ORIGINAL ARTICLES

Eosinophilic/T-Cell Chorionic Vasculitis

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ABSTRACT

Chorionic vasculitis is the hallmark of a fetal response in chorioamnionitis. There are five highly characteristic findings: (1) leukocyte migration is not concentric but rather radiates toward the infected amniotic fluid; (2) the infiltrate is primarily neutrophils; (3) multiple chorionic vessels, first veins and then arteries, are usually involved; (4) the infiltrate never extends into the vasculature of stem villi; and (5) it is rare in the absence of chorioamnionitis (or its precursors). Here we describe a new form of chorionic vasculitis characterized by an infiltrate composed primarily of eosinophils and CD3+ T lymphocytes that very focally involves a single chorionic vessel (artery or vein), that radiates away from the amniotic fluid (i.e., toward the intervillous spaces), and that may extend into the stem villous vasculature; this lesion occurs in the absence of any evidence of chorioamnionitis. During the past 7+ years, using accepted placental review criteria, we have examined 7104 placentas and identified 14 cases of eosinophilic/T-cell chorionic vasculitis (or related lesions). Although the frequency of diagnosis in the placentas examined was 0.197%, its true incidence cannot be estimated because of its very focal nature and the limited nature of placental disk sampling. Its etiology and significance are unknown, but it may represent a focal immune-mediated vasculitis.

Key words: eosinophils, T lymphocytes, chorionic vasculitis, placenta, chorioamnionitis

INTRODUCTION

Chorioamnionitis (CA) is generally considered to be caused by (or the result of) an ascending infection characterized by an acute inflammatory infiltrate (i.e., neutrophils). The maternal inflammatory response to the presence of bacterial toxins in the amniotic fluid results in an initial margination of neutrophils in the subchorionic fibrin layer of the placental disk and in the decidua capsularis of the peripheral membranes. These polymorphonuclear leukocytes then migrate inward across the chorion and amnion to reach the amniotic cavity and the fetus. This inflammatory infiltrate is eventually of dual origin, as fetal neutrophils also contribute by migrating from the blood vessels of the placental chorionic plate (i.e., chorionic vasculitis [CV]) and umbilical cord (umbilical cord phlebitis arteritis and funisitis). CA has several important associations and is known to be both a cause and a result of premature membrane rupture as well as preterm labor [1].

In addition to the conventional acute CA, a chronic form (i.e., lymphocytic inflammation of the fetal membranes) has also been described;
chronic CA has been less well characterized but is not related to ascending infection and is commonly associated with nonspecific chronic villitis of unknown etiology [2]. Chronic CA is not generally associated with CV.

**METHODS AND RESULTS**

Over the past 7+ years, 7104 placentas have been reviewed at our institution using accepted placental review criteria [3]. Examinations have included a detailed gross description and microscopical review of formalin-fixed, paraffin-embedded 4-μm sections stained with hematoxylin and eosin (H&E). Sections from the umbilical cord (n = 1), fetal membranes (n = 1), and placental disk (n = 2) were reviewed. In 12 instances (10 singleton and 2 twin), we found a peculiar form of CV characterized by very focal involvement of a single chorionic vessel (artery or vein) that was infiltrated by eosinophils; in the majority of these cases, mononuclear cell infiltrates could also be seen with H&E staining (Fig. 1) while in other cases these mononuclear cells were not readily apparent. When eosinophilic CV was identified, serial sections from these blocks were stained using immunoperoxidase for T lymphocytes (CD3; clone PC3/188A; Dako), B lymphocytes (CD 20; clone L26; Dako), macrophages (CD68; clone KP1; Dako), cytomegalovirus (Dako), and herpes simplex viruses I and II (Dako). Normal placentas were used as controls. CD3⁺ T lymphocytes were present in all 12 cases along with scattered CD68⁺ macrophages. B lymphocytes were not found in any case. In each instance, the inflammatory cells migrated away from the amniotic fluid (i.e., towards the intervillous space). This type of lesion has not been previously described and we have referred to it as eosinophilic/T-cell chorionic vasculitis (E/TCV). In some cases, up to 30 additional blocks from documented regions of the involved placental disk were examined in an attempt to determine the extent of the inflammatory process. In no instance was an additional focus of E/TCV identified; however, in 1 of these 12 cases there was additional focal involvement of a single umbilical vessel artery and in a 13th case, an apparently identical process was seen localized to a single umbilical vein (i.e., no CV was identified). Finally, we identified one case (i.e., case 14) in which the lesion involved only a single vessel in a stem villous near its insertion into the chorionic plate. In none of these 14 cases was there evidence of subchorionic intervillousitis, chorioamnionitis, villitis, or intervillousitis. In two instances (cases 3 and 12), gross meconium staining was present. One case (10) was associated with a large umbilical cord hemangioma.

In addition, all the patients’ charts were reviewed for maternal, obstetrical, and perinatal histories. The clinicopathological findings are reviewed in Table 1. We noted a seemingly high proportion of mothers having a blood type of either A positive or O positive (13 of 14). However, in our population this is not totally unexpected, as the prevalence of A or O blood types is 85% with 83% Rh positive.

**DISCUSSION**

There is only a very scanty literature pertaining to eosinophilic infiltrates in the placenta. Although eosinophils are not generally considered by placental pathologists to be characteristic contributors to CA, Salafia et al. have reported that eosinophils derived from chorionic vessels may be present in up to 19% of placentas of preterm deliveries before 32 weeks [4]. However, in each of their cases, eosinophils comprised only a small portion of the total, predominately neutrophilic, infiltrates and were seen exclusively in the perivascular chorionic plate radiating toward the amniotic fluid. These authors speculated that eosinophils, when they appear as a component of CA in preterm placentas, represent a sign of fetal myeloid depletion [4]. Clearly our cases differ, as there was no associated CA and the eosinophils migrated away from the amniotic fluid; furthermore, none of our placentas were the product of premature deliveries.

A retrospective report from the veterinary literature by van Moll et al. [5] was the only other report of eosinophils participating in a placental vasculitis that we were able to identify. This report describes necrotizing placental lesions and a vasculitis in the placentas of aborted bovine and ovine fetuses infected with *Coxiella burnetii*. It is exceedingly unlikely that this organism plays any role in the current cases, as prior human case reports of placental infection with *C. burnetii* have been associated with extensive necrosis [6,7]. Further-