Pathogenesis of secondary hypertrophic osteoarthropathy: a hypothesis

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ABSTRACT: Wide ranges both in the location and the pathological state of the primary disease associated with hypertrophic osteoarthropathy (HO) have been noted. The combined distribution of the glossopharyngeal and vagus nerves appears to coincide with the range of locations of the primary disease associated with HO. These two nerves are believed to contribute to the innervation of the blood vessels in this same area. This hypothesis states that: i) some of this innervation is part of a blood volume control system; and ii) by an inappropriate stimulation of this system, as a result of blood-flow in an anomalous vascular rearrangement lying close to the primary disease associated with HO, a cerebral salt centre is stimulated to retain extra-cellular sodium. A secondary atrial natriuretic peptide oversecretion ensues and a “near steady-state” is established, with the presence of excess fluid and dilated vessels in all four limbs. Thus, the pathogenesis of HO and the distribution of an extra-renal volume control system are reciprocal facets of the same question.

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Background

The lungs are the predominant site for the primary disease associated with hypertrophic osteoarthropathy (HO). Association of HO with primary diseases in a number of other organs has also been reported, e.g. oesophagitis, infected diverticulum of the stomach, cirrhosis of the liver and a number of benign or malignant tumours, including pleural fibroma, neurilemoma of the diaphragm and both myoma and carcinoma of the oesophagus [1].

In HO, a common factor in the organs which may be the site of the primary disease has been suggested [1] - these organs are all in the distribution of the homologous, composite, branchial nerves, the glossopharyngeal and the vagus. These two nerves are believed to supply branches to all arteries which lie in the distribution of these same nerves [2].

It is hereby suggested that some of the branches of these nerves to the arteries in this distribution are part of an extra-renal volume receptor system. Evidence for the existence of an extra-renal volume receptor system has been presented previously [3, 4].

One of the characteristic features of HO is the presence of bilateral, symmetrical edematous swelling of feet, ankles, hands and wrists (sometimes the legs and forearms). This swelling must be due to excessive intra- and extra-vascular fluid, as the swelling subsides quickly after resection of the primary tumour or after an appropriate vagotomy (bilateral, or in the neck) [5].

Lung cancer is the commonest primary disease associated with HO. Close to some primary lung tumours, the presence of pre-capillary broncho-pulmonary arterial shunts has been clearly demonstrated [6]. In this abnormal vascular rearrangement, there will be anomalous blood flow between the bronchial and pulmonary arteries, with the possibility of an abnormal deflation with each pulse (by means of back-flow and/or a Venturi effect) of a segment of either the bronchial or pulmonary artery. If this localized segment of artery were the site of the volume receptors, then an inappropriate signal would be transmitted by the vagus to its dorsal sensory nucleus, and thence to other parts of the brain.

Hypothesis

The cardinal points of this hypothesis are that the inappropriate stimulation of one system of volume receptors results in fluid retention in the absence of cardiac, renal or hepatic disease and that this is effected by means of a hormone or system of hormones, released by the brain and acting finally on the renal tubules.

An increased secretion of atrial natriuretic peptide would counterbalance, and thereby limit, the excess fluid retention and may also account for the dilated state of the vessels in the limbs in HO [7].

There is evidence for brain involvement in sodium homeostasis, e.g. in the cerebral salt wasting state secondary to injury or damage by disease to the brain [8–10]. Thus, HO might be considered as the very antithesis of the cerebral salt wasting state.
The lungs have a double circulation and this fact might account for the greater frequency of HO with lung disease than with diseases of the oesophagus, liver, stomach, diaphragm etc., where an abnormal vascular rearrangement (as in lung cancer cases with HO) would rarely occur.

Finally, HO associated with disease in a specific organ might be considered as a marker for the presence, in the arteries supplying that organ, of receptors in a volume control system. A corollary is that by plotting out the sites of the primary diseases associated with HO the wide, but none the less clearly defined, limits of the distribution of a system of extra-renal volume receptors are determined, namely the arteries in the distribution of the glosopharyngeal and vagus nerves.

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References

La pathogenèse de l'ostéoarthropathie hypertrophiante secondaire: une hypothèse. L. Doyle
RÉSUMÉ: L'on a noté de larges variations, à la fois dans les localisations et dans les états pathologiques de la maladie primaire associée à une ostéo-arthropathie hypertrophiante. La distribution combinée du nerf glosopharyngé et du nerf vague semble coïncider avec la zone de localisation des maladies primitives associées à l'ostéo-arthropathie hypertrophiante. Dans cette zone particulière, ces deux nerfs contribuent probablement à l'innervation des vaisseaux sanguins correspondants. Cette hypothèse suppose que 1) une partie de cette innervation appartient au système de contrôle du volume sanguin; et 2) par une stimulation inappropriée de ce système, consécutive à un réarrangement vasculaire anormal à proximité de la maladie pulmonaire associée à l'ostéo-arthropathie, un centre cérébral du sel est stimulé pour retenir le sodium extra-cellulaire. Il s'ensuivrait une hypersecrétion d'un peptide natriurétique de l'oreillette, avec établissement d'un "état quasi stable", avec présence d'excès de liquide et de dilatation des vaisseaux dans les quatre membres. Ainsi donc, la pathogenèse de l'ostéo-arthropathie hypertrophiante et la distribution d'un système de contrôle du volume extra-rénal, seraient des facettes réciproques de la même questionère.