (15).

RP34 was examined macroscopically and subjected to radiological analysis to identify differences in mineral density. Then, the specimen underwent computed tomography scan at the department of Radiology of the GB Morgagni-Pierantoni city Hospital

Figure 1. On the left, the white dot is the position of the Church of the Conversion of San Paul in north of Italy (Roccapelago, Modena district); on the right, the church.

in Forlì. The parameters of acquisition included: 1.25 slice thickness, with an interval of reconstruction of 0.7 mm; 120 kV and 140-300 mA. Radiological images of the chest were taken in anterior view (Fig. 2a). Additionally, the computed tomography image data were segmented using Avizo Lite 9.2.0 software (Visualization Sciences Group Inc.) to generate 3D digital surfaces. The 3D digital models were imported into Geomagic Design X (3D Systems, Rock Hill, South Carolina, USA), post-processed (i.e., cleaning processes and correction of defects to create fully closed surfaces), and virtually repositioned in anatomical position. The post-processing of radiological images was performed at the Laboratory of Anthropology and Ancient DNA of the Department of Cultural Heritage of Ravenna University of Bologna.

Results

The right hemithorax, consisting of nine ribs, shows the costovertebral articulations and the posterior arches affected by a severe synostosis, while the third and the fourth ribs appear fused for their entire length (Fig. 2b). The morphology of the archway is altered with the ribs that fanning out in a crab-like morphology, as highlighted by the 3D digital model (Fig. 3 a, b, c, d). The posterior arches of the first two ribs are fused with what seems to be the transverse process of a thoracic vertebrae (Fig. 4); The left chest is represented by six ribs divided into two groups; the first one consists of four ribs with synostotic costovertebral articulations, with the synostosis of part of the posterior arch of the third and fourth ribs from above the second group consists of two ribs with synostosis only of the costovertebral joint processes (Fig. 3 c, d). These ribs also show the characteristic crab-like morphology (Fig. 3 a, b). Radiological trophism and size are compatible with a newborn.

Discussion and Conclusions

Differential diagnosis

The differential diagnosis of similar spinal and ribs disorganization in a fetus includes several diseases that often affect both the skeletal system and the soft tissues. The differential diagnosis applied to RP34, exclusively takes into account the morphology of the chest, ribs and degree of dysplasia, which can be estimated on recovered bone remains (Table 1). Due to the shortage of osteological material and the typology of deposition, genetic analysis was excluded a priori. We also evaluated the advantages and disadvantages of a paleogenetic analysis but, RP34 is essentially constituted by spongy bones, that usually contain scarce amount of endogenous DNA respect to petrous bones or teeth (16, 17). The marker targeted by this study should also be the nuclear DNA, usually present in few cop-

Figure 2. On the left (A), Radiological images, anterior view, of the chest. On the right (B), photo of the same view.

