Title: White scar-like lesions in a female infant with bilious emesis and 6th nerve palsy

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Case:

A 10-day old otherwise healthy full-term female was admitted under a surgical team for bilious emesis and abdominal distension. Until her admission she had been feeding normally and was otherwise well. Parents were non-consanguineous and family history was unremarkable. Workup was negative for bowel obstruction or malrotation, however inflammatory markers were elevated (CRP 111). She had a history of three congenital, discrete, atrophic porcelain-white skin lesions with surrounding erythema. During the admission period the skin lesions appeared to be resolving, and as she was improving clinically, she was treated conservatively for septic ileus, and discharged.

At 8 weeks of age, she presented urgently to the Pediatric Dermatology clinic with the progressive appearance of multiple new atrophic porcelain-white lesions with an erythematous surrounding border as well as older lesions that had developed a necrotic or ulcerated center (Figures 1&2) . At this visit, she also had an acute inability to abduct her left eye, and bloody stools A clinical diagnosis was made and she was admitted urgently. A skin biopsy was also performed (Figures 3&4). During her admission she developed numerous complications including pericardial effusions, coagulopathy, liver and pancreatic dysfunction. MRI/MRA of the brain showed multiple evolving anterior cerebral and posterior cerebral artery branch infarcts. Comprehensive infectious disease workup including for TORCH infections, HIV, VZV and HSV was negative. Autoimmune workup showed weakly positive p-ANCA, however other labs including ANA, dsDNA, and complement levels were unremarkable.

What is the diagnosis?

Diagnosis: Infantile Degos Disease with Systemic Involvement

Skin biopsy histology showed focal epidermal necrosis and a sparse lymphocytic infiltrate. The patient was treated conservatively with antibiotics, IV methylprednisolone and TPN. Unfortunately, her condition worsened, she was transitioned to comfort care and ultimately expired.

Degos disease, or "malignant atrophic papulosis" is named after its description by the French Dermatologist Robert Degos in 1942, and is an extremely rare disorder in children. Most cases occur in middle-aged adults, with only a handful of cases ever reported in infancy (1-3), and a congenital presentation is even rarer with only two cases ever reported prior to this patient (4).

The clinical presentation of the skin lesions is characteristically described as the appearance and evolution of discrete, atrophic, porcelain-white skin lesions with surrounding erythema and typical natural history. Initially however lesions appear as pink papules on the trunk and extremities that umbilicate, and then develop the characteristic "porcelain white" centres that can become necrotic and/or ulcerated. The morphologic differential diagnosis for these lesions includes: progressive systemic sclerosis, cutaneous lupus erythematosus, and other medium vessel vasculitides.

The condition has been classified into "malignant" and "benign cutaneous" subtypes, with the former having a severe and progressive course and is characterised by systemic involvement(5). In the benign variant of Degos disease, lesions can appear in recurrent crops and manifestations are exclusively cutaneous. In the progressive systemic variant, following the appearance of skin lesions, there can be associated multisystem involvement, most commonly gastrointestinal and neurologic as illustrated by our case. Neurological and ophthalmic features are protean, and include ischemic and hemorrhagic stroke, seizures, ophthalmoplegia and visual field defect(1). Gastrointestinal manifestations can include upper or lower GI bleeding, pain, and intestinal perforation, which is an important cause of death in this condition(5). Importantly, extracutaneous manifestations herald a poor prognosis(5).

A majority of the pediatric cases reported in the literature fit into the malignant subtype. Although our patient had a progressive fatal course, it is not yet clear if congenital onset portends a poorer prognosis. Of the two congenital cases reported, one followed a progressive course and the other is systemically well at 18 months old on treatment(4).

Laboratory testing including basic screening for autoimmune diseases (such as ANA, dsDNA, complement) or systemic inflammation (ESR, CRP) can be normal and unhelpful in this condition(1, 2). Although skin biopsy findings canvary, the finding of a wedge-shaped zone of sclerosis in the dermis with thickened vascular channels has been suggested to be characteristic of this condition(6).

The exact pathogenic mechanisms at work in this disorder are not known, however the clinical feature of multisystemic infarctions and histologic observation of increased prothrombotic chemokines in affected skin suggest a vasculopathic process(6). In general the condition is sporadic, however a rare case of mother to infant daughter inheritance, or perhaps transmission, has been described(7).

There are no proven treatments for the malignant and progressive version of this condition, and in particular there is no data on treatment of infants. Treatments trialed include aspirin and other antiplatelet therapies, calcium channel blockers, steroids and other immunosuppressive medications(8), and there is limited reported success in single cases in adulthood with the complement inhibitor Eculizumab and the prostacyclin analogue Trepostinil(9, 10). As illustrated by our case, this condition can have a devastating and fatal outcome.

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