Amnion Nodosum and Congenital Ichthyosis

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Garcia, Aparecida G. P., Consorte, Sônia Maria, Lana, Ana Maria Arruda, and Friede, Roldão: Amnion nodosum and congenital ichthyosis. Am J Clin Pathol 67: 567–572, 1977. Histologic characteristics of the placentas in four cases of amnion nodosum and congenital ichthyosis, a rare association, are presented. Two cases were missed abortions of a single multiparous woman, supporting the hypothesis that in congenital ichthyosis amnion and skin share an abnormal genetic trait. As the amnion showed no hyperkeratosis, it is likely that the amniotic lesions are related to an increased deposition of keratotic plugs on the amnion. Oligohydramnios was verified in two cases; urinary tract malformations were absent in all. The histologic characteristics of the placentas were similar. Noteworthy was the aspect of the chorionic vessels, whose lumens were reduced or obliterated. Perhaps this feature contributed to the poor nutrition of the amnion, a fact assumed by some authors to explain lesions of amnion nodosum. As these vascular alterations are common after fetal death, it is only in the placenta of the newborn that the vascular changes, compatible with rubella vasculitis, may have altered the nutrition of the amnion. (Key words: Amnion nodosum; Ichthyosis; Placenta.)

THE ASSOCIATION of amnion nodosum and congenital ichthyosis is rare.[2] The purpose of this paper is to describe the histologic characteristics of the placentas in four cases of congenital ichthyosis: amnion nodosum was present in all.

Methods

The tissues in this study were obtained from the Pathology Service of the Institute Fernandes Figueira. The material was fixed in 10% formalin and embedded in paraffin. The slides were stained with hematoxylin–eosin. Selected tissues were stained with phosphotungstic acid–hematoxylin, periodic acid–Schiff (PAS), Gomori's one-step trichrome, and Alcian blue.

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Report of Four Cases

Case 1. The fetus was the product of a missed abortion of a 33-year-old diabetic multiparous woman (five children, three alive and well, two dead in the second month of life, unknown cause). Actual pregnancy had lasted 22 weeks, with slight vaginal bleeding. The ovum, weighing 125 g, was eliminated *in toto*. Scarce yellow-tan material flowed out when the cavity was opened. A severely macerated fetus (13 cm crown–heel, 6 cm crown–rump) was found. Despite autolysis, somatic characteristics of ichthyosis were identified. No internal malformation was detected; the urinary tract was normal. The insertion of the cord was marginal and the membranes had extensive lesions of the amnion in the form of flat plaques on the fetal surface of the disk and on the free membranes (Fig. 1).

Case 2. The mother later had two normal children and, six years after the first abortion, a 20-week-pregnancy ended in a missed abortion,with the fetus manifesting more severe cutaneous lesions, easily recognized as congenital ichthyosis (Fig. 2); no other malformation was present. The placenta, which weighed 35 g, was fragmented by curettage. The extraplacental amnion contained numerous nodules, varying in size from slightly visible to several millimeters in diameter. They were rounded, protuberant, shiny or dull, gray-yellowish or reddish, equally distributed over the free membranes (Fig. 3).

Microscopic examination revealed similar lesions in both cases. The nodules appeared as eosinophilic amorphous or granular masses apposed to the amnion, although some of them were detached from the mem-

