Choriodecidual Haemosiderin Staining

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41.1 Introduction

The amniochorial membranes are normally translucent. Opacity or duskiness of the membranes is usually due to acute chorioamnionitis (Chap. 44), prolonged retention of stillbirth or prolonged rupture of the membranes. Discoloration due to the presence of pigment-laden macrophages in the amniochorial membranes can sometimes be evident grossly and is usually due to meconium (Chap. 40) or iron uptake by macrophages in the amniochorion. Haemosiderin is a breakdown product of red blood cells.

41.2 Definitions

Choriodecidual haemosiderin staining is defined as the presence of iron, preferably confirmed by using histochemical stains, in the amniochorial membranes or the chorionic plate.

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41.3 Synonyms

Iron pigment staining in the membranes and in the chorionic plate has been termed diffuse chorioamnionic haemosiderosis [1]. The objection to this term is that "diffuse" is not clearly defined and haemosiderosis by iron staining can be seen in about half of placentas examined [2] and thus may be normal (see below) [2, 3]. The presence of iron in the basal plate or placental membranes has been referred to as decidual haemosiderosis [4], albeit the basal place contains also the extravillous trophoblast.

41.4 Epidemiology

Some degree of iron pigment staining is seen in approximately 50% of placentas when unselected placentas were stained with an iron stain [2]. Previous studies with lower prevalences, 2.2% [1] and 4.2% [5], either excluded cases with history of meconium staining or histological finding suggestive of meconium [1] or performed iron stains following light microscopic determination of pigment in the membranes and chorionic plate [5]. Decidual haemosiderosis was seen in 43% of placentas <32 weeks gestation but only in 0.8% of term placentas [4]. Choriodecidual haemosiderosis (defined on haematoxylin- and eosin-stained slides without routine iron histochemistry stain)

T. Y. Khong et al. (eds.), *Pathology of the Placenta*, https://doi.org/10.1007/978-3-319-97214-5_41

was seen in 5% of 3382 non-selected placentas from high-risk pregnancies [6]. Haemosiderosis in the amniochorial membranes, chorionic plate and/or basal plate is seen in approximately 50% of delivered placentas if they are stained for iron. There are no specific associations in low-risk cohorts [2].

However, placentas submitted to pathology for clinical indications do have specific associations in cases diagnosed with *diffuse chorioamnionic haemosiderosis*. Diffuse chorioamnionic haemosiderosis is an objective marker of chronic peripheral placental separation, clinically called the chronic abruption-oligohydramnios sequence. This finding is associated with circumvallate placentas, old peripheral clots, increased chorionic villous macrophages and green discolouration [1]. It also clusters with clinical and histological features of placental abruption [6]. It is not more common in chronic hypertension (4.7% vs 5.0%) and it is unclear whether preeclampsia affects this frequency [7, 8].

Diffuse haemosiderosis is more common with membrane laminar necrosis (8%), chorionic microcysts [9] and cord compromise [10]. Finally, diffuse haemosiderin deposits in the chorionic plate have been described in association with massive subchorial haematoma [11].

41.5 Gross Findings

A greenish-brown or "rusty" discolouration of the membranes may be seen, but it is essentially a microscopic diagnosis.

41.6 Histopathology and Special Stains

The differential diagnosis of pigment staining in the membranes can be due to haemosiderin deposition or meconium uptake by macrophages. Haemosiderin staining can be suspected by refractibility on haematoxylin and eosin staining [3] and confirmed by using an iron stain, such as Perls' Prussian blue, Gomori or Berlin blue.

Placentas are not usually routinely stained for iron. On haematoxylin and eosin staining, haemosiderin deposition is indistinguishable from deposition elsewhere in the body (Fig. 41.1). The iron deposition may be seen on histochemistry staining as a clustered stippling of dots, as a ring around nuclei or as a dark irregular spot (Fig. 41.2a–c). The staining is usually seen in the chorion laeve layer alone or in both the chorion and decidual layers. The cells in Fig. 41.2b resemble chorion laeve cytotrophoblast.

