Bilateral Spontaneous Carotid-Cavernous Fistulae in Ehlers-Danlos Syndrome

Case Report

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Ehlers-Danlos syndrome is a familial hereditary disorder characterized by fragility of the skin and other tissues, gastrointestinal diverticula, arterial aneurysms, and ocular abnormalities. The clinical features of this syndrome were first pointed out by van Meek’ren, who in 1682 described a 23-year-old man who could stretch the skin of his right pectoral area to his left ear. Two hundred years later, Ehlers drew attention to loose-jointness and subcutaneous hemorrhages, while Danlos described subcutaneous tumors in these patients.

Vascular abnormalities in association with Ehlers-Danlos and correlated syndromes have been described, but Rubinstein and Cohen were the first to report intracranial aneurysms in this disease.

Two cases of carotid-cavernous fistulae in association with this syndrome treated by carotid ligation were recently described by Graf. In both instances, signs and symptoms disappeared following carotid ligation, only to recur at a later date.

The following is the first report of bilateral spontaneous carotid-cavernous fistulae in Ehlers-Danlos syndrome.

Case Report

A 39-year-old married woman was admitted to the University of Kansas Medical Center with proptosis and redness of her left eye and noise in her head of 2 weeks duration.

History. The patient had a life-long history of hyperextensibility of joints and easy bruising. Both she and her 29-year-old daughter suffered severe perineal lacerations with difficult surgical repair during childbirth. A sample of perineal tissue obtained from her daughter during delivery revealed histological hallmarks of Ehlers-Danlos syndrome. The patient’s mother died at age 33 of a cerebrovascular accident of unknown type and a brother from a perforated viscus.

Three years before admission the patient suddenly developed numbness and weakness of her left side, which cleared in approximately 1 month. Four months before her current complaint, she suffered spontaneous rupture of the sigmoid colon which was repaired; it was followed by an uncomplicated postoperative course and no recurrence.

Two weeks preceding admission she noted scleral injection, decreased visual acuity, and protrusion of her left eye with diplopia and heard a swishing sound in her head synchronous with her pulse. There was no history of trauma.

Examination. The patient was an alert woman with proptosis, decreased vision, ophthalmoplegia, and scleral injection of the left eye. A loud bruit which could be obliterated by left carotid artery compression, synchronous with her heart beat, was heard over the precordium, with no other abnormal cardiac signs.

Laboratory Studies. Routine blood count, urinalysis, bleeding and clotting time, clot retraction time, prothrombin time, partial thromboplastin test, and platelets were normal.

Hospital Course. Carotid arteriography revealed a left carotid-cavernous fistula. The patient tolerated compression of the left carotid artery for 10 minutes without difficulty. Intracranial ligation of the left internal carotid artery was contemplated but considered too hazardous. Consequently, ligations of the left common, external, and internal carotid arteries were performed under local anesthesia. The fragility of her arteries was exemplified by the superior thyroid artery which separated from the external carotid artery with normal ease when resected for histological examination. Immediate obliteration of the bruit in her left eye was noted by the anesthesiologist and the patient following carotid ligation. Two hours following surgery, a faint bruit was heard for the first time over her right eye, which could be obliterated by gentle compression of the right carotid artery.

During the ensuing 8 weeks, her left eye became normal whereas her right eye showed progressive proptosis, injection, and diminution of vision. A right carotid arteriogram demonstrated a right carotid-cavernous fistula. We were thus confronted anew with the danger of fatal hemorrhage, this time from a right carotid-cavernous fistula. Contemplation of right carotid artery ligation required proper evaluation of her vertebral circulation, and thus an angiographic study of the aortic arch was performed. Under fluoroscopic control a catheter was introduced to the aortic arch by way of the femoral artery to what appeared a satisfactory placement. Approximately 2 minutes following catheterization, the patient complained suddenly of chest pain, lost consciousness, and despite attempts at resuscitation, died a few minutes later.

Autopsy. A massive hemorrhage (600 cc) in the pericardial sac resulting from a double intimal tear of the ascending aorta was found at autopsy. The aorta and other major arteries were smaller and thinner than normal. The pulmonary artery and its principal branches showed the most marked diminution in wall thickness in comparison to other main arteries. Fragility

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of vessels became strikingly evident when gentle manipulation of kidneys and spleen resulted in detachment of the splenic and renal arteries from their respective hiluses.

Consistent with the recent appearance of right proptosis, dissection of the right internal carotid artery within the cavernous sinus revealed a 3-mm rent on its posterior surface. The left internal carotid artery showed evidence of resolution of a former carotid-cavernous fistula with focal roughness of the adventia but no patent communication between the artery and cavernous sinus.

Other features consistent with connective tissue abnormalities were the extreme thinness of abdominal skin, particularly the dermal layer, and diminished size and weight of lungs in the absence of emphysema. The lung weights were 25% of normal, with the left lung weighing 120 gm and the right 150 gm (average for 6- and 9-year-old children respectively).