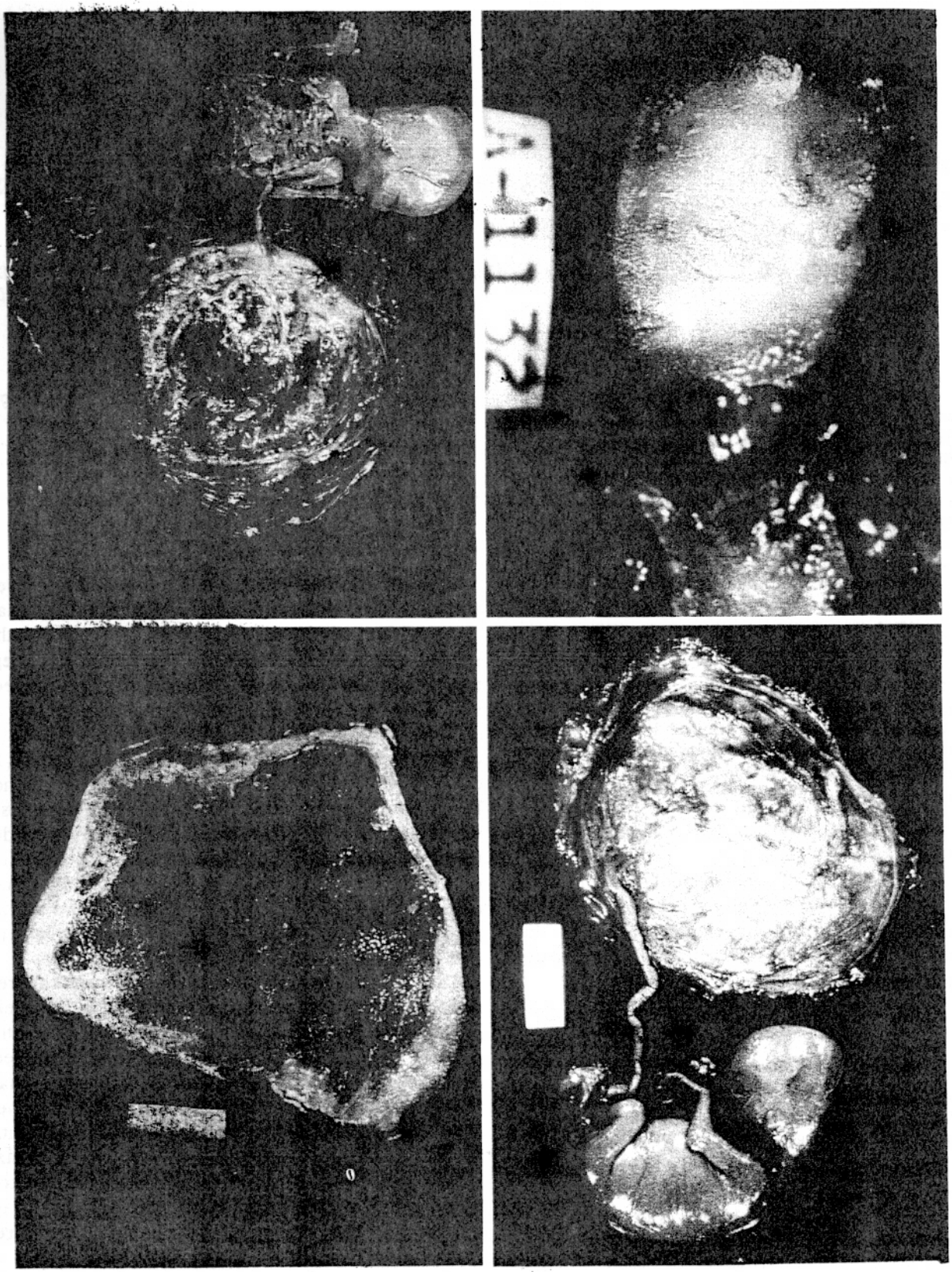

FIG. 1 (*upper, left*). Severely macerated fetus, showing the characteristics of ichthyosis on the face and hands. Note the presence of flat plaques on the free membranes (Case 1).

FIG. 2 (*upper, right*). Missed abortion with typical facies of congenital ichthyosis. (Case 2).

FIG. 3 (*lower, left*). Extraplacental amnion, showing numerous rounded nodules of variable size.

FIG. 4 (*lower, right*). Missed abortion, showing the signs of ichthyosis on the face and hands. Numerous adherent nodules can be seen on the fetal surface of the placenta.

