Article

A visual tool inclusive of fetal ultrasound and autopsy findings to reach a balanced approach to counselling on trisomy 18 in early second trimester

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Abstract: Identified by the eponym "Edwards' Syndrome," trisomy 18 (T18) represents the second most common autosomal trisomy after T21. The pathophysiology underlying the extra chromosome 18 is a nondisjunction error, mainly linked with the advanced maternal age. More frequent in female fetuses, the syndrome portends high mortality, reaching a rate of 80% of miscarriages or stillbirths. The three-step evaluation includes first trimester screening for fetal aneuploidy using a combination of maternal age, fetal nuchal translucency thickness, fetal heart rate and maternal serum free ß-hCG and PAPP-A; followed by the research for fragments of fetal DNA in maternal blood; and, finally, invasive techniques leave to the established diagnosis. Starting with the first trimester scan, selected ultrasound findings should be investigated to define not only the impact of the genetic problem on the fetus, but also to address the prenatal counselling. Previous series underline that T18 is not uniformly lethal. An active dialogue on the choices in the management of infants with T18 has emerged, sustained by the transition from the comfort care to the intervention attitude. Survival rates for individuals with supposedly fatal conditions have increased. In this novel scenario, an ad hoc counselling is pivotal. To support it, a comparative analysis by pictorial assays between ultrasound and autopsy findings could be beneficial. We provide an illustrative tool from a clinical case managed in early second trimester, with the purpose to strive a balanced approach in the hard choice faced by couples of fetuses with T18.

Keywords: Trisomy 18; diagnosis; ultrasound; counselling; autopsy.

1. Introduction

First described by Edwards in 1960, trisomy 18 (T18) is defined as a chromosomal disorder characterized by the presence of an extra chromosome 18 [1]. It is the second most common trisomy after Down's syndrome, with a live born prevalence of 1/6,000 and an overall prevalence of 1/2,500 [2]. The gap between these two estimates rescan can be justified by taking into account both the high

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rate of miscarriage and the predominant choice of therapeutic abortion, as the syndrome's poor prognosis leads to voluntary pregnancy termination in up to 86% of cases [3]. The T18 phenotype results from a nondisjunction error leading to an extra chromosome. Similarly, to other autosomal trisomies, the frequency of nondisjunction errors increases with maternal age [2,3]. Conversely, individuals carrying the mosaicism represent less than 5% of cases and manifest variable phenotypes, ranging from early mortality to physiologically developed adults [4]. The partial trisomy form occurs when only a segment of the chromosome's long arm is triplicated as a result of a balanced translocation or inversion, accounting for about 2% of individuals with T18 [5]. There is a predominance of affected females, with a male: female ratio of 1:3 [6-8].

Commonly known findings in children born with T18 include pre- and post-natal growth retardation, congenital structural heart defects, upper airway obstruction, early onset pulmonary hypertension, ocular abnormalities, external ear abnormalities, hearing impairment, genitourinary tract defects, structural abnormalities of the central nervous system (CNS) feeding issues, and an increased risk of developing certain types of neoplasia (Tab. 1) [9-13]. In addition, making the prognosis worse, there are severe alterations in psychomotor and intellectual development [14]. As a final result, a low life expectancy is accounted, with only 5-10% of children surviving beyond their first year of life [9,14].

Table 1. Principal abnormalities observed in Trisomy 18.

Visceral malformation	**Dysmorphic signes**
Central nervosous system	
- Agenesis of corpum callosum	
- Microgyria	*Skull and face*
- Cerebellar hypoplasia	- High foerhead
- Meningomyelocele	- Prominent occiput
- Hydrocephalus	- Hypertelorism
- Dolichocefaly	- Short palpebral fissures
- Wide fontanels	- Slender bridge of nose
- Microencephaly	- Nares upturned
	- Narrow palatal arch
Heart	- Micrognathia
- Ventricular septal defect	- Microstomia
- Patent ductus arteriosus	- Retrognathia
- Atrial septal defect	- Ears, low set and malformed
- Polyvalvular heart disease	
	Thorax
Lung	- Short webbed neck
- Malsegmentation to absence of right lung	- Short sternum
	- Small nipples
Abdomen	*Pelvis*
- Omphalocele	- Limited hip abduction
- Tracheoesophageal fistula	
- Pyloric stenosis	*Hands*
- Ileal atresia	- Hyperflexed position
- Meckel's diverticulum and intestinal malrotation	- Clenched hand
	- Camptodactyly
- Ancomplete fixation of the colon	- Clinodactyly
- Agenesis of the appendix	- Overlapping of index finger over third
- Extra-hepatic biliary atresia	- Fifth finger over fourth
- Abnormal liver lobulation	
- Hypoplastic gallbladder	*Foot*
- Heterotopic pancreas	- Hyperflexed position
- accessory spleen	- Rocker bottom feet
- Inguinal / umbilical hernia	- Syndactyly of second and third toes
-	
Kidneys	

