Review

Perinatal pathology reports: A guide for obstetricians

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Abstract

This article will provide the practising obstetrician with a general guide to the structure and interpretation of the histopathology report, with a focus on placental and perinatal autopsy reports. The relevance and readability of a histopathology report is heavily dependent on the quality of clinical information provided by the referring clinician. Walkthroughs of example placental and autopsy reports are provided, along with examples of pathologies and their possible significance to the underlying diagnosis.

Keywords: autopsy; pathology; perinatal; placenta

Introduction

Practising obstetricians generally have few spontaneous interactions with paediatric and perinatal histopathologists (hereafter referred to as ‘pathologists’ for brevity). The specialties are so different that, to an observer, it may seem unlikely that they share a common root derived from ‘pluripotent’ medical students. The environments in which pathologists and obstetricians work are markedly different, with the rhythms and urgency of the delivery suite and operating theatre uncommon within pathology laboratories. However, decisions made within both arenas can have significant consequences for families. Specialists from both will meet at fetal MDTs (often along with geneticists) to discuss the presentation and management of complicated pregnancies. Face-to-face encounters may also occur in court (usually Coroner's court, in the context of an unexplained neonatal death or following intra-partum complications).

As such, there are few arenas that permit trainees to learn from one another in a safe and constructive manner. Considerable doubt about how to interpret findings may therefore arise, particularly for junior doctors or new consultants. This article will provide the practising obstetrician with a general guide to the structure and interpretation of the histopathology report, with a focus on placental and perinatal autopsy reports. Maternal deaths are beyond the scope of the article and will not be further considered. Similarly, histopathological review of specimens submitted to exclude or confirm potential gestational trophoblastic disease is not covered, but reviews can be found elsewhere.

The examples are based on real cases but have been altered to protect patient confidentiality.

Generating a useful pathology report

Following a request being placed by a clinician, the placenta is collected and sent to the histopathology laboratory. The relevance and readability of the histopathology report generated at the end of this process is heavily dependent on the quality of clinical information provided by the referring clinician, since interpretation of histological features may be strongly related to the context in which they are found. Request forms should be completed by staff who understands the reason for the request and the general information required for histological evaluation. The histopathology report represents the opinion of a specialist in tissue examination and clinical information informs the subjective interpretation of objective histological findings. This is analogous to a clinician assessing a clinical presentation of, for example, abdominal pain, in which context is highly important in addition to the objective examination findings. The reporting pathologist may not be able to provide correct interpretation of microscopic features present in the absence of satisfactory clinical information. Two practical examples of this are illustrated below:

1. A pathologist deciding whether the acute chorioamnionitis present in the placental membranes (objective finding) could reasonably have contributed (subjective interpretation) to a term baby born in unexpectedly poor condition (minimum clinical information). Knowledge of stillbirth versus livebirth, presence or absence of raised inflammatory markers, positive cultures, suspected aetiological agents (e.g. Group B Strep) and maternal symptoms of infection may help the pathologist to provide a clinically useful comment in this case.
2. A pathologist deciding whether marginal haemorrhage/clot present on the maternal surface of a placenta (objective finding) could represent an abruption (subjective opinion) in the context of PV bleeding (minimum clinical information) and

significant antepartum haemorrhage versus a clinically incidental finding.

Clinical information may also be referenced within a report by the reporting pathologist to corroborate or refute a specific diagnosis (e.g. reporting the presence or absence of sickled maternal erythrocytes or Plasmodia in the assessment of placental histology of a feverish woman of East African origin).

If a pathologist judges that insufficient clinical information is present, they may only provide a ‘morphological description’; consisting of a technical description of the objective findings present, without commenting on the clinical significance of these changes. In such cases if the pathology report would be influenced and improved by providing additional information (or by correcting misleading clinical information written on the request form in error), contacting the pathologist in question will afford them the opportunity to provide a more meaningful report in an addendum.