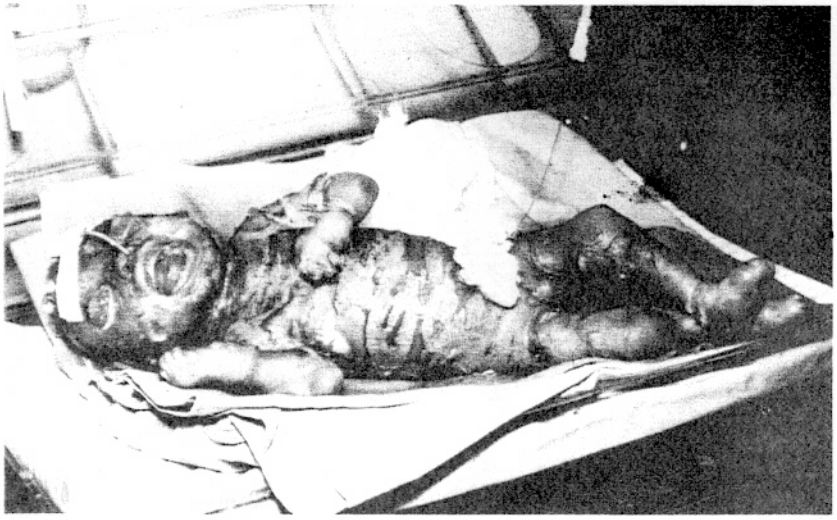

FIG. 5. The baby has dry, scaly skin typical of ichthyosis.

brane. Details could not be seen, due to the extent of autolysis of the tissues, but in some of them a thin layer of flatter cells was also observed to be covering most of the free surface of the nodules. The chorionic vessels were partially or completely obliterated, rarely thrombosed. The villi were avascular and fibrous, encased in a thick layer of fibrinoid material. In Case 2, the extraplacental amnion showed numerous rounded or oval masses containing barely visible squamous cells, presumably from the amniotic fluid, within a collagenous matrix. The masses were located on the amnion surface or embedded in its mesoderm. There was no amniotic epithelium on most of the nodules; in contrast, some of them appeared completely surrounded by the amniotic epithelium Figs. 6 and 7. These probably represented cross sections of pedunculated lesions. The interamniochorial space was not visible over wide areas. Degenerative nonspecific lesions of the local cells and areas of necrosis were observed in the decidua. Both umbilical cords contained three vessels.

Case 3. The fetus was from a missed abortion, product of a 25-week-pregnancy of a 27-years-old primiparous woman. Fever and disseminated pruriginous spots had occurred in the second month of pregnancy, followed by slight vaginal bleeding. The ovum was eliminated whole and had a gray-yellowish surface; when opened, a few drops of grumous grayish fluid flowed. The membranes were opalescent; on the fetal surface of the placenta numerous adherent reddish nodules were seen. The cord was thick and had only two vessels. The placenta weighed 22 g and the fetus, 20 g. Despite autolysis, features suggestive of congenital ichthyosis were observed (Fig. 4), and no other malformation was seen. Histologic examination of the placenta showed features identical to those in Cases 1 and 2. It is worthy of note that the second umbilical artery was actually hypoplastic.

Case 4. The mother, a 25-year-old woman, gravida 4, delivered in her thirty-ninth week of pregnancy. The prenatal course had been uneventful. The amniotic sac was ruptured artificially, flowing out fluid with grumous material; there is no reference to oligohydramnios. The mother stated that there had been "skin malformations" in her two previous stillborn infants and that the third gestation had ended in a normal child, alive and well. The parents are third cousins. The newborn lived 12 days. The urethral meatus was visible and the newborn urinated normally after birth. At autopsy, the baby had the dry scaly skin characteristics of ichthyosis; the whole cutaneous surface appeared as a deeply fissured horny cuirass (Fig. 5). Beside this lesion, the postmortem examination revealed septicemia accompanied by intravascular coagulation, as well as visceral, vascular, and placental lesions attributed to fetal rubella. There was no internal malformation; the urinary tract was normal; the ureters had normal caliber and walls of normal thickness, as did the urinary bladder, whose mucosa was edematous with petechial hemorrhages. The left renal artery was duplicated. The placenta weighed 340 g, measuring $22 \times 18 \times 2$ cm. It had numerous plaques covering the placental amnion and the membranes were remarkably thick. Microscopic examination showed a very thick amnion deprived of epithelium over extensive areas and diffusely infiltrated by pigmented macrophages. The nodules appeared to be composed of amorphous necrotic material intermingled with cellular debris and squames (Figs. 8 and 9). They invaded the amniotic mesoderm, and the epithelium adjacent to the nodules showed degenerative lesions; calcium deposits were also seen, but fragments of hair were not present. The chorion was thick