- Horseshoe defect
- Hydronephrosis
- Polycystic kidney

Genitalia

Male: cryptorchidism
Female: hypoplasia of labia majora,
hypoplasia of ovaries

Others visceral malformation

- Tracheo-esophageal fistula
- Esophageal atresia
- Thymic and adrenal hypoplasia

Neoplasia

- Wilms tumors

Hepatoblastoma

In early gestation, the diagnosis relies upon some specific ultrasonographic fetal findings (i.e., increased nuchal translucency (NT), absence of the nasal bone, reversed a-wave in ductus venosus (DV), tricuspid regurgitation) and abnormal maternal serum markers, assessed during the first trimester routine screening and generally followed by invasive testing techniques to confirm the suspected diagnosis [15,16]. The probability of fetal survival increases with increasing gestational age. Specifically, at 12 and 39 weeks of gestation only 30% and 67% of viable pregnancies result in live birth, respectively [17]. After diagnosis of T18, prenatal counseling and postnatal care have traditionally been based on assumptions that these aneuploidies are either lethal or associated with a poor quality of life [4,18]. However, this view is now being challenged. Recent evidence suggests that the assumptions on quality of life are rather subjective and that there is a certain variability in postnatal outcomes, which may be improved by postnatal interventions [19]. Parental advocacy for their infant's best interest mimics this variability as requests for resuscitation, neonatal intensive care, and surgical intervention are becoming more frequent [19]. Consequently, a balanced approach to counseling families of the newborn with T18 at the time of diagnosis is recommended. The counseling process should include presentation of accurate survival figures, comparison between aggressive versus non-aggressive interventions, avoidance of language that assumes outcome, communication of developmental outcome that does not presuppose perception of quality of life, and respect for the family's choice, whether it be comfort care or intervention [19].

At the best of our knowledge, no previous investigations have developed a photographic instrument to be used by clinicians to support the parental decision-making process after a well-established T18 diagnosis. Moving from our clinical experience in managing a case of pregnancy complicated by T18, we performed a comparative analysis by pictorial assays between ultrasound and autopsy findings, in order to provide a visual tool for striving a balanced approach in the hard choice for couples of fetuses with T18.

2. Case description

A 40-year-old woman, gravida 2, para 1 of non-consanguineous marriage was admitted to our unit at 15+4 weeks of amenorrhea for pelvic pain. Any routine obstetric assessment was performed previously. At admission, an appropriate ultrasound evaluation was assessed, leading to a correct datation of pregnancy based on crown-rump length corresponding to 13 weeks and 1 day. A combined screening for aneuploidies, preeclampsia (PE) and smallness for gestational age (SGA) was accomplished.