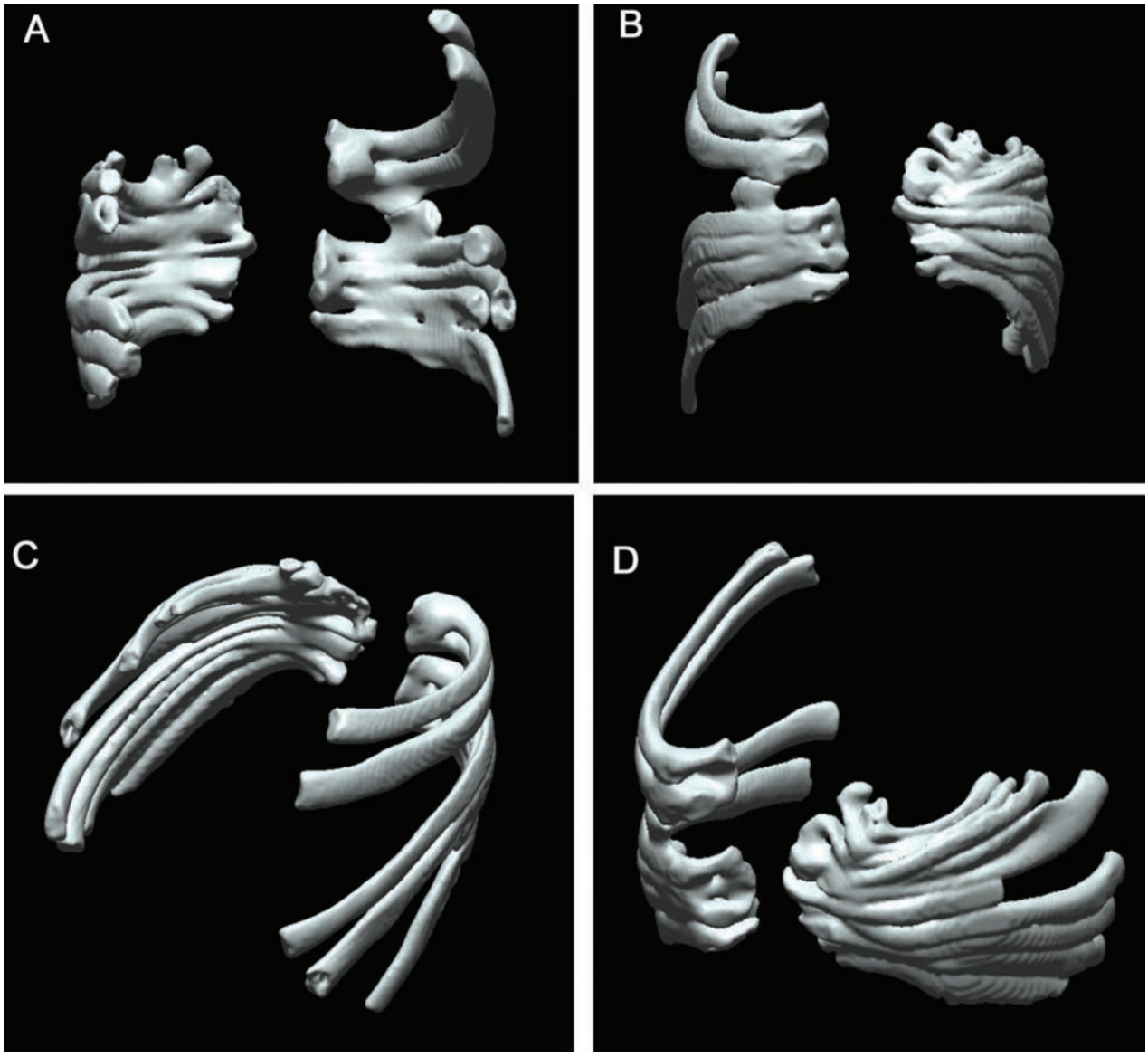

Figure 3. 3D digital model: A anterior view of the chest; B posterior view; C anatomical vision of the typical crab-like morphology, anterior view; D synostosis of the ribs of the right hemithorax.

ies respect to mitochondrial DNA (18, 19). For these circumstances the molecular approach, on the case of RP34, was not the first diagnostic line, therefore this analysis was excluded.

Differential diagnosis for an archeoanthropological case of Jarcho-Levine syndrome, is to be associated with those pathologies that are mainly characterized by severe skeletal disorders. Below are discussed the disorders considered for differential diagnosis:

- Dyssegmental dysplasia is characterized by severe micromelia, with extreme shortening of all segments of the extremities and occipital cephalocele, narrow chest with no ribs fusion. Crab-like appearance of the chest is lacking. Three variants are known: the Rolland-Desbuquois type, Silverman-Handmaker type and glaucoma syndrome. RP34 has a crab like chest, with fusion of numerous ribs, it is therefore quite dis-

Figure 4. Right hemithorax, external view. The red rectangle highlights the synostosis of part of the posterior transverse process of the thoracic vertebrae with ribs.

tinct from the morphology observed in Dyssegmental dysplasia (20).