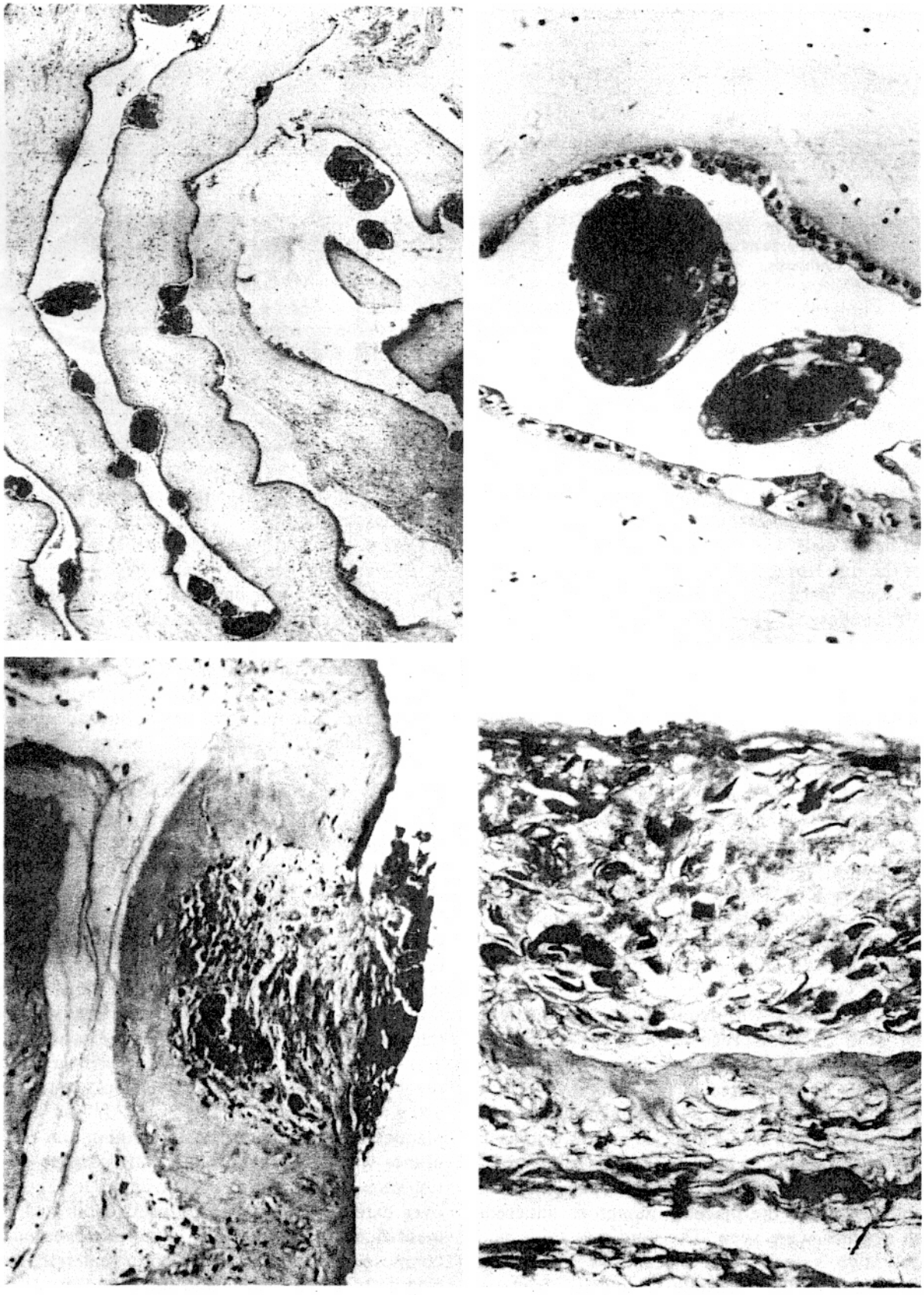

FIG. 6 (*upper, left*). (Case 2) Extraplacental amnion, showing numerous nodules on the surface or embedded in the mesoderm. Hematoxylin and eosin. ×44.

FIG. 7 (*upper, right*). Nodules entirely covered by amniotic epithelium in the plane of the section. Hematoxylin and eosin. ×125.

FIG. 8 (*lower, left*). Nodule in the amniotic mesoderm composed of amorphous material intermingled with cellular debris. Hematoxylin and eosin. ×125.

FIG. 9 (*lower, right*). Squames embedded in hyaline ground substance. Phosphotungstic acid–hematoxylin. ×560.

