HYPEROSTOTIC SPONDYLOSIS AND DIABETES MELLITUS

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Forestier and Rotès-Querol (1950) described a disease of the spinal column, occurring mostly in elderly persons and frequently mistaken for ankylosing spondylitis, which they designated "hyperostose ankylosante vertébrale sénile".

The clinical manifestations of this disease are characterized by a decreased mobility of the spine, caused by bony outgrowths bridging the anterior and lateral faces of the vertebral bodies and extending across the intervertebral space. A typical *post mortem* specimen is shown in Fig. 1 (opposite).

This disease was described long ago by Wenzel (1824), Rokitsky (1856), and Bechterew (1899). It was mentioned as "moniliform hyperostosis of the right side of the thoracic spinal column" by Meyer and Forster (1938) and Oppenheimer (1942). Lacapère, Delaville, and Drieux (1954) called it "spondylorheostosis"; in 1949 Lacapère had used the term "vertebral melorheostosis". Forestier and Certonciny (1956) discarded the adjective "senile" after the condition had been found in younger people.

Ott (1953) used the term "hyperostotic spondylosis".

Pathological Anatomy

The changes are produced by paravertebral ossifications, which are most marked in the thoracic spine, particularly from D4 downwards. The anterior and lateral faces of the vertebral bodies become coated with a continuous bony layer, resembling sugar-icing (Zuckerguss). At the level of the vertebral body the bridging is a few millimetres thick, while across the intervertebral space it may be several centimetres thick. These ossifications may extend over two vertebrae or more and sometimes involve the whole thoracic spine. They tend to be more marked on the right side, since on the left side the pulsation of the aorta interferes with their formation (Fig. 2a and b, overleaf).

In the lumbar spine, these bony outgrowths are often discontinuous; they may be shaped like a candle-flame or the snout of a tapir, and may project upwards or downwards. In the lumbar region they develop on both the right and left sides (Fig. 3, overleaf).

In the cervical spine (Fig. 4, overleaf), there may be continuous ossification, or bridging similar to that in the lumbar region.

There is no ankylosis of the intervertebral and costovertebral joints, like that characteristic of ankylosing spondylitis, no ossification of the short spinal ligaments, and no obliterations of the sacroiliac joints like that seen in ankylosing spondylarthritis (Fig. 5, overleaf).

On the basis of the findings of de Sèze, Lacapère, and Amoudruz (1952), who studied the embryonic development of the spinal column, Ott (1953) suggested that these ossifications originate in the loose vascular connective tissue which persists from the embryonic stage and in which vasomotor changes and oedema may develop. Such tissue shows a strong tendency to undergo transformation into any kind of connective tissue including bone, and various mechanical, inflammatory, or hormonal influences may lead to the formation of pathological ossifications.

Clinical Findings

The disease usually affects persons between 50 and 70 years of age, the mean age at radiological diagnosis being about 65 years. Juvenile cases of spinal hyperostosis also occur involving the lumbar region only (de Sèze and Claisse, 1960; Claisse, 1961; Bastin, 1962), Forestier at first found the condition only in males, but it is now thought that the incidence in females is about equal. Besides the involvement of the spinal column, degenerative processes, sometimes very severe, may be observed in other joints especially the hip joints. The affected persons are

Fig. 1.—Necropsy specimen of vertebrae.

most often muscular, pycnic, or obese. Subjective symptoms may be absent or insidious back pain may persist for years. The thoracic rigidity with exclusively abdominal respiration, which is regularly found in ankylosing spondylitis, is mostly absent. Limitation of movement is most marked in the thoracic spine, where measurements disclose a reduction of Stibor's distance, while the lumbar and cervical regions retain their normal mobility. Spinal rigidity is never so severe as in ankylosing spondylitis, because this bony layer forms only on the anterior and lateral faces of the vertebral bodies and there is no true ankylosis of the vertebral arches. The development of kyphosis of the thoracic spine probably represents the sequelae of Scheuermann's disease.

There is no atrophy of the dorsal and gluteal muscles. Laboratory investigations show no evidence of an inflammatory process and no deviations in the metabolism of calcium or phosphorus.

Discussion

The aetiology of this condition has not yet been elucidated. Ott (1953), Vignon, Durant, Pansu, Bertrand, and Truchot (1961) and Smith, Pugh, and Polley (1955) suggested that it is merely one form of spinal degeneration, differing only quantitatively from the common spondyloses. Rubens-Duval, Villiaume, and Lubetzki (1961) suggested that this hyperostosis of the spine is due to dystrophies affecting the somatic growth in adolescence and develops in later life when the spinal column is subjected to excessive strain.