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Evidence of increased NT (3.2mm), presence of the nasal bone, reversed a-wave in DV (pulsatility index (PI), 0.98), absence of tricuspid valve regurgitation, pathological mean uterine arteries PI (1.1) were recorded. The combined risk for T13, T18, T21 PE and SGA were 1.52, 1:10554, 1:51, 1:4524, 1:48 and 1:83, respectively. Preventive therapy by aspirin 150mg per day was indicated. A Non-Invasive Prenatal Testing (NIPT) was suggested, leading to the risk for T18 with a sensitivity of 96% at 7% of cell free rate of fetal DNA. At 16 weeks of gestation, a sonographic morphological assessment of the female fetus was carried out in order to identify one or more detectable structural abnormalities. Major cardiac malformations, CNS anomalies, and gastrointestinal abnormalities or abdominal wall defects were ruled out. Among facial anomalies, short ear length and micrognathia were suspected. In the evaluation of skeletal anomalies associated to fetal T18, both camptodactyly, defined as an antero-posterior flexion deformity of the proximal interphalangeal joint of the fingers, and clinodactyly, defined as radio-ulnar deviation of the fingers, were supposed. A concomitant invasive prenatal diagnostic procedure was performed, finding a karyotype with a T18 (47, XX, +18). A detailed counselling session was planned, discussing clinical and prognostic aspects detected until that time of pregnancy. Swiss experience detailed in one of the largest with respect to the number of cases of children with T18 was provided, reporting a median survival of 17 days for the 53 females born at term, without esophageal atresia, and 4% of them lived for longer than 10 years [20]. Additional information available in the literature regarding the use of a patient-centered care approach and the impact of surgical interventions on the long-term outcomes were also communicated [2,3,6,8,14,25-44]. Following a painful decision-making process, a final request for therapeutic termination of pregnancy was made. By using vaginal misoprostol at the dose of 800 mcg repeated after 6 hours, a stillborn female fetus, corresponding to 18 weeks of gestation, was delivered. A subsequent manual extraction of placenta followed by an intra-uterine curettage was performed. The placenta and the fetus underwent to histological and autoptic examination. The patient was discharged the day after delivery, with a psychological support and an appointment to discuss the histological results.

3. Comparison between ultrasound assessment and autopsy findings

A heterogeneous spectrum of ultrasound features might be observed at time of the prenatal assessment suggestive of T18. Early ultrasonographic findings, including NT, absence of the nasal bone, reversed flow in the DV, tricuspid valve regurgitation, omphalocele, abnormal posturing of the hands, megacystis, abnormal four-chamber view of the heart and single umbilical artery might be identified during the routine scan at 11-13 weeks [8]. Further findings, more easily detectable in the second and third trimester, comprise meningomyelocele, ventriculomegaly, chorioid plexus cysts, posterior fossa anomalies, cleft lip and palate, micrognathia, low-set ears, microphtalmia, hypertelorism, short radial ray, clenched hands with overriding index fingers, club or rocker bottom feet, diaphragmatic hernia, renal anomalies, cardiac defects, polyhydramnios, and growth retardation. According to the topographic criterion, a summary of principal abnormalities observed in T18 are summarized in Tab. 1. A comparative analysis among well-known postnatal characteristics in children with T18 and the combination of prenatal images at scan evaluation and autoptic elements is detailed below, inclusive of images taken from the clinical case.

3.1 Skull and face

At postnatal evaluation, the skull of newborns with T18 is dysmorphic, with narrow bifrontal diameter and prominent occipitus; enlarged fontanels and microcephaly may be present. The face has a typical triangular shape because the forehead is high and wide with a small chin associated with micrognathia and microstomia. Palpebral fissures are narrow, the nose and mouth are small, the palate is narrow and high. The ears are dysplastic and low-set, resembling faun ears, and may be associated with preauricular tags. Cleft lip is reported in 5% of cases, and cleft palate in other 5%

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[10,11]. Choanal atresia may also be present. Less frequent anomalies include hypoplasia of the supracilliary ridges, Wormian bones, eye abnormalities such as corneal opacities, microphtalmia, coloboma, cataract, glaucoma, blue sclera, oblique or narrow palpebral fissures, epicanthic folds, ptosis, abnormally thickened eyelids, abnormally long or sparse eyelashes, blepharophimosis, hypertelorism, strabismus and nystagmus.