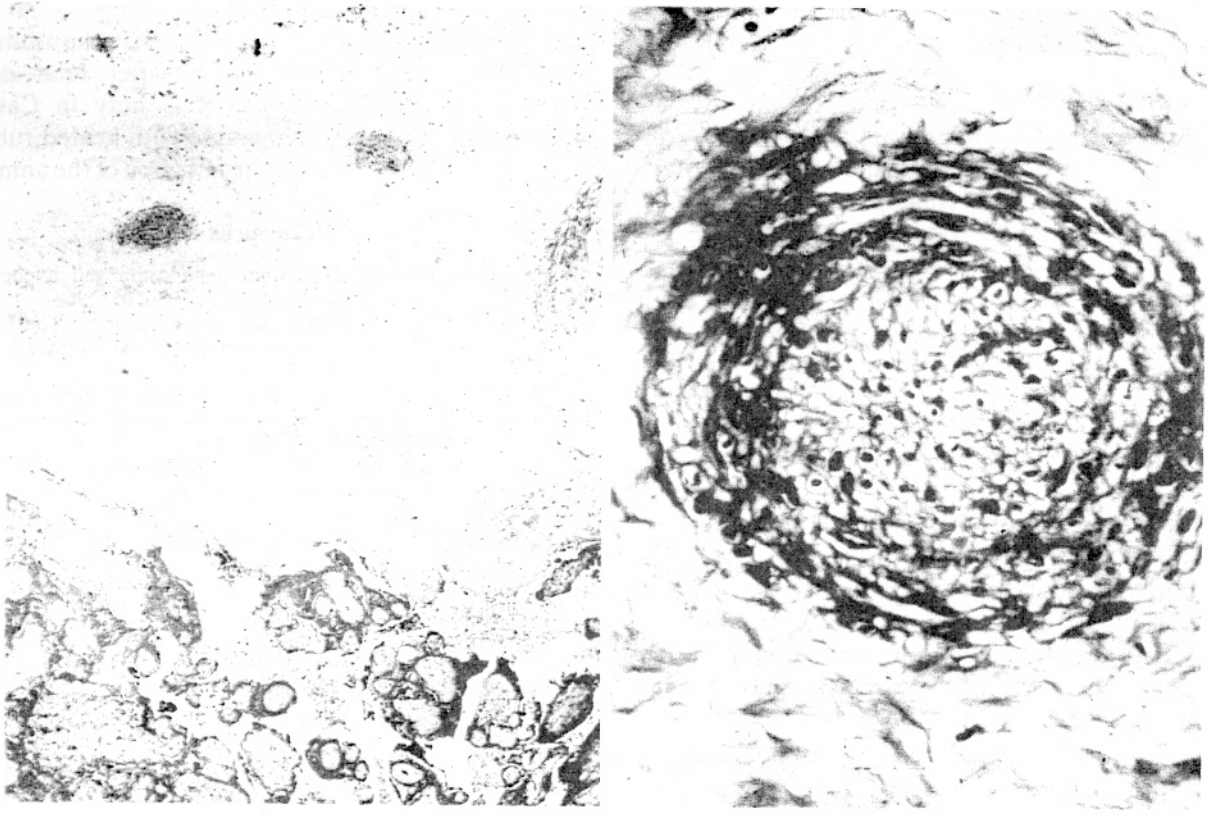

FIG. 10 (*left*). Chorionic vessels, showing reduced or obliterated lumens and an abnormal structure of the walls. Hematoxylin and eosin. ×44.

FIG. 11 (*right*). Chorionic vessel. The structure is more visible with the special staining. Phosphotungstic acid–hematoxylin. ×560.

and contained a diffuse mononuclear infiltrate. The vessels of the chorion had a reduced or completely obliterated lumen (Figs. 10 and 11), rarely with thrombosis. The villi showed scarce vascularization and increased cellularity, mainly due to an increase in number of Hofbauer cells and mononuclear infiltrates. In the decidual cells, besides the nonspecific degenerative lesions, inclusions, attributed to the rubella virus, were identified.

Sections of the skin showed hyperkeratosis, parakeratosis, keratotic plugs, irregular acanthosis, and papillomatosis. The granular layer could be seen in some places and was absent in others. Groups of vacuolated cells were observed in the upper Malpighian layer. In the dermis there was only edema and dilatation of the blood vessels.

Comment

Benirschke[2] mentions that it would be interesting to know whether amnion nodosum was associated with congenital ichthyosis, but states that he has not been able to study such specimens. He quotes other investigators who surveyed the literature regarding this possible association, referring only to a single case, while all other placentas of congenital ichthyosis described had normal membranes.[2] He believes that the abnormal genetic trait of the epidermis may be shared by the amnion in this condition. The simultaneous occurrence of ichthyosis and amnion nodosum in two successive missed abortions of one multiparous woman (Cases 1 and 2) supports this hypothesis. Since the amnion itself showed no evidence of hyperkeratosis, it is, however, just as likely that the abundance of amniotic nodules in ichthyosis is related to an increased deposition of keratotic masses on the amnion.