Interpretation of a placental pathology report

The structure of a placental pathology report: clinical details and supporting information

This section reflects the comments provided by the requesting clinician on the paper form or electronic requisition accompanying the specimen. RCPath/RCOG guidelines for placental examination are available but common clinical indications for pathological examination of the singleton placenta include:

1. Intra-uterine death or stillbirth
2. Baby born in unexpectedly poor condition
3. Suspected maternal or neonatal infection or sepsis
4. Suspicion of growth restriction or small for gestational age or clinical symptoms of pre-eclampsia
5. Suspicion of morbidly adherent placenta
6. Antepartum haemorrhage
7. Suspected umbilical cord pathology

In multiple pregnancies, placental examination may also be requested in the context of twin-to-twin transfusion syndrome, twin anaemia-polycythaemia sequence and for confirmation of chronicity (although this is now rarely indicated if early ultrasound examinations are performed), in addition to the above list. Placental examination is sometimes requested in the context of fetal anomalies (e.g. Trisomy 21, spina bifida), however, in most cases, placental examination adds little useful additional clinical information in the context of a confirmed anomaly and few fetal anomalies have specific associated placental abnormalities.

In the anonymised example provided (Figure 1), placental examination has been requested by the clinical team due to the presence of clinical fetal growth restriction (450 g at 28 weeks’ gestation), clinically-identified antepartum haemorrhage, and intrauterine death. This history raises the possibility of multiple pathologies, several of which can be assessed at macroscopic examination. The laboratory contact details are provided in the top left hand corner, along with the seal of UKAS (United Kingdom Accreditation Society), which indicates that the laboratory reporting the specimen is meeting medical laboratory standard ISO 15189. These standards are rigorous and intended to ensure quality and competence within diagnostic services. Main UKAS inspections are generally performed every three years, with interim inspections occurring more frequently.

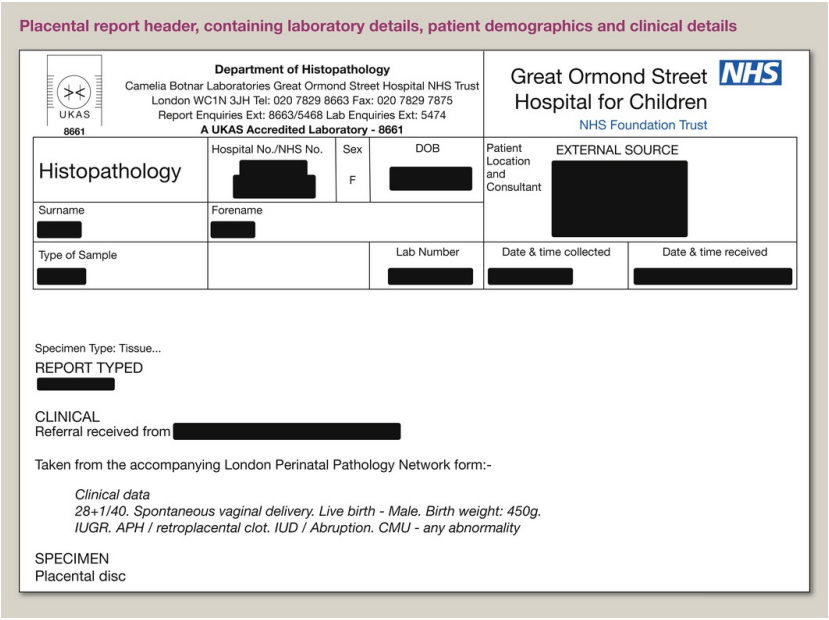

Figure 1

alt-text: Figure 1

The structure of a placental pathology report: macroscopic examination

Macroscopic examination (or gross examination) is usually performed following confirmation of matching patient identifiers on the specimen container and request form by the receiving laboratory. This section of the report describes the appearances of the cord, membranes, fetal surface, maternal surface and placental parenchyma, along with the dimensions (including a trimmed weight) and the presence of any abnormalities identified. Some commonly seen macroscopic abnormalities and the related pathologies are summarised in Table 1 below.