At ultrasound assessment in the first half of pregnancy, the majority of these characteristics might be difficult to recognize. The leading feature remains the sonographic appearance of subcutaneous accumulation of fluid behind the fetal neck in the first trimester of pregnancy, known as NT. The term translucency is used irrespective of whether it is septated or not and whether it is confined to the neck or envelopes the whole fetus [17]. Of note, its impact on chromosomal abnormalities is more closely related to the size rather than its appearance. In about one-third of fetuses and, in about 75% of cases, the chromosomal abnormalities are associated with T18 or T21, with some involvement on fetal cardiovascular and pulmonary defects, skeletal dysplasias, congenital infections and metabolic and hematological disorders; consequently, the prognosis for chromosomally normal fetuses with nuchal edema is poor [16]. In the present case, a fetal edema confined to the neck was observed at the first ultrasound scan (Fig. 1a) and confirmed at the autopsy (Fig. 1b). Additional features can be inspected. First, a likely narrow bifrontal diameter was suspected (Fig. 2a, 2b). Second, a prominent occipitus was identified (Fig. 3a), but associated with the edema of the NT (Fig. 3b). Third, the nasal bone was easily visualized by sonography, although slightly short (Fig. 4a), as confirmed at the autopsy, with anteverted nostrils (Fig. 4b). Four, as a non-specific finding in a wide range of genetic syndromes and chromosomal defects, signs of micrognathia were found. A prenatal suspect was made (Fig. 5a), subsequently confirmed by post-mortem evaluation in our case (Fig. 5b), showing a triangular face (Figg. 2b, 4b). Finally, microcephaly should be suspected in chromosomal defects, albeit its accurate estimation belongs to advanced gestational ages.

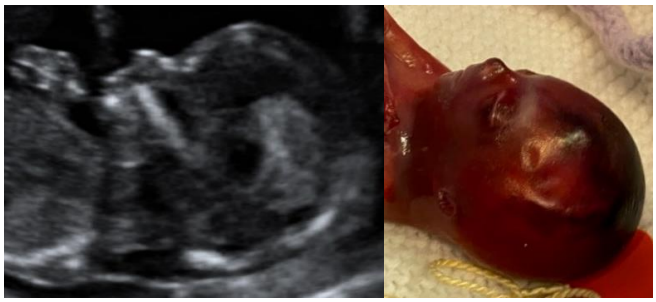

Figure 1. Fetal nuchal translucency at 13 weeks of gestation (left side, a) and persistent nucal edema at autopsy (right side, b).

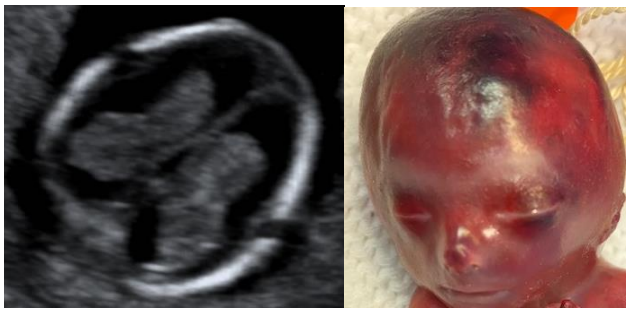

Figure 2. A narrow bifrontal diameter suspected at 13 weeks of gestation (left side, a). A high forehead is evident (right side, b).

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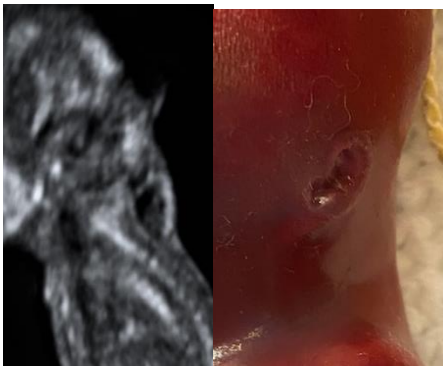

Figure 3. The prominent occipitus identified prenatally (left side, a), associated with the edema of the nucal thickness and low set ear (right side, b).

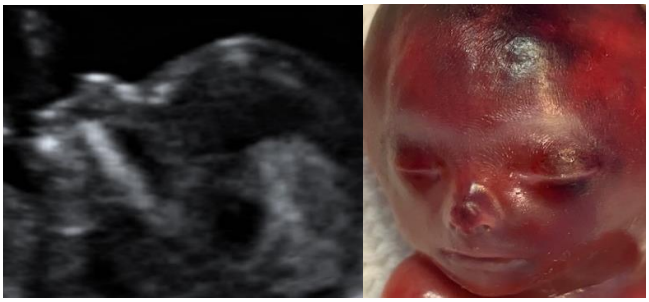

Figure 4. Short nasal bone assessed during the 11-13 weeks scan (a) and bulbous nose with anteverted nostrils (b).

