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EHLERS-DANLOS SYNDROME

A case with some skeletal changes.

By

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The Ehlers-Danlos syndrome (hereafter referred to as E-D) is an inherited systemic tissue disorder presenting several interesting features even to the orthopedic surgeon. It is primarily characterized by the triade: 1) hyperelasticity of skin, 2) increased fragility of skin and blood vessels and 3) increased laxity and mobility of joints. Several other symptoms may occur. Cases are reported where the syndrome is incomplete or even subclinical. These *"formes frustes"* may be very confusing to the clinician (*Johnson & Falls* 1949, *Leider* 1949, *Broberger, Eriksson & Wedin* 1959).

A detailed survey of the various manifestations of the disease will be found in *McKusick*'s comprehensive study (1960), hence only a short general survey will be given below.

McKusick, on going through the literature, found approximately 100 cases of E-D, but the disease is certainly more frequent than this number indicates. Apart from Ehlers original report (1901), the Scandinavian literature comprises papers by *Haxthausen* (1936), *Strandberg* (1938), *Wigers* (1950), *Huseby* (1925), *Kornstad* (1953), *Sæmundson* (1956) and *Broberger et al.* (1959).

The fundamental defect in this connective tissue disorder remains controversial. It is probably due to a *collagen* defect. *Jansen* (1955) has advanced the theory that E-D is a disorder of the organization of collagen fibrils into bundles, and of the bundles into a strong network ("defective wicker work"). This view has been recently opposed by *Wechsler & Fisher* (1964), who claim that the basic defect is shortness of collagen tissue. There is no uniform agreement as to the histological picture. Normal, increased or decreased amounts of elastic tissue or collagen have all been reported.

Autosomal dominance with variable penetrance is the usual form of inheritance, although other genotypes may occur.

The clinical features are variable. The syndrome is commonly noticed in early childhood. The patients are usually mentally normal. They are often small, short and poorly developed. The face may be normal or with a broad nasal bridge, widely spaced eyes and epicanthus. Various ocular changes have been recorded. Blue sclerae are seen. As a whole, the defective collagen and the normal elastic tissue will explain several of the clinical features. The skin has a characteristic velvety appearance. It can be pulled away in large folds, but retracts instantly upon release. The elasticity decreases with increasing age, and loose folds appear in elderly people. The skin is abnormally fragile or brittle. Minor trauma or surgery produces gaping "fish mouth wounds" which are hard to close and heal only slowly. Stitches hold poorly in the skin, and operation wounds reopen easily. Paper-thin, atrophic scars are other characteristics. Minor blows may results in considerable hematomas which may organize to form pseudotumors. Pseudotumors also tend to form at pressure points. Histologically, they show connective tissue proliferation, increased vascularity, islets of fatty degeneration and cyst formation. Subcutaneous nodules on the limbs are frequently seen, composed of encapsulated fat with a diameter of 2-8 mm. They often calcify, which may permit the radiologist to make the diagnosis of E-D. Acrocyanosis has been a prominent feature of several previous case reports.

The hemorrhagic tendency has been ascribed to a vascular defect based upon poor collagen support of blood vessels. Recently some cases with abnormal coagulation mechanism have been reported, but the majority of cases have shown no abnormality as to coagulation factors (*Day & Zarafonetis* 1961, *Wigzell & Ogston* 1963).

The hyperextensibility of joints is often striking ("India rubber men"). It tends to become less marked as the patient becomes older. In addition, muscular hypotonicity and underdevelopment seem to exist in these patients. The result is a number of musculoskeletal abnormalities. Abnormal positions of extremities and digits are characteristic. There is a marked tendency to habitual dislocation of different joints (hip, shoulder, patella, radius, clavicle etc). Joint effusions, probably due to repeated trauma, are frequent. Kyfoscoliosis is likely to develop. Flat feet commonly occur. Finally, the literature comprises more or less sporadic reports on spina bifida occulta, arachnodactylia, club foot, acroosteolysis of finger phalanges, radio-ulnar synostosis,

pigeonbreast, high arched palate and dental abnormalities in connection with E-D (*McKusick, Johnson & Falls*).

The disturbances in the joints may be noted when the child starts to walk. It is particularly obvious if the changes of the knee and ankle joints allow much subluxation. In some cases the condition has even been diagnosed as myotonia congenita due to the patient's waddling gait or inability to walk or run fast.