Table 1 Possible macroscopic abnormalities at placental examination with associated pathology

alt-text: Table 1

Macroscopic abnormality	Related pathology
Opaque membranes	Ascending maternal genital tract infection
Green, slippery membranes	Intrauterine meconium release
Circumvallation of membranes	Chronic abruption sequence or incidental
Barber-shop pole cord	Funisitis
Two vessel cord (single umbilical artery)	May be associated with fetal anomalies or incidental
Marginal or velamentous cord insertion	Haemorrhage, thrombosis, mechanical impingement of cord during labour or incidental
Distorted and dilated chorionic plate vessels	Placental mesenchymal dysplasia
Organising thrombi within chorionic plate vessels	Fetal vascular malperfusion
Clot distorting fetal surface	Sub-amniotic haemorrhage (may be artefactual)
Maternal surface ragged	Potential for retained products of conception

Diffuse increase in fibrin throughout the disc	Massive perivillous fibrin
Discrete white foci within parenchyma	Possible infarctions or intervillous thrombi
Adherent clot indenting maternal surface	Premature placental separation or artefact/incidental
Intervillous thrombus	Extensive thrombus may represent feto-maternal haemorrhage, most incidental
Focal white areas on maternal surface	Morbidly adherent placenta vs calcification (calcification may be normal at term)

It is important to note that many pathologies, including chronic histiocytic intervillositis, villitis of unknown aetiology, maternovascular malperfusion and viral infection of the feto-placental unit may show no macroscopic abnormalities. The presence of knots in the cord and abnormal coiling (“over” or “under” coiling) should be described within the macroscopic examination section if present; however, the significance of these findings is controversial and requires close clinical correlation with the history and any other pathological features.

“Trimmed weight” refers to the weight of the placenta disc following the removal of the cord and free membranes. There are abundant reference charts for the expected trimmed weights of placenta specimens from singleton and twin pregnancies by gestation. Data regarding placental trimmed weight from the first trimester are generally less reliable, due to the fragmented nature of placental specimens retrieved at early gestations and uncertainty regarding the intrauterine interval in cases of intrauterine death. Fetal weight can be assessed in relation to the trimmed weight of the placenta (the “feto-placental ratio”). Abnormal feto-placental ratio has been reported in association with poor pregnancy outcomes but the overall value of placental weight measurement remains uncertain.

At gross examination, the placenta is serially cut for examination and postage stamp-sized pieces of placental parenchyma (extending from the fetal membranes to the maternal surface) along with samples of the cord and membranes are dissected and submitted for histological processing (progressive dehydration of the tissue followed by infiltration with paraffin wax under heat and pressure). Slides can then be prepared from the formalin fixed paraffin embedded (FFPE) tissue. This process (including subsequent slide production) takes approximately 12 hours after macroscopic examination, though the necessity of batch processing usually means that non-urgent specimens take up to 24 hours for slides to be created following macroscopic examination.

In the example provided (Figure 2), the trimmed weight is low for the stated gestation (10th centile; 214 g is 50th centile at 28 weeks).

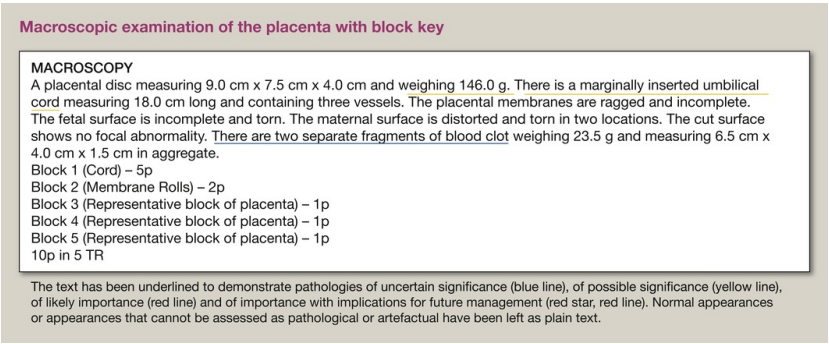

Figure 2

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Of note, two additional separate blood clots are reported to be present along with the placenta; these could potentially represent artefact related to delivery (it is essentially impossible for the pathologist to comment on the significance of separate clots in isolation). The description of the maternal surface (“torn”, “distorted”) and fetal membranes (“ragged and incomplete”) raises the possibility of retained placental fragments.