While amnion nodosum is more common at the end of gestation, it has also been described to occur in abortions.[7] As Bartman and Driscoll[1] noted, it is possible that the amniotic lesions seen in late pregnancy are not recent, but represent the final result of an abnormal process beginning earlier in development. Our observations give support to this hypothesis. Perhaps the ichthyosis, with increased cellular desquamation, may have precociously initiated the amniotic lesions. Presently, on the basis of ultrastructural observations, there is no doubt that the main component of the nodules is the epithelial cells,[5] confirming

the belief that the amniotic lesions originated from apposition of desquamated fetal skin elements on the amniotic epithelium.

Blanc[3] considers that the localization of the nodules on the extraplacental membranes is rare, but in Cases 1 and 2 they abounded on the free membranes and were fewer on the placental disk.

Oligohydramnios was verified in two cases (Cases 1 and 3). It is well known that there is a decrease in the amount of amniotic fluid in missed abortion, secondary to its reabsorption after retention of a dead fetus. Landing had already stressed[4] that amnion nodosum may occur in some cases of intrauterine deaths of normally formed fetuses when abortion is delayed for a sufficiently long period after the death of the fetus.

The histologic features of the placentas in all four cases were identical. Noteworthy was the aspect of the chorionic vessels, whose lumens were reduced or entirely obliterated, even in the liveborn baby (Case 4). Perhaps this feature contributed to the poor nutrition of the amnion, a condition assumed by some investigators to explain the initial lesions of amnion nodosum.[2–6] It should be stressed that the obliterative changes are normal events after fetal death (Cases 1, 2 and 3) and that it is only in Case 4 that vascular changes, compatible with healed rubella vasculitis, may have altered the nutrition of the amnion.

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