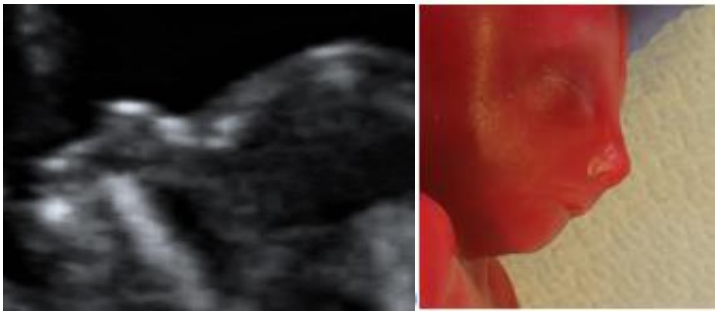

Figure 5. Micrognathia suspected during the first trimester scan (a), requiring a successive assessment and its confirmation at autopsy (b).

3.2 Thorax

Short neck with excess hair, short sternum, small nipples, umbilical or inguinal hernia and/or diastasis of the rectus muscles, narrow pelvis and limitation of the hip abduction may be noticed. The chest may be relatively wide, with or without widely spaced nipples. Other findings include incomplete ossification of the clavicle, hemivertebrae, fused vertebrae, scoliosis, rib anomalies, pectus excavatum and hip dislocation.

Early ultrasound scans failed to find any significant abnormalities in thoracic conformation, while during the external examination of the autopsy a short sternum associated with a short-webbed neck might be identified, as described in our case (Figg. 3b, 6a, 6b).

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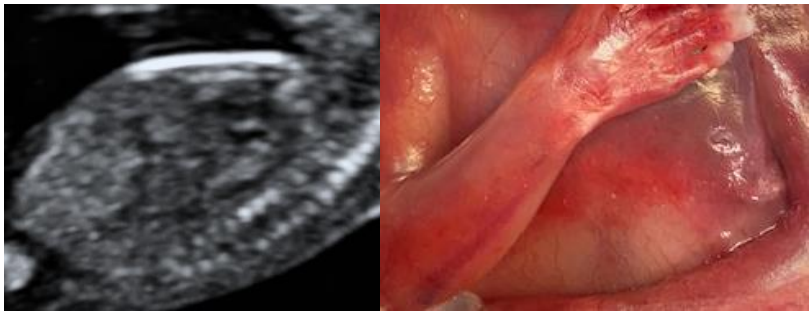

Figure 6. A short sternum associated with a short-webbed neck, less evident at scan (a) than at autopsy (b).

3.3 Visceral malformations

T18 is clinically associated with various major and minor multisystem anomalies, including cardiovascular, neurological, renal, gastrointestinal, respiratory, and skeletal malformations, as detailed below:

- CNS malformations occur in nearly 30% of cases, with frequent cerebellar hypoplasia, heterotopy of the granule cells in the white matter, and anomalies of the corpus callosum [10-14]. Other abnormalities include hydrocephalus, anencephaly, myelomeningocele, facial palsy, Arnold-Chiari malformation, arachnoid cysts and periventricular heterotopia of the brain [12-14].
- Congenital heart defects are often described and are considered almost a rule. The frequency of heart defects reported in autopsies and echocardiography studies is greater than 90%. A wide spectrum of heart defects is reported in patients with T18, with most individuals presenting with multiple defects. Ventricular septal defects and patent ductus arteriosus were described in the original report written by Edwards [1] and are considered as major anomalies. Some authors consider polivalvular heart disease (characterized by the involvement of two or more atrioventricular and/or semilunar valves) as a pathognomonic finding [10,11].
- The most frequent anomaly in the organs of the immune system is the atrophy or hypoplasia of the thymus. The decreased lymphocyte count in the spleen, lymph nodes and intestinal tract has also been described. Thyroid or adrenal hypoplasia may be present.
- Malformations of the digestive system include esophageal atresia with or without tracheoesophageal fistula, omphalocele, pyloric stenosis, extra-hepatic biliary atresia, ileal atresia, Meckel's diverticulum and intestinal malrotation. Thyroglossal duct cyst, hypoplastic gallbladder, gallstones, abnormal liver lobulation, heterotopic pancreas, incomplete fixation of the colon, agenesis of the appendix, accessory spleen, cloacal exstrophy, imperforate or misplaced anus can also be observed.
- Several types of renal abnormalities have been observed, the most frequent being the horseshoe, polycystic, ectopic or hypoplastic kidneys, renal agenesis, hydronephrosis, hydroureter and ureteral duplication.
- Neoplastic diseases have been occasionally reported in individuals with T18 and include Wilms' tumor and hepatoblastoma.