The structure of a placental pathology report: microscopic examination

The reporting pathologist will review the clinical details and macroscopic appearances in association with examination of the slides. The pathologist will then systematically examine the tissue present on the slides, prior to requesting any additional work needed including deeper levels within the wax block, tinctorial stains to highlight infectious organisms (e.g. Gram, Grocott silver, Ziehl-Neelsen), ferric iron/haemosiderin (Perls) or immunohistochemistry (e.g. CD3 to highlight T-cell aggregates within villi in VUE or some infectious agents (e.g. CMV, toxoplasma).

Similar to the structure of macroscopic examination, the pathologist will typically comment on the appearances of the fetal membranes, cord, chorionic plate vessels, placental parenchyma and maternal decidua. Table 2 shows some potential abnormalities identified on microscopy and their significance.

Table 2 Possible microscopic abnormalities at placental examination with associated pathology

alt-text: Table 2

Microscopic abnormality	Related pathology
Neutrophil infiltration of membranes	Ascending maternal genital tract infection
Haemosiderin within the membranes	Previous premature placental separation/marginal haemorrhage
Umbilical vein phlebitis/vasculitis/funisitis	Ascending maternal genital tract infection with fetal inflammatory response
Thrombi within chorionic plate vessels/avascular villi	Fetal vascular occlusion
Frequent immature villi after 34 gw	Delayed villous maturation
Abundant knots with over-mature villi	Accelerated villous maturation/maternovascular malperfusion
Lymphocytes within villi with villous damage	Villitis of unknown aetiology
Macrophages within maternal space with agglutination of villi	Chronic histiocytic intervillositis
Low density villi with few, thin-calibre terminal villi (over 34 weeks)	Distal villous hypoplasia/maternovascular malperfusion
Plasma cells within the maternal decidua	Chronic deciduitis
Atherosis of maternal spiral arterioles	Maternal vascular malperfusion/vasculopathy
Sickled maternal erythrocytes	Possible maternal sickle cell trait
Over-abundance of nucleated fetal erythrocytes in late second to third trimester	Possible fetal hypoxia

In the example provided, the microscopy is structured into sections, reporting on the cord, followed by the extraplacental membranes, chorionic plate, and lastly the placental parenchyma with decidua.

The reporting pathologist describes three-vessel funisitis without inflammation of the extraplacental membranes examined microscopically (however, these were disrupted and incomplete in the macroscopic examination). The chorionic plate shows acute inflammation. In combination with the funisitis, the description is of ascending maternal genital tract infection with a fetal inflammatory response (Figure 3).

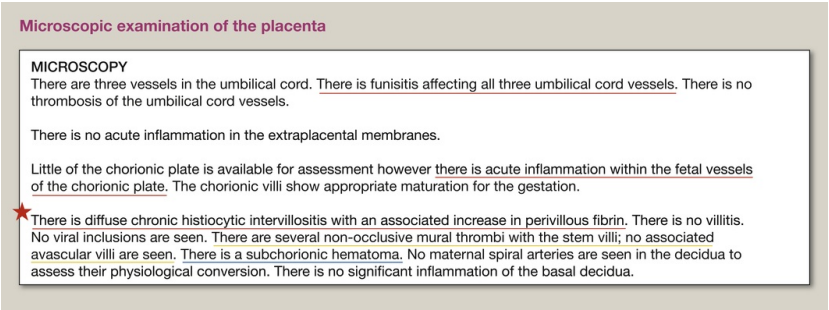

Figure 3

alt-text: Figure 3

In addition to the presence of acute inflammation, there is co-morbid chronic histiocytic intervillositis (CHI) within the description of the parenchyma. This represents a significant abnormality with a high recurrence rate that has implications for counselling regarding future pregnancies.

The structure of a placental pathology report: comment and conclusion

Most clinicians will be familiar with the conclusion section of a histopathology report. The presence of a “comment” section should flag to the reader that the case is particularly interesting, challenging, or has implications for clinical management, and should prompt the reader to look at the whole report carefully. The comment section is, in general, used by a pathologist to highlight important findings or to express varying degrees of confidence about the subjective importance of an objective finding. In this case, the pathologist describes the perceived importance of the abnormalities present (Figure 4).