Umbilical and inguinal hernias are common, and cases of diaphragmatic hernia also occur.

In recent years there has been an increased interest in the internal manifestations of the E-D. They include ectasia of portions of the alimentary tract, spontaneous rupture of the lung, recurrent hemoptysis, dissecting aneurysm of the aorta, multiple intracranial aneurysms, sinus of Valsalva aneurysm and spontaneous perforation of the bowel with gastrointestinal hemorrhage (*McKusick, Robitaille* 1964, *Madison, Bradley & Castillo* 1963, *Tucker, Miller & Jacoby* 1963, *Rubinstein & Cohen* 1964). E-D associated with multiple neurofibromatosis has also been reported (*Turkington & Grode* 1964).

There is no treatment for this disorder. Trauma should be avoided. Surgical procedures should be undertaken with great care because of the friability and hyperelasticity of skin and internal structures. Prognosis for life is usually good, although deaths occur from various internal manifestations.

CASE REPORT

The patient, a 54 year old woman, was admitted to our hospital on suspicion of a malleolar fracture. Her gait had been waddling since childhood, and her finger joints had always been extremely mobile. In younger years, she repeatedly suffered from dislocations in both shoulder joints, but this had not occurred for the last 12–15 years. Even the smallest trauma caused large skin bleedings. She did not bleed more than other people on accidental cuts in fingers etc. 23 years old, she had a cesarian section. She was told that she had a contracted pelvis and other skeletal deformities due to serious rachitis in childhood.

On *admission* she appeared mentally normal. As will be seen from Figure 1 she had a curious frame of body. She had a number of subcutaneous hematomas due to the trauma. A peculiar, gaping wound was seen on her right leg. The ankle joints appeared lumpy and deformed. The skin could be pulled away in large folds (Figure 2), but rapidly resumed its normal position on release. Histological examination of the skin revealed a obvious shortness on collagen fibers and even the elastic fibers were scarce. Typical pseudotumors were observed on the anterior aspects of the legs. There were also numerous calcified subcutaneous modules on the limbs (Figure 8). The skin was extremely brittle, and sutures cut through it.

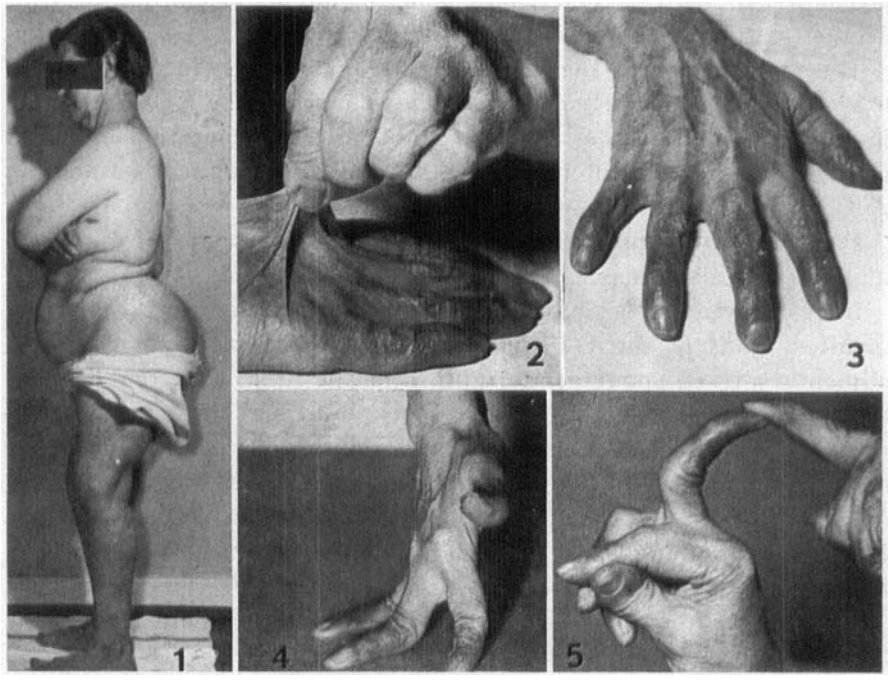


Figure 1. Figure 2. Hyperelasticity of the skin. Figure 3. Acrocyanosis. Figure 4. Hypermobility of fingers. Figure 5. Hypermobility of fingers.