In our case, no visceral malformations were at ultrasound scans and found at autopsy. Weight, shape and histological development of organs corresponded to the gestational age.

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3.4 Limb abnormalities

T21, T18, triploidy and Turner syndrome are associated with relative shortening of long bones. Typically, the fists are clenched, with overlapping of the second over the third and of the fifth over the fourth fingers. The distal crease of the fifth finger and, less frequently, of the third and fourth fingers may be lacking. Analysis of the dermatoglyphics usually shows a pattern of increased arches at the digital pulps of six or more fingers. Single palmar crease and clinodactyly of the fifth fingers may also be present. The nails are hypoplastic. Clubfoot and prominent calcaneus are common, and there may be rocker-bottom (or rocking chair) foot. The hallux is shortened and dorsiflexed. Syndactyly of the second and third toes is also a common finding. Less frequent anomalies include syndactyly of the third and fourth fingers, polydactyly, ectrodactyly, thumb aplasia and hypoplasia/aplasia of the radius.

In our case, an antero-posterior flexion deformity of the proximal interphalangeal joint of the fingers (camptodactyly) and radio-ulnar deviation of the fingers (clinodactyly) were suspected during the scan at 16 weeks of gestation (Fig. 7a), confirmed at autopsy (Fig. 7b).

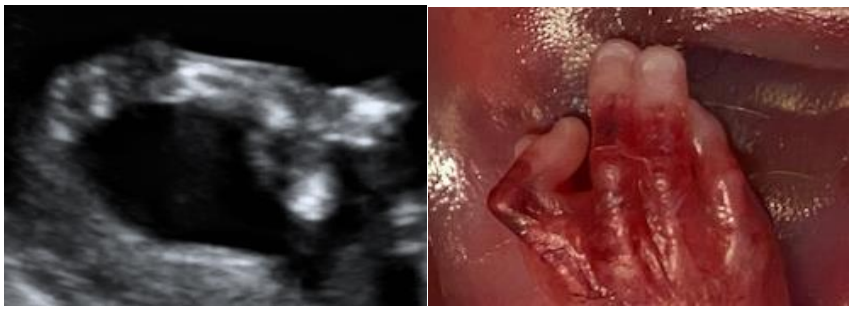

Figure 7. Antero-posterior flexion deformity of the proximal interphalangeal joint of the fingers (camptodactyly) and radio-ulnar deviation of the fingers (clinodactyly) suspected during the scan at 16 weeks of gestation (a) and its confirmation at autopsy (b).

3.5 Impaired neurological development

Mental retardation is frequent and usually severe in infants born with this syndrome. The hypotonia, observed in the neonatal period, is followed by hypertonia. The cry is weak and the response to sounds is reduced. Suction difficulties are common. Severe cognitive and motor development dysfunctions are frequently observed. Nevertheless, individuals with T18 usually reach some degree of psychomotor maturity and keep learning continuously. Interestingly, cases of T18 mosaicism with normal intelligence have been reported.

Due to the pregnancy voluntary termination, we cannot describe these particular aspects for our case.

4. Discussion

Growing attention is being paid to obstetric quality of care, primarily supported by the epidemiological change of pregnancy, which is planned later and less, with higher rates of complications [45]. In this novel scenario, assessing the quality of care of the feto-maternal dyad include at least two aspects. First, to achieve a patient-centered care, advocated by an individual's specific health needs and desired health outcomes, which are the driving force behind all health care decisions and quality measurements [46, 47]. Second, to apply lessons learned from the management

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of other diseases to those who could benefit from them. With regard to T18, patient-centered care represents not only a new achievement for patient management, but also it encourages the active collaboration and decision-making to design an individualized care plan [19]. To support it, changes in managing offspring affected by T21, supported by the desire to share progression in developmental areas and a longer-term survival by the families involved, might be beneficial also in T18 condition.