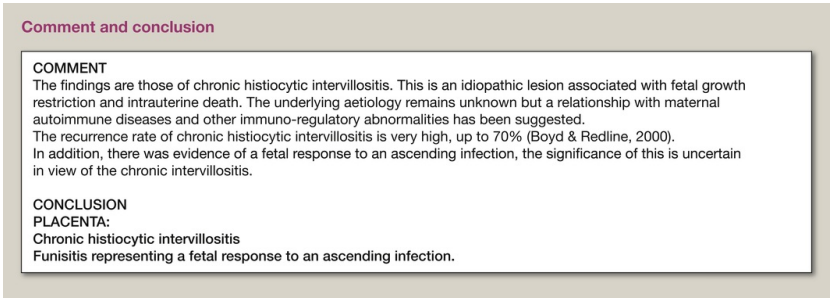

Figure 4

alt-text: Figure 4

Placenta reports: integrating findings and counselling

The placental histopathology report represents a long-exposure snapshot of one third of the maternal-fetal-placental unit. As such, it is essential that the appearances are interpreted in the light of the clinical context of the mother and infant. For example, villitis of unknown aetiology (VUE) may be identified in 5–10% of placentas from normal deliveries with health babies and healthy mothers. In this clinical context, the VUE present in the placenta is almost certainly incidental, and although the risk of recurrence in future pregnancies is probably higher than that of the background population, the risk of pathology in future pregnancies is unknown. However, in a case with maternal hypertension, diabetes, and intra-uterine growth restriction, VUE found within the disc is more likely (but still not certain) to represent a pathological correlate of the clinical presentation. Similarly, in a term stillbirth with minor sub-chorionitis and no additional pathological or clinical evidence of fetal or maternal inflammation, the sub-chorionitis is unlikely to represent the cause of intra-uterine demise but rather be a secondary or incidental event. In contrast, some entities are always pathological; for example, chronic histiocytic intervillositis (CHI)(This abbreviation has been defined in the paragraph above and can be removed.), or placental mesenchymal dysplasia. All such cases should be discussed with a fetal medicine specialist to optimise future management.

In some senses, counselling of mothers following a placental pathology report is more difficult than counselling following a post-mortem report, as there is more room for subjective interpretation and unconscious bias when faced with a ‘possible’ cause of pathology from analysis based on one-third of the picture. Consideration of the clinico-pathological presentation will help to prevent over diagnosis and further potential over-investigation of the mother and/or baby for pathology.

The structure of a post-mortem report

The structure of a post-mortem report: clinical details & supporting information

In general, the types of post-mortem performed by pathologists can be divided by clinical presentation as follows:

1. Intrauterine fetal death (IUFD):
2. Termination of pregnancy (ToP):
3. Peripartum stillbirth/Intrapartum stillbirth
4. Neonatal death
5. Deaths in infancy, including sudden unexpected death in infancy (SUDI)

6. Deaths in childhood, including sudden unexpected death in childhood (SUDC)

Many neonatal deaths, infant deaths and childhood deaths are medicolegal in nature being mandated by the Coroner in the jurisdiction where death occurred, and are beyond the scope of this article.

Investigation of the remaining categories of perinatal deaths usually involves a search for placental, fetal or maternal factors that could be involved in the death, with the aim of providing a unifying diagnosis. In ToP cases, autopsy may confirm the antenatally diagnosed anomalies, acts as a potential source of tissue for further genetic studies, and may identify additional features (either from gross anatomical findings or on microscopy) that point towards an overarching diagnosis or syndrome. Reports are often presented in a similar fashion to surgical reports (please see full report), with demographic details and details of the performing centre. If the mother has given the baby with a name, it may be used within the report demographics, or mentioned within the comment section. The title section usually confirms the type of examination performed (in this case, a limited autopsy with micro-CT imaging), along with the summary of major pathological findings (Figure 5).