- Spondylo-epiphyseal dysplasia is a chondrodysplasia characterized by disproportionate short stature (short trunk), abnormal epiphyses, flattened vertebral bodies and short ribs. Skeletal features are manifested at birth and evolve with time. The presence of fused ribs and of average physiological length on RP34, associated with the crablike chest, does not find similarities with Spondylo-epiphyseal dysplasia (21).
- Vacterl syndrome is an acronym that describes a non-random constellation of congenital anomalies. The acronym derives from V (vertebral anomalies, hemivertebrae, congenital scoliosis, caudal regression, spina bifida), A (anorectal anomalies, anal atresia), C (cardiac anomalies, cleft lip), TE (tracheo-oesophageal fistula +/- oesophageal atresia), R (renal anomalies, radial ray anomalies), L (limb anomalies, polydactyly, oligodactyly). Vacterl syndrome does not appear with crab-like chest, and the fusion of ribs, though rare, is always limited to a few ribs. RP34 has a typical crablike chest, with at least fifteen fused and dysplastic ribs; the greatest severity and extent, associated with the crablike chest, differ from the clinical picture of the Vacterl syndrome (22).
- Robinow syndrome is characterized by dysmorphic features like mesomelic limb shortening, hypoplastic external *genitalia* in males, and renal and vertebral anomalies. Patients may exhibit abnormal depression of the bone forming the center of the chest with a "funnel chest" morphology, or *pectus excavatum*, fusion and/or absence of certain ribs is also possible, although very rarely the defect extends to the entire chest. The abnormality of RP34, so extensive and characteristic in the crablike chest morphology, tends to exclude Robinow syndrome (23).
- Casamassima syndrome is a spondylothoracic dysplasia, similar to the costovertebral dysplasia and the Jarcho-Levin syndrome. The thorax has a crab-like configuration with fused ribs. The association of anal atresia, single umbilical artery, and urogenital anomalies suggested that this is a distinct entity compared to the Jarcho-Levin syndrome. Since it is not possible to evaluate the urogenital apparatus of RP34, Casamassima syndrome can not be excluded, in spite of the extreme rarity of the pathology (24).
- Poland syndrome is a congenital unilateral ab-

Table 1. Evaluated items for differential diagnosis

	Crab-like chest	Rib fusion	Short rib	Widespread chest anomaly
Jarcho-Levin Syndrome	yes	yes	no	yes
Dyssegmental dysplasia	no	no	no	yes
Spondylo-epiphyseal dysplasia	no	no	yes	yes
Vacterl syndrome	no	yes	possible	yes
Robinow syndrome	no	yes	no	no
Casamassima syndrome	yes	yes	no	Yes
Poland syndrome	no	no	yes	no
RP34	yes	yes	no	yes

sence of the pectoralis major and minor muscles, with unilateral chest wall hypoplasia, short ribs and hand modifications. The abnormality of RP34, bilateral and characterized by crablike chest morphology, without particular hypoplasia of the ribs, exclude Poland syndrome (25).

- Jarcho-Levine syndrome is a genetic birth defect which causes malformed bones in the vertebrae and ribs. Patients with Jarcho-Levin syndrome have short necks with limited movement, short stature and difficulty breathing, due to small, malformed chests that have a distinctive crab-like appearance with fused ribs. The alterations of RP34, due to morphological characteristics, is very similar to Jarcho-Levine syndrome with its very evident crab-like chest and fused but normal-sized ribs.

In the light of the severe degree of morphological compromise of the chest, which probably resulted in immediate death at moments after childbirth, except for Jarcho-Levine syndrome, the other diagnostic hypotheses are likely to be excluded, presenting them all in more benign forms; Casamassima syndrome is not completely excluded, it is associated with urogenital malformations, which can not be investigated on our case.

The severe deformity and the almost total lack of elasticity of the chest have probably resulted in death due to respiratory failure. Jarcho-Levin syndrome commonly leads to respiratory insufficiency and death during the first years of life, usually by 15 months of age. The severe form of Jarcho-Levin syndrome, as probably the case under study (SCD type), is considered a uniformly lethal condition. RP34, as far as the authors know, appears to be the first case of Jarcho-Levin syndrome on ancient cases, and the oldest documented case of this disease, dated before the Authors codified it in the scientific literature.

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