Boulet, Serre, and Mirouze (1954), Serre and Mirouze (1955), and Mirouze (1961) support the hypothesis that the condition is due to an excessive output of the pituitary growth hormone (somatotropin) which occurs in humans when the secretion of gonadal hormones declines. In addition to its stimulating effects on the growth of organs and tissues, somatotropin has an important metabolic action, and may induce a hyperplasia and proliferation of connective tissue, increasing their inflammatory potency, or producing an ossification of paravertebral and pararticular tissues. Experimental studies have shown that the administration of extracts of the pituitary or of a purified growth hormone resulted in periosteal new bone formation, while the cells of the joint cartilage showed a tendency towards enchondral ossification.

This hypothesis that the growth hormone promotes the development of spinal hyperostosis is supported by the incidence of hyperostotic spondylosis in diabetics, as well as by the high frequency of

Fig. 2(a).—Antero-posterior view of dorsal vertebrae, showing bony outgrowths, more marked on the right side. 2(b).—Lateral view of dorsal vertebrae, showing hyperostosis covering the disks and vertebral bodies.

Fig. 3.—Antero-posterior view of lumbar vertebrae, showing "candle-flame" and interrupted bridging ossifications.

diabetes mellitus or of prediabetic glycosuria in cases of acromegaly, which is commonly associated with paravertebral or paraarticular hyperostosis. The problems of diabetes do not concern the pancreas alone. The islets of Langerhans are under the control of neuro-endocrine regulatory mechanisms, and the pituitary hormones (*i.e.* somatotropin, corticotropin, and TSH) are antagonistic to insulin. The growth hormone has a diabetogenic action and

Fig. 4.—Lateral view of cervical vertebrae, showing large bony outgrowths on the anterior aspect of the vertebral bodies.

induces hyperglycaemia, glycosuria, and ketonuria, and it also has an important effect on the metabolism of proteins, fats, calcium, and phosphorus. In addition somatotropin promotes glycogenolysis in the liver and influences the output of alpha-cells of the pancreatic islets, containing glucagon which in turn raises the blood-sugar level and to a certain degree counteracts the biological activity of insulin. Insulin, which is produced by beta-cells of the islets of Langerhans, promotes the uptake of glucose by the cells and its phosphorylation to glucose-6-phosphate. This is subsequently utilized both in the production of glycogen and in the gradual splitting up to pyruvic acid. The phosphorylation of glucose to glucose-6-phosphate is produced by

Fig. 5.—Antero-posterior view of the pelvis. There is no obliteration of the sacro-iliac joints.

the enzyme hexokinase, acting as a catalysator during the formation of glucose-6-phosphoric acid from glucose and from adenosine triphosphoric acid. In older people the diabetogenic action of the growth hormone may be due either to its action on the carbohydrate metabolism by depressing the secretion of insulin, or by influencing the peripheral utilization of glucose through the inhibition of hexokinase activity. Through a mobilization of lipids and an excessive oxidation of fats, the growth hormone actually increases the severity of symptoms caused by a deficiency of insulin (Straub, 1960).

According to Boulet and others (1954), Serre and Mirouze (1955), and Ott, Schwenkenbecher, and Iser (1963), both the diabetogenic disturbance

and the increased osteoplastic activity of the subligamentous connective tissue may be due to a common factor, *i.e.* to the increased output of the growth hormone. Osteoporosis of the spinal column was the first spinal disease reported in association with diabetes mellitus; its development was explained as due to metabolic and endocrine disturbances and the presence of mild pain was attributed to diabetic neuropathy.

Boulet, Serre, Mirouze, and Mandin (1953) and Boulet and others (1954) drew attention to the relatively high incidence of hyperostotic spondylitis in patients suffering from diabetes. This association had been previously described in occasional cases by Ott. The problem has been studied

in more detail by Ott (1964) and Ott and others (1963), and in Czechoslovakia by Weiszer, Ďurčo, and Kratinová (1964). Ott and others (1963) found a hyperostotic spondylosis in almost 50 per cent. of 82 patients with clinically manifest diabetes; this series included old people with a benign type of diabetes. According to Boulet and others (1954), hyperostotic changes may develop as late as 12 years after the onset of diabetes; they are not confined to the spine and develop in various sites.

Ott and others (1963) and Einaudi and Viara (1960) reported that, in many patients with hyperostotic spondylosis, the glucose tolerance test yielded a hyperglycaemic curve. Ott and others (1963) observed this phenomenon in 25 out of 100 patients suffering from hyperostosis, but Klunker (1964) found no positive correlation between hyperostotic spondylosis and a disturbance of the carbohydrate metabolism.

During the study of spinal hyperostosis, we have tried to ascertain whether diabetes had any influence on its development. We have investigated altogether 101 diabetics whose ages ranged from 40 to 86 years (including 44 patients treated at our Institute for diseases of the locomotor system and 57 patients followed-up at an out-patient department for diabetes).

The Table shows that 83 of our 101 patients were women whereas Ott's series consisted mainly of men. We found hyperostotic spondylosis in six of eighteen men and in 34 of 83 women (*i.e.* in 41 per cent. of females and 33.3 per cent. of males). The mean age of the diabetics with hyperostotic spondylosis was higher than that of those without.