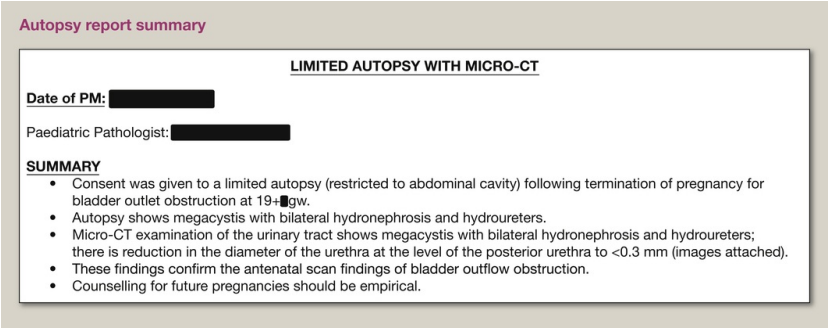

Figure 5

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Of note in this case, the pathologist provides a comment explaining the major findings, including the source and anatomical level of obstruction. These match the antenatal findings, with no further action recommended regarding additional genetic investigations. A comment section is then provided, which explores the findings and aetiologies in more detail. This may be useful for parents in understanding how the anomalies arose in utero, in this case (Figure 6).

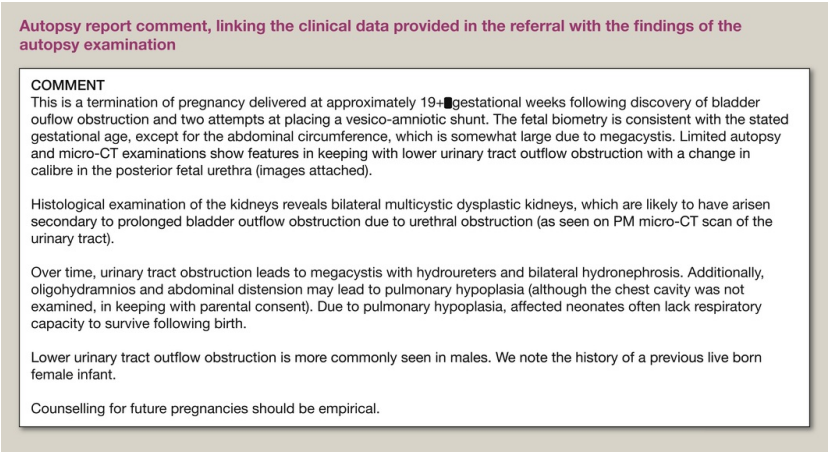

Figure 6

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Providing the summary of major findings and comment enables an accessible summary without the need to wade through detailed anatomical descriptions, which may be upsetting for relatives. There follows a summary of the clinical history as provided by the referring team. This is not intended to be exhaustive and is reliant on the quality of the referral and accompanying information provided. Copies of antenatal scan results are extremely useful for ToP cases and many pathologists will refuse to proceed with an autopsy without reviewing them.

Following the clinical history, a brief summary of the consent details of the case are documented within the report (see full report). This directly reflects the option chosen on the consent form by the parents, along with any limitations to the consent provided. In this case, consent is provided for a limited autopsy of the abdomen only, but with additional consent for teaching, research, retention of genetic material and audit. In this case, micro-CT was performed as part of direct clinical care with parental consent in order to visualise the level of the urinary tract obstruction.

The structure of a post-mortem report: external examination

External examination findings are then described, including a detailed examination of the body for evidence of dysmorphic features, malformations, or evidence of disease. If medical devices are present, these are described and their location documented. In children who have lived for a period prior to death, marks of resuscitation and injuries are noted. In this example, there is mild abdominal distension but no other external anomalies are noted.

A brief table of potential abnormalities discovered at external examination and related pathologies is provided in Table 3.