Microscopic Examination. Microscopic studies of blood vessels, skin, and viscera revealed a generalized deficiency and abnormal distribution of elastic fibers.

The common carotid arteries were of normal size but revealed marked reduction of elastic fibers. The internal elastic membrane was quite fragmented with many sectors completely devoid of these fibers. Regions of the intracavernous portion of the left internal carotid artery revealed an organizing thrombus occupying the rupture site (Fig. 1). The right internal carotid artery (1 cm proximal to its recent rupture) showed a disruption of the internal elastic membrane and replacement of a segment of the arterial wall by fibrous tissue (Fig. 2). The circle of Willis and its branches showed no histological abnormalities.

In the aortic arch, elastic fibers were decreased in number, frayed, and arranged haphazardly without orderly lamination (Fig. 3). The abdominal aorta, however, showed relatively normal elastic laminae of the media.

Several major veins, particularly the splenic and renal, showed irregular elastic fiber distribution with heavy accumulations in some foci and complete absence in other areas.

The epiglottis, normally consisting of elastic cartilage, showed a marked reduction and in some portions a focal absence of elastic fibers (Figs. 4 and 5). The pulmonary alveolar septa and bronchial and bronchiolar walls showed very few elastic fibers. The dermis of the abdominal skin was abnormally thin with its elastic fibers more fragmented than usual although apparently normal in quantity.

Discussion

Despite the fact that Ehler-Danlos syndrome has been recognized for a considerable period, its underlying defect and its nature as a clinical entity are still poorly understood. The fact that this disease is usually inherited in a dominant autosomal manner and is exemplified by our patient's family in which both sexes were apparently affected. The patient's mother died at age 33 of a "cerebrovascular accident," while her brother succumbed to a "ruptured viscus" most likely due to this disease. Tissue biopsy from her daughter's episiotomy confirmed the presence of elastic tissue abnormality in her skin.

Because of obvious changes in skin elasticity
FIG. 2. Section from the right internal carotid artery 1 cm proximal to its rupture shows clearly the segmental absence of the internal elastic membrane. Note that collagenous components of the wall are actually thickened in the area of defect. (Verhoeff-van Gieson stain).

(see van Meek'ren’s original report on De dilatabilitate extraordinaria cutis19) the disease classically has been regarded as an abnormality of elastic tissue. Recently, however, alterations of collagen tissues have been emphasized. Jansen,13 in his electron microscopic studies, was unable to detect abnormalities of individual collagen fibers, but was impressed by the loose “wickerwork” of collagen in this disease. Other authors have referred subsequently to collagenous tissue as the site of the defect.16,19

Our case also demonstrated a certain deficiency of collagen, as was evident in the unusually thin dermis of the abdomen, and thinness of some blood vessel walls. We believe, however, that the role of elastic tissue in this condition deserves re-emphasis. The defects and severe fragmentation of elastic membranes in the large blood vessels could not be attributed solely to a poorly-organized collagen framework. We find it significant that the lungs, normally so rich in elastic tissue, weighed disproportionately less than other organs. (One of the dreaded complications of this condition is spontaneous rupture of the lungs.) It is of interest that, despite major structural anomalies of her lung, our patient had no respiratory difficulties. The generalized deficiency of elastic tissue was also strikingly manifest in the epiglottis which normally has an abundance of elastic fibers in its cartilage.

Although several authors5,6,7,15 have described altered clotting mechanisms in this syndrome, no hematological abnormalities were evident in our case.

Abortive forms of Ehlers-Danlos syndrome are
believed to occur not infrequently and may be the basis of some unusual vascular and gastrointestinal accidents. The possibility that some unexplained “spontaneous” carotid-cavernous fistulae may actually represent a “forme fruste” of Ehlers-Danlos syndrome should be considered.

The importance of this type of underlying tissue abnormality is evident particularly if diagnostic measures such as arteriography are contemplated.

Summary

We have reported what we believe to be the first case of bilateral, spontaneous, carotid-cavernous fistulae in a patient with Ehler-Danlos syndrome. The patient originally developed a left carotid-cavernous fistula. Following therapeutic ligation of the left carotid artery, a similar fistula developed in the right cavernous sinus. The patient died of aortic arch rupture during arteriography.

Postmortem examination showed marked elastic tissue deficiency in major blood vessels, lungs, and epiglottis. While abnormalities of collagen are regarded by many as the major feature of this disease, our case points to the role of elastic tissue changes, which we believe play a major part in the disruption of blood vessels and viscera.

Acknowledgment

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References


18. Meek'hen, J. *Observationes medico-chirurgicae.* Amsterdam: T. Boom, 1882, 392 pp. (See Ch. 32, De dilatabilitate extraordinaria cutis.)