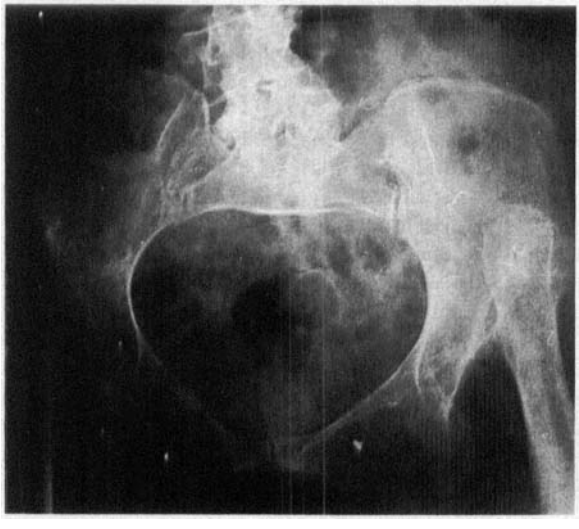
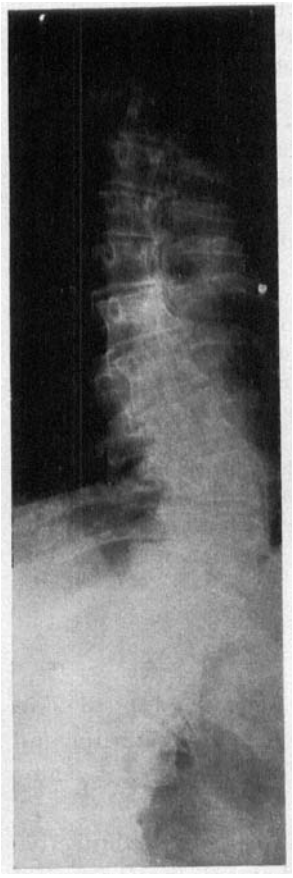


Figure 7. Bilateral dislocation of the hip joints.

Figure 6. Deformity of the spine.



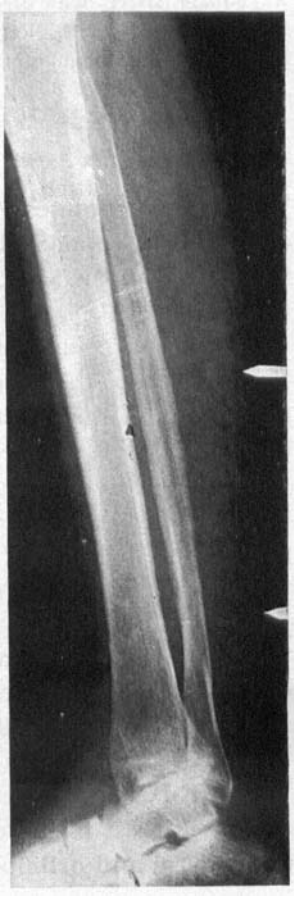


Figure 8. Lateral radiograph of leg. Subcutaneous calcified nodules. Slight dorsal displacement of the distal end of the fibula.

Acrocyanosis was seen on the fingers (Figure 3). There was a marked hypermobility of the fingers (Figures 4 and 5) and some other joints. Finally, there was a walnut-sized umbilical hernia and subluxation of several toe joints with bilateral hallux valgus.

X-ray examination revealed a considerable kyfoscoliosis (Figure 6) with torsion and secondary changes of the vertebrae and discs. Furthermore, there was a bilateral dislocation of the hip joints (Figure 7). Regarding the changes in the legs and ankle joints, it was obvious that the leg bones were twisted in relation to each other probably due to a subluxation of the fibula. There were some alterations of the shape of the talus and the heel bone. X-ray examination of the skull, hands and clavicle disclosed no obvious changes.

Biochemical tests showed normal values for serum calcium, phosphorus, alkaline and acid phosphatase, and proteins. The thymol turbidity tests, bleeding time, coagulation time, hemoglobin, prothrombin time, thrombocyt count and white blood cell count were all normal. Multiple bleedings were observed on the Rumpel-Leede's test.