Table 3 Possible external abnormalities at autopsy examination with associated pathology

alt-text: Table 3

Macroscopic abnormality (external examination)	Possible related pathology
Abnormal head shape	Craniosynostosis
Encephalocoele	Meckle (Typo identified, this should be "Meckel Gruber syndrome")Gruber syndrome, neural tube defect
Cryptophthalmos	Fraser syndrome
Hypertelorism	Noonan syndrome, Opitz G syndrome
Broad nasal bridge, low set ears, hypertelorism	Potter sequence
Cystic hygroma	Monosomy X, Trisomy 21, Noonan syndrome
Polydactyly	Ciliopathy, skeletal dysplasia, Trisomy 13
Absent thumb	VACTERL association, Fanconi anaemia, Thombocytopaenia-absent radius syndrome
Chest and abdominal wall defects, externalisation of the heart	Pentalogy of Cantrell
Anal atresia	VACTERL, caudal regression syndrome
Lower limb abnormalities	Skeletal dysplasia, fibular aplasia spectrum
Ambiguous genitalia	Denys-Drash syndrome, Lissencephaly

In addition, linear measurements and body weight at the time of post-mortem are provided and assessed with regards to the normal reference tables for the gestational age of the fetus. This may help to identify cases of intrauterine growth restriction or syndromic disorders, however, measurements taken at post-mortem are greatly affected by the degree of maceration of the fetus; care must be taken to distinguish post-mortem artefacts from true pathology.

The structure of a post-mortem report: post-mortem radiology

Most centres perform routine plain radiography on cases of IUFD and ToP, however, there is little additional diagnostic yield in doing so where a clinical abnormality is not suspected. While a full review of post-mortem radiology is beyond the scope of this article, a range of additonal post-mortem imaging techniques may be used from 8 weeks gestation (micro-CT) to full term (mostly MRI or ultrasound, CT in some circumstances). The imaging report is then integrated into the pathology report.

Discrepancies are usually commented on within the report and the cause of death (and responsibility for the overall report) remains that of the reporting pathologist. Some pathology specialties have begun to develop guidelines for further integration of post-mortem imaging into autopsy practice. In the example provided, the plain X-ray shows no abnormalities. Micro-CT was performed on the extracted block containing renal tract and bladder, which confirmed the anatomy of the obstruction along with obstructive type cystic changes present in the kidneys.

The structure of a post-mortem report: internal examination

The internal examination section describes the findings of the pathologist's systematic examination of internal anatomy following dissection. Table 4 demonstrates some examples of the types of pathology that may be found in each body system. In addition, the weights of the internal organs are recorded.

Table 4 Possible internal abnormalities at autopsy examination with associated pathology

alt-text: Table 4

Body system	Examples of possible internal abnormalities
CNS (brain, spinal cord)	Neural tube defect, abnormal gyration, ventriculomegaly, intracranial haemorrhage, calcifications, absent corpus callosum, posterior fossa cyst, vermian hypoplasia
CVS (Heart, great vessels, peripheral vascular system)	Abnormal segmental anatomy (atria, ventricular or outflow tract level), abnormal coronary artery anatomy, cardiomyopathy, single umbilical artery, infarction
Respiratory (upper and lower respiratory tract, lungs)	Atresia, fistula, pulmonary hypoplasia, diaphragmatic hernia, anatomical isomerism, pleural effusion
GI	Atresia, malrotation, perforation, volvulus, abnormal connection, ascites, biliary atresia
GU	Cystic renal dysplasia, Renal agenesis/dysgenesis, duplex ureter, megacystis, cloacal anomaly
LR	Splenomegaly, lymphadenopathy, cystic hygroma, thymic hypoplasia/aplasia, anatomical abnormality
Endocrine	Abnormal anatomy (e.g. annular pancreas), atresia, pituitary/adrenal haemorrhage
MSK	Abnormal skeletal or muscle formation, abnormal muscle bulk, fixed flexion deformity

In the context of IUFD, ToP and stillbirth, the diagnostic yield of routine histology of macroscopically normal organs is low, with placental examination being the most important histological component. However, in some clinical circumstances (e.g. intrapartum stillbirth or complex series of fetal anomalies), histology of macroscopically normal organs may be of use in identifying factors contributing to death or refining the diagnosis (Table 5). In this case, histology taken from the kidneys and bladder showed changes related to obstruction, with no histological evidence of heritable cystic renal disease. In addition, no ductal plate malformation was identified within the liver. These findings are reassuring with regards to future genetic counselling, with most cases of bladder outflow obstruction occurring sporadically in male fetuses. Joint pathology-radiology review of the micro-CT images in this case identified the presence of posterior urethral valves distal to the prostatic urethra.