Based on histochemistry staining for iron, the extent of haemosiderin deposition is classi-

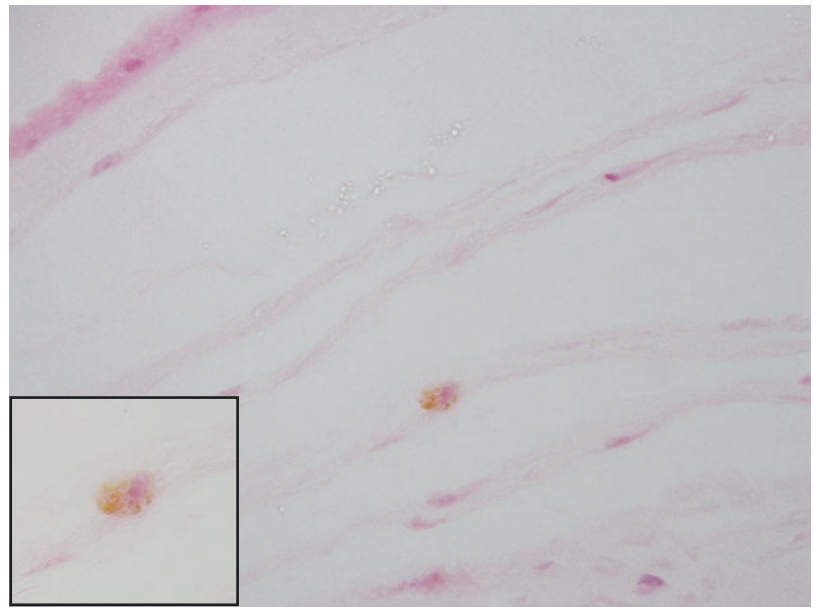

Fig. 41.1 Haemosiderin deposition in the amnion mesenchyme of the amniochorial membranes showing golden-brown granules phagocytosed by macrophage. (Haematoxylin and eosin-staining)

fied as diffuse when haemosiderin deposition is seen in five or more adjacent high-power fields (HPF × 20 objective lens) or as localised when present in fewer than five HPF. The density is defined as high when there are ten or more haemosiderin-laden cells or as low when there are fewer than ten haemosiderin-laden cells in one HPF (×20 objective lens). The haemosiderin deposition can be graded as mild, moderate or severe, based on the extent and density of haemosiderin deposition: sections with a localised and low density are graded as mild; sections with diffuse and high density are graded as severe and the rest as moderate (Fig. 41.3a–c) [2].

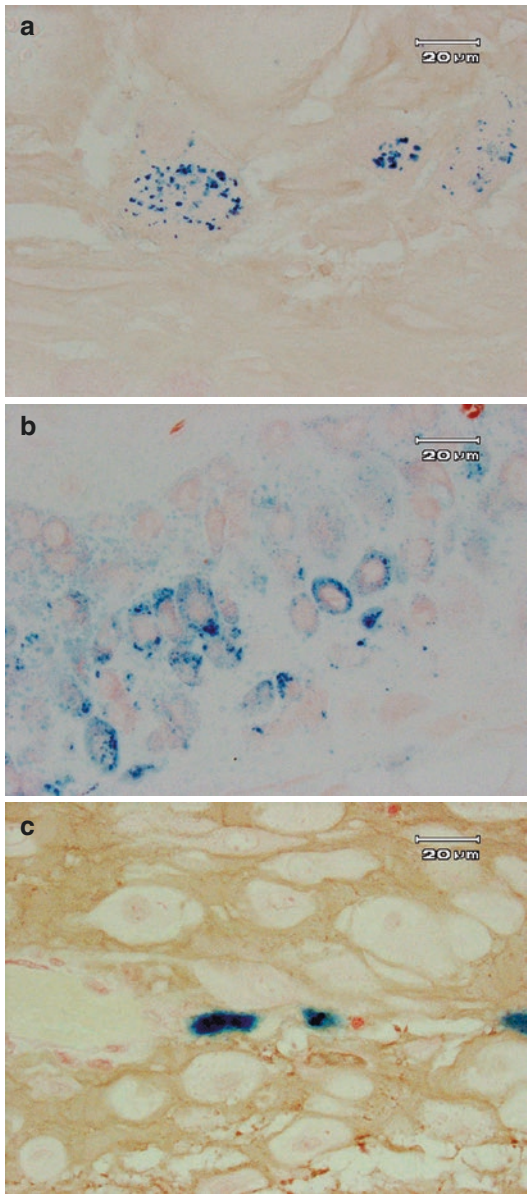

Fig. 41.2 Different patterns of iron deposition in the amniochorial membranes: (**a**) clustered stippling of dots, (**b**) perinuclear ring and (**c**) dark irregular spot (Perls' Prussian blue stain) (with permission from Pathology 2010;42:119–124)