A more thorough study of the hereditary aspects of this case was not possible. A younger sister, who died from sepsis in 1942, showed symptoms analogous to those of our patient. Neither her parents, nor her other 6 brothers and sisters, her son and granddaughter or other known relatives had symptoms indicating E-D.

DISCUSSION

The patient shows several features of the E-D with the typical skin and joint affections, the bleeding tendency, the umbilical hernia and the acrocyanosis. Her sister undoubtedly suffered from the same disease.

It is of course difficult to establish the importance of the connective tissue defect in the development of the hip joint dislocation. Congenital dislocation of the hip has been reported in a case of E-D (*Debré & Semelaigne* 1938), and according to McKusick some cases of habitual hip joint dislocation have also been reported. It is noteworthy that the patient's sister also had symptoms indicating hip joint dislocation. The patient was deprived of the tendency to shoulder joint dislocations in her fourth decade of life, which is in accordance with the general experience with the E-D. As mentioned before, kyfoscoliosis is a fairly common skeletal manifestation of the E-D. In some cases a wedge-shaped deformity of the vertebral bodies has been demonstrated (*Kornstad* 1953, *MacFarlane* 1959, *Coventry* 1961). The other skeletal manifestations of our case are commonly seen in cases of E-D.

The E-D has for a long time been regarded as a disease of particular interest to the dermatologist. However, it is also of interest to the general and orthopedic surgeon. It is frequently a typical surgical

condition that makes the patient seek medical help. This is evident from the abovementioned Scandinavian papers. 2 patients saw a doctor owing to habitual dislocation of the shoulder (*Wigers*) and repeated ankle distortions (*Huseby*) respectively. 3 patients reported by *Kornstad* had suffered from shoulder luxation, and one patient saw a doctor owing to repeated dislocations of various fingers on one hand. *Strandberg's* patient was admitted to a surgical ward with a large femoral hematoma accompanying a minor trauma.

SUMMARY

The signs and symptoms of the Ehlers-Danlos syndrome are described briefly. The surgeon should be aware of this disease owing to the bleeding tendency and the frequency of dislocation and skeletal deformities. The author reports on a 54 year old woman suffering from bilateral hip dislocation, marked kyfoscoliosis, twisting of the leg bones as well as subdislocations of several toe joints. She had also suffered habitual dislocations of the shoulder joints, butt this had been cured spontaneously in the fourth decade of her life. It is frequently the skeletal or joint manifestations of the Ehlers-Danlos syndrome that makes the patient seek medical advice,—most commonly a general or an orthopedic surgeon.

RESUME

Les signes et symptômes du syndrome Ehlers-Danlos sont succinctement décrits. Le chirurgien doit veiller à cette maladie due à la tendance aux hémorragies et à la fréquence des dislocations et des déformités squelettiques. L'auteur rapportte le cas d'une femme âgée de 54 ans, souffrant d'une dislocation bilatérale de la hanche, d'une cyphoscoliose marquée tordant les os de la jambe, ainsi que de subdislocations de différentes articulations. Elle avait souffert aussi des dislocations habituelles des articulations de l'épaule, mais celles-ci s'étaient guéries spontanément dans la quarantaine. Il arrive fréquemment que ce sont les manifesttations squelottiques ou articulaires du syndrome Ehlers-Danlos qui amènent le malade à consulter un médecin—le plus souvent un praticien de médecine générale ou un chirurgien orthopédiste.

ZUSAMMENFASSUNG

Die Kennzeichen des Ehlers-Danlos Syndrome wurden kurz beschrieben. Der Chirurg sollte auf diese Erkrankung wegen der Blutungsbereitsschaft und der Häufigkeit von Verrenkungen und Skelettdeformiteten aufmerksam sein. Der Verfasser berichtet über eine 54 Jahre alte Patientin, dia an doppelseitiger Hüftgelenksverrenkung, ausgesprochener Kyphoskoliose, Torsion der Unterschenkelknochen und auch an Subluxation mehrerer Gelenke litt. Sie hatte auch an habitueller Luxation der Schultergelenke gelitten, doch kam es hier zu einer spontanen Heilung im vierten Jahrzehnt ihres Lebens. Häufig sind es die Skelett oder Gelenkserscheinungen des Ehlers-Danlos Syndrome, die den Patienten zum Arzt führen,—meist zum allgemeinen oder orthopädischen Chirurgen.

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