Table 5 Possible microscopic abnormalities at autopsy examination with associated pathology

alt-text: Table 5

Body system	Examples of possible histological abnormalities[a]
CNS (brain, spinal cord)	Neuronal migration defect, periventricular leukomalacia, detato-olivary dysplasia, hippocampal sclerosis, hypoxic ischaemic encephalopathy, inflammation, haemorrhage
CVS (Heart, great vessels, peripheral vascular system)	Myocarditis, abnormal accumulation of material (e.g. glycogen), giant mitochondria, fibrosis, cardiomyopathy
Respiratory (upper and lower respiratory tract, lungs)	Fetal pneumonia, alveolar capillary dysplasia ± misalignment of pulmonary veins, bronchial atresia, cystic malformations, lung growth defects, immaturity, interstitial lung disease
GI	Aganglionosis, extra muscle layers, ischaemia, neutrophils within the lumen
GU	Cystic renal disease (including subtype), haemorrhage, glomerular developmental anomalies, nephronophthisis, nephrogenic rests

LR	Lymphoproliferative disorder, abnormal accumulation of material (e.g. glycogen)
Endocrine	Polyendocrinopathy, adrenal fat accumulation
MSK	Abnormal mineralisation, abnormal ossification; inflammation, fibrosis or atrophy of muscle

[a] Haemorrhage, infarction, thrombosis, or viral cytopathic changes may be seen in any system.

Lastly, a section within the report summarises tissue stored or retained (where appropriate consent is present) for further ancilliary studies, including frozen tissue, retained organs, genetic studies, microbiology, virology and biochemistry.

Post-mortem pathology reports: integration of findings

Post-mortem reports effectively represent external review and integration of the clinical documentation and phenotyping of the fetus and placenta at a macroscopic and microscopic level. Ancillary investigations such as genetic studies (which add a futher layer of depth to the analysis) may not be known to the pathologist at the time of issuing the post-mortem report. Once all outstanding investigations have been collated and acknowledged, the clinician should have an overview of the clinical presentation (clinical remit), phenotype of the body and placenta, with review of the notes (histopathology remit) and genetic phenotype (usually molecular or cytogenetics remit, or both). If there is a suspicion of heritable disease from any of the separate strands of investigation, this should be highlighted within the respective report and the case should be further discussed at a regional fetal dysmorphology and genetics meeting to guide further management in difficult or unusual cases. Where a cause of death is not apparent and no abnormalities are identified (a “negative autopsy”), counselling for future pregnancies will be empirical, based on the clinical presentation and history. When in doubt, most paediatric and perinatal pathologists will be happy to discuss the findings of one of their cases in order to clarify issues within the report. Unfortunately, a majority of IUFD cases remain unexplained despite full autopsy examination. In these cases, the mechanism of death is presumed to be placental dysfunction that fails to manifest on examination by light microscopy. As proteomic and molecular investigations improve and exapnd (Typo identified, the correct wording is "expand")to include formalin fixed tissue, research may help to shed light on the pathogenic mechanisms involved.

Practice points

- Pathologist interpretation of the clinical significance of objective findings in both placental and post-mortem reports is reliant on both objective findings and adequate clinical information
- Histology of the placenta is the most important investigation in IUFD, providing a cause of death in approximately 20–25 % of cases
- Some placental pathologies have high recurrence rates (CHI, high-grade VUE); others may be incidental
- Counselling for future pregnancies following post-mortem examination should take into account clinical presentation, pathological phenotype, and any genetic or other ancillary findings

Queries and Answers

Query: Please check the hierarchy of the section headings.
Answer: Checked, these appear correct, thank you.

Query: Correctly acknowledging the primary funders and grant IDs of your research is important to ensure compliance with funder policies. We could not find any acknowledgement of funding sources in your text. Is this correct?
Answer: This is correct, I have double-checked this with Prof. Sebire.

Query: Please confirm that given names and surnames have been identified correctly and are presented in the desired order and please carefully verify the spelling of all authors’ names.
Answer: These are both correct in spelling and layout. I would be grateful if you could indicate that Neil Sebire is the corresponding author.