JOURNAL OF FORENSIC SCIENCES

J Forensic Sci, September 2011, Vol. 56, No. 5
doi: 10.1111/j.1556-4029.2011.01857.x
Available online at: onlinelibrary.wiley.com

Commentary on: Shields LB, Rolf CM, Davis GJ, Hunsaker JC 3rd. Sudden and unexpected death in three cases of Ehlers-Danlos syndrome type IV. J Forensic Sci 2010;55(6):1641–5.

Sir,

We read with attention the recent case report by Shields et al. (1) concerning three cases of sudden death in patients affected by Ehlers–Danlos syndrome (EDS) type IV.

EDS is a group of rare inherited connective tissue disorders characterized by common features such as loose and unstable joints, hyperelastic and delicate easy-bruising skin, and slow and poor healing of wounds with abnormal scarring. In EDS type IV (*vascular*), involvement of joints is minimal and limited to small joints, while tissue and vascular fragility is increased because of a defect of *collagen type III*, a component of skin and vessel walls (2).

Our interest for the manuscript was enhanced when we observed the case of a 16-year-old boy who was taken to the emergency department because he complained of persistent pain in his right side after sustaining minor trauma. After computed tomography revealed a retroperitoneal hematoma, urgent evacuation of the hematoma via nephrectomy was performed. The postoperative period was characterized by hemodynamic instability with continuous internal bleeding. He developed a mesenteric hemorrhage treated by ileal resection and finally an aortic dissection extending both to the epiaortic branches and to the thoracic tract, which proved fatal despite surgery. The case was referred to the pathology unit for autopsy. Autopsy revealed no external abnormalities. Internal examination revealed residual retroperitoneal hemorrhage. An intact, appropriately attached, synthetic arterial graft replaced the epiaortic branches (Fig. 1*A*). During autopsy, to perform genetic examinations, sterile skin/subcutaneous tissue, lung, and artery were collected. Fibroblast culture was attempted but was unsuccessful. Histological examination of the vascular walls documented areas of myxoid degeneration and a diffuse alteration of the elastic-collagen structure with decreased type III collagen which presented a disorganized appearance (Fig. 1*B–D*).

At colonic level, examination showed wall ischemia areas with diffuse necrosis and the presence of lymphocyte inflammatory infiltrate. The morphologic specimen, in combination with clinical history, was considered highly suggestive of a diagnosis of EDS type IV.

We believe that postmortem EDS type IV diagnosis, especially in those cases when it is not possible to use genetic testing to establish a definitive diagnosis, could be strongly suggested on the basis of clinical history and autopsy macroscopic and microscopic findings, in cases of "characteristic facial features, thin and transparent skin with apparent subcutaneous vasculature, and excessively friable vasculature, soft tissues, and viscera" (1, p. 1645), leading to spontaneous artery dissections/ruptures or gastrointestinal perforations/ruptures that are apparently "*sine materia.*" We would also like to point out that, as reported by Perdu et al. (3) diagnostic accuracy for genetic tests is nevertheless not higher than 61%. Therefore, genetic tests should be reserved for cases in which the classic signs and symptoms of EDS type IV are not present or are so mild that they are not clinically evident, with past unclear medical history and autopsy findings.

Finally, we invite all pathologists who suspect a diagnosis of EDS type IV, as in our case, even in the absence of postmortem genetic confirmation, to inform the direct relatives of the deceased

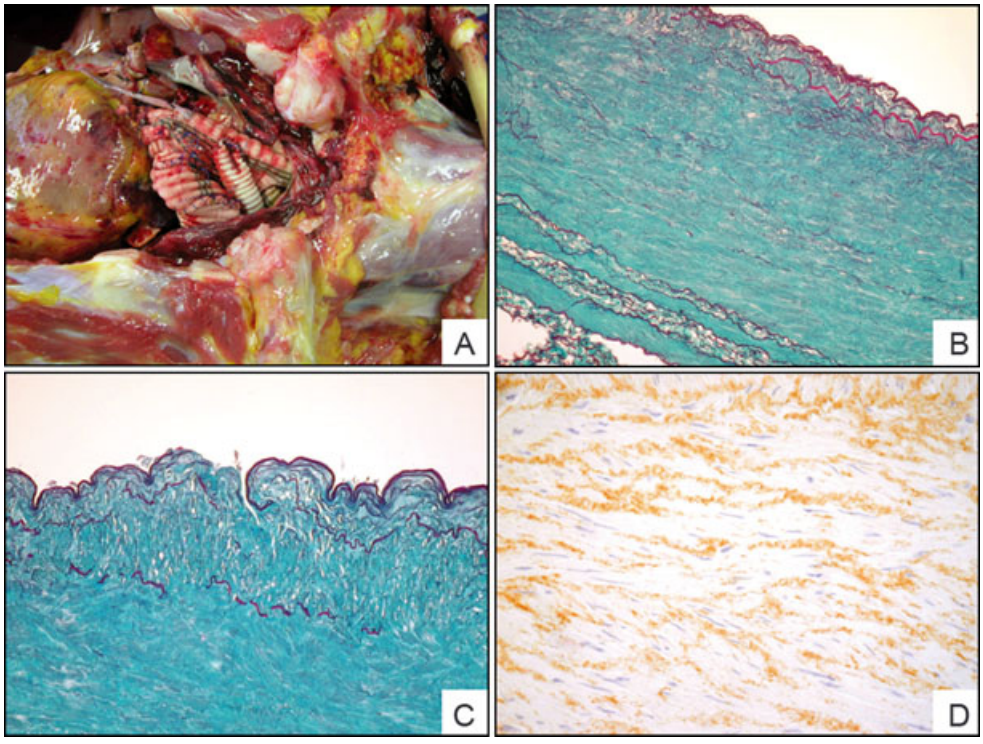

FIG. 1—*(A) Macroscopic image of the synthetic arterial graft at the epiaortic branches level; (B, C) microscopic images (Elastic Van Gieson) of the vascular walls documented a diffuse alteration of the elastic-collagen structure; and (D) decrease type III collagen with disorganized appearance.*

that they may benefit from genetic screening and, if necessary, to advise them to adopt a lifestyle compatible with this disease.

Acknowledgment

We thank Mr. Egidio Stigliano for his technical support.

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Fabio De-Giorgio,[1] M.D., Ph.D.; Vincenzo M. Grassi,[1] M.D.; Giuseppe Vetrugno,[1] M.D.; and Vincenzo Arena,[2] M.D.
[1]Institute of Legal Medicine, Catholic University, Largo Francesco Vito 1, 00168 Rome, Italy
[2]Institute of Pathologic Anatomy, Catholic University, Largo Francesco Vito 1, 00168 Rome, Italy
E-mail: fabio.degiorgio@rm.unicatt.it