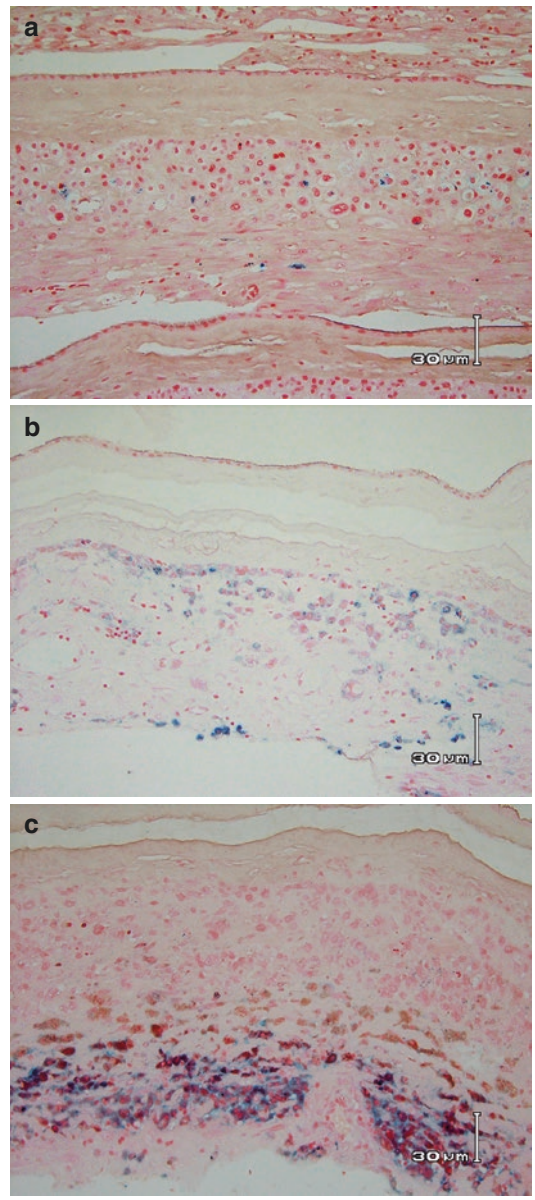

Fig. 41.3 Amniochorial membranes showing haemosiderin deposition graded as (**a**) mild, (**b**) moderate and (**c**) severe. (Perls' Prussian blue stain) (with permission from Pathology 2010;42:119–124)

Haemosiderin deposition can be observed not only in the extraplacental membranes but also in the chorionic plate and basal plate. Placental haemosiderosis is a wider term than choriodecidual haemosiderosis as iron deposition can be revealed in mineralization of basement membranes of chorionic villi or haemosiderin granules in the villi. Both can be diffuse as in retained stillbirth [12], aneuploid pregnancies, placental oedema or infections or lobular as in fetal vascular malperfusion (Chaps. 19, 21, 24) [3].

41.7 Prognosis and Predictive Factors

None known at present.

41.8 Further Studies

Choriodecidual haemosiderin staining, as defined, did not differentiate in which cells the iron staining was found. Transferrin receptors, which are needed to internalise iron into a cell, are expressed in macrophages [13] but not in chorion laeve cytotrophoblast [14]. Neutrophil gelatinase-associated lipocalin can bind and transport iron and has been localised to chorion laeve cytotrophoblast [15]. Studies on the role of iron transport proteins and homeostasis at the local level in the chorion laeve cytotrophoblast and macrophages in normal and abnormal pregnancy may reveal the clinical significance of choriodecidual haemosiderosis. Furthermore, the clinical significance of various stages and grades of choriodecidual haemosiderosis needs to be determined.

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