The incidence of hyperostotic spondylosis is compared with the duration of diabetes and the age of the patients in Fig. 6, which shows that the older the patient and the longer the duration of diabetes, the higher was the frequency of hyperostotic spondylosis.

In our series of hyperostotic and diabetic patients, the diabetes was mild or moderately severe, of the so-called sthenic form. Eighteen cases were controlled by dietary restriction alone, eleven took antidiabetic drugs by mouth and eleven received insulin up to 40 units/day.

Fig. 6.—Frequency of spondylosis, by age of patient and duration of diabetes.

The associated complications were compatible with the advanced age of the patients as well as with the underlying disease. The most common were cardiovascular diseases (hypertension, ischaemic heart disease, myocardial infarction, endarteritis, systemic arteriosclerosis, thrombophlebitis), slightly less frequent were cholecystopathies, diabetic polyneuritis, and retinopathies, and there was one case of a diabetic pseudotabes. There were also a few cases of pulmonary or spinal tuberculosis, Reiter's syndrome, infectious hepatitis, gastric ulcer, and pyelonephritis. Two cases of vascular nephropathy included one early stage and one suspected Kimmelstiel-Wilson's glomerulo-hyalinosis.

Conclusion

There are no substantial differences between the radiological appearances and the clinical symptoms of hyperostotic spondylosis in patients with and without diabetes mellitus. Although a disturbance of the carbohydrate metabolism cannot be the unique aetiological factor responsible for the development of hyperostotic spondylosis, the relatively high incidence of this spinal condition in diabetics

TABLE
INCIDENCE OF HYPEROSTOTIC SPONDYLOSIS IN 101 DIABETICS, BY AGE AND SEX

Hyperostotic Spondylosis				Present		Absent	
				No. of Cases	Mean Age (yrs)	No. of Cases	Mean Age (yrs)
Sex	Male			6	68.1	12	61.7
	Female			34	66.7	49	61.5
	Total			40	67.4	61	61.6

supports the view that the association is not due to chance alone. The hyperostotic spondylosis is associated only with certain forms of diabetes (*i.e.* those occurring in middle age or old age* and easily controlled by dietary restrictions or anti-diabetic medication).

The frequency of hyperostotic spondylosis increased with advancing age and with the duration of diabetes.

Summary

Hyperostotic spondylosis is often mistaken for ankylosing spondylarthritis. This spinal disorder develops in older people and is associated with the formation of bony bridges extending throughout the intervertebral spaces, and of a bony layer coating the anterior and lateral faces of the vertebral bodies, most commonly involving the thoracic spine. The aetiology of this degenerative spinal process is still unknown. It has been suggested that an increased output of the pituitary growth hormone may assist the production of these paravertebral ossifications. Hyperostotic spondylosis is found relatively frequently in patients suffering from diabetes mellitus (*e.g.* in about 40 per cent. of our series of 101 diabetics). Older patients in whom diabetes developed at a more advanced age and had a benign but prolonged course, showed a higher frequency of spinal hyperostosis.

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La spondylose hyperostotique et le diabète sucré

RÉSUMÉ

La spondylose hyperostotique est souvent confondue avec la spondylarthrite ankylosante. Ce trouble vertébral survient chez des personnes âgées et est associé à la formation des ponts osseux traversant tous les espaces intervertébraux, et des couches osseuses couvrant les faces antérieure et latérale des corps vertébraux, impliquant le plus souvent la colonne dorsale. On n'en connaît pas l'étiologie. On a avancé une hypothèse selon laquelle la sécrétion augmentée de l'hormone pituitaire de croissance pourrait favoriser la production de ces ossifications paravertébrales. La spondylose hyperostotique est relativement fréquente chez les malades atteints de diabète sucré (en 40 pour cent de notre série de 101 diabétiques). Des plus vieux malades, chez qui le diabète avait commencé plus tard et était benin mais prolongé, accusaient une fréquence plus grande d'hyperostose vertébrale.

La espondilosis hiperostósica y la diabetes mellitus

SUMARIO

La espondilosis hiperostósica se ve a menudo confundida con la espondilartrosis anquilosante. Este trastorno vertebral ocurre en personas de edad avanzada y se ve asociada con la formación de puentes óseos que atraviesan todos los espacios intervertebrales y de capas óseas que cubren los aspectos anterior y lateral de los cuerpos vertebrales y que afectan muy comunamente la columna

* The average age at onset of diabetes in our patients was 55.2 yrs.

dorsal. Su etiología no se conoce, pero se sugiere que la secreción aumentada de la hormona hipofisaria de crecimiento pudiera favorecer la producción de estas osificaciones paravertebrales. La espondilosis hipero-
stósica es relativamente frecuente en enfermos con

diabetes mellitus (un 40 por ciento en nuestra serie de 101 diabéticos). Los enfermos de edad más avanzada, cuya diabetes había empezado más tarde y fué benigna aunque prolongada, acusaban una frecuencia mayor de hipero-
stosis vertebral.