With the increase in the number of women delaying childbearing and the development of prenatal screening tests such as cell-free fetal DNA technologies, there is a parallel increase in the number T18 prenatal diagnoses [20]. Albeit it is characterized by variable clinical manifestations, with involvement of multiple organs and systems and counting more than 130 different anomalies, which may affect virtually all organs and systems, recent studies seem to encourage the shift from traditional palliative care to therapeutic procedures [8,34,38,39,44], with a parallel increases in survival rates (Fig. 8).

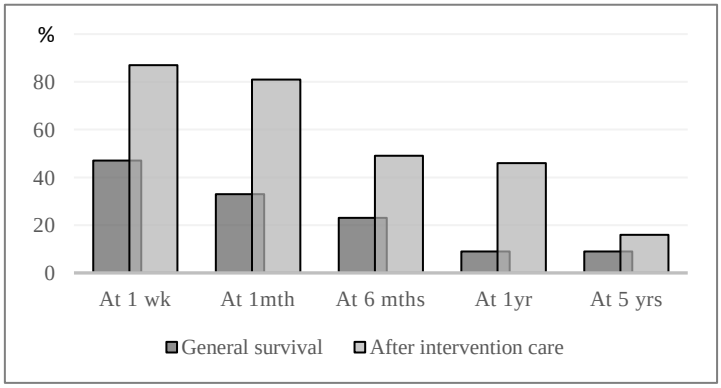

Figure 8. Summary of postnatal survival rates among children with T18, segregated into general and after intervention care, as reported in literature (see Tab. 2).

Consequently, changes in prenatal counseling and postnatal management, traditionally based on poor neonatal survival rates and significant cognitive and motor disabilities in alive children, are nowadays inclusive of the offer of care opportunities with parents, together with a longer survival. A growing body of evidence is available from several tertiary centers, including comparison between palliative care versus interventions for malformative conditions susceptible of postnatal correction [8,34,38,39,44]. This concept implies an added effort in performing an effective counselling, minimizing the impact of the physician's personal preferences upon those of the families. Indeed, moving from the fundamental aspects of the effective prenatal counselling process based on the 'best interest of the patient', parental autonomy and available medical resources [48], a synergetic multidisciplinary team including feto-maternal specialists, geneticists, neonatologists, pediatric surgeons, psychologists is nowadays necessary. Since the prenatal diagnosis of a seriously malformed fetus is a stressful event in the life of expecting parents, the counseling offered by competent physicians seems helpful, irrespective of the final decision. In some cases, parents can choose to continue pregnancy because of moral beliefs, either personal or religious, followed by child-centered reasons involving the value of life and love for their child. In other ones, parents may choose to terminate the pregnancy because of fear of managing a child who is problematic under several aspects, including that of home healthcare. In both situations, previous experiences and visualization of the disease's characteristics might aid to better understand the extent of the problem.

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Relevant research studies provide detailed information concerning genetic counselling for parents and their families and life prognosis, prior to applying intensive management to newborns with T18. Kato et al. have identified as factors for survival the longer gestation period, larger physique, the absence of an extremely low birthweight infant, the absence of esophageal atresia and/or cardiovascular defects [43]. Imataka et al have investigated the effect of the medical progression and prognosis, reporting improvements in life prognosis at six months after birth [39]. Likewise, in the Canadian retrospective analysis completed by Nelson et al covering a 21-year period, 10% to 13% of children who underwent surgical interventions survived for 10 years [38]. A summarized report on survival among children with T18 is showed in Fig. 8. Data extraction from previous published studies (Tab. 2) allows speculating on improved survival rates if an intervention approach is chosen, while accepting the general mortality for T18.

Table. 2. Summary of reported survival of live-born with trisomy 18, expressed in percentage (%).

Author, year	Country	Sample size (n)	Study period	At one week (%)	At one month (%)	At six months (%)	At one year (%)	At five years (%)	Mean survival (days)
Weber, 1967[6]	Multicenter	192	1963-1966	89	72	13	8	1	70
Carter, 1985[25]	Australia	43	1972-1982	35	11	5	4	-	5
Young, 1986[26]	United Kingdom	21	1980-1985	32	18	-	0	-	2.5
Goldstein, 1988[27]	Denmark	76	1977-1986	44	21	3	0	-	6
Root, 1994[28]	USA	64	1979-1988	45	34	9	5	-	4
Embleton, 1996[2]	United Kingdom	34	1986-1992	-	15	-	0	-	3
Brewer, 2002[29]	United Kingdom	84	1974-1997	43	25	-	2	-	6
Rasmussen, 2003[30]	USA	114	1979-1997	50	38	15	8	-	14.5
Niedrist, 2005[14]	Switzerland	161	1964-2003	40	22	9	6	2	4
Lin, 2006[8]	Taiwan	39 (20[1]/19[2])	1988-2004	46	16	3	3	-	18[1]/145[2]
Imataka, 2007[31]	Japan	179	1997-2003	68	43	17	9	-	-
Kosho, 2008[32]	Japan	24	2003-2008	87	83	45	25	-	152.5
Vendola,	USA	200	1999-	52	30	-	3	-	7

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2010[33]			2003						
Irving, 2011[3]	United Kingdom	301	1985-2007	36	27	-	6	-	-
Subramaniam, 2015[34]	USA	54 (5[1]/49[2])	2004-2014	-	-	64	7	7	12[1]/24[2]
Russo, 2015[35]	Italy	60	1985-2011	39	11	-	-	-	-
Meyer, 2016[36]	USA	1113	1999-2007	53	37	-	13	12.3	8
Negase, 2015[37]	Japan	73	1993-2009	43	33	-	3	-	-
Nelson, 2016[38]	Canada	254 (219[1]/35[2])	1991-2012	-	29[1]/83[2]	-	13[1]/69[2]	10	9
Imataka, 2016[39]	Japan	44 (20[1]/24[2])	1992-2013	70[1]/87[2]	50[1]/79[2]	15[1]/33[2]	10[1]/12.5[2]	-	38.5 (3-97)[1]/ 112 (47-260)[2]
Dogan, 2017[40]	Turkey	43	1996-2016	9	36	27	9	-	60
Duque, 2018[41]	Brasil	11	1994-2017	45	9	-	0	-	2
Iida, 2019[42]	Japan	69 (28[1]/41[2])	2003-2017	-	-	51[1]/65[2]	30[1]/50[2]	13[1]/11[2]	-
Kato, 2019[43]	Japan	117 (61[1]/52[2])	2000-2015	-	72	43	5[1]/53[2]	0[1]/20[2]	20[1]/384[2]
Goel, 2019[44]	Multicenter	122	1974-2014	58	20	-	12	8	-

[1]Neonates managed by palliative care ; [2]Neonates treated by agressive interventive care.

Figure 8. Summary of postnatal survival rates among children with T18, segregated into general and after intervetion care, as reported in literature (see also Tab. 2).

In contrast to the efforts performed until now to provide details on survival for an optimal prenatal counselling, visual tools to facilitate the comprehension of the defects suspected at obstetric ultrasound are truly lacking. In general, the practice of translating information into a visual context makes information easier for the human brain to understand. In a scenario of medical counselling, the benefits from the visualization might include not only the ability to absorb information rapidly, but also to reach an increased understanding of the subsequent steps of the treatment process. Therefore, we provide a catalog of ultrasound and autopsy images from our clinical case, with a

special focus on dysmorphic signs attributable to T18. Regardless of the couple's final decision and based also on the absence of a multi-organ involvement, the visual tool can support the transition from non-concrete to concrete cognitive functioning, making the issue more tangible and preparing the couple to make a more conscious choice.

5. Conclusions

In conclusion, due to the growing maternal age at birth, diagnoses of T18 are destined to increase. Improvements in care achieved in similar conditions, such as T21, and the novel approach based on the patient-centered care lead the dialogue enriched with the complex and multi faced questions surrounding the cases of fetuses affected by T18. An appropriate counselling should be based on strong elements, such as updated data from literature and visual tools for a better understanding.

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