Deposition of aluminum and iron in benign bone tumors (exostosis)

Fig. 1. X-ray image of an exostosis (red arrow) developed on the side of the femur in a 14 y.o. girl.

An exostosis is an outgrowth of new bone from the surface of a bone into the muscles; it is a frequent benign tumor in children. An exostosis causes discomfort and chronic pain, depending on its size and location. The tumor usually develops on the long bones (femur, tibia, humerus) but also on shoulders, elbows and hips. There are some forms of hereditary diseases characterized by the existence of multiples tumors (MHE-Multiple Hereditary Exostoses) that affect 1 in 50,000 individuals. The surgical treatment consists in resection of the tumor. Although the occurrence mechanism is not fully understood, exostoses seem be due to an abnormal and uncontrolled activity of cartilage and bone forming cells. Under the microscope, the tumor has usually a mushroom-shape with a cape of proliferating cartilage covering a bone shell.

Bone is the major structural and supportive tissue of the body, elaborated by bone-forming cells. It is both elastic and rigid. Elasticity is conferred by a high amount of collagen and rigidity is obtained by the deposition of a mineral phase composed of calcium/phosphate crystals (coined hydroxyapatite) between the collagen fibrils. Hydroxyapatite crystals can be modified by several ions that can replace the phosphate, the calcium or the hydroxide groups. Calcium can be replaced by metallic ions such as lead, zinc, iron, strontium and aluminum. This replacement modifies the quality of the mineral phase and has deleterious consequences at both the tissue and the cell level. Iron deposition in the bone is well known in some diseases associated with iron metabolism.

Aluminum deposition in bone and brain was evidenced in the seventies in dialyzed patients with renal failure who developed encephalopathy and osteomalacia (the adult form of rickets due to mineralization impairment). The discontinuation of alumina gels to purify water in the water treatment plants has led to the disappearance of the disease.

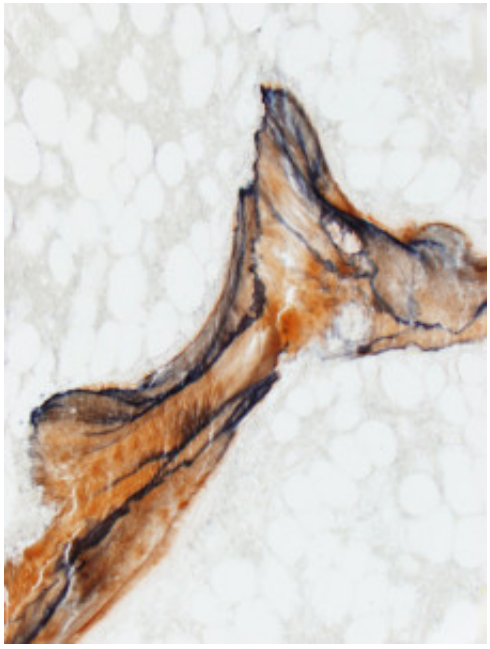

Fig. 2. Detection of aluminum in the calcified bone of an exostosis, microscopic section. Bone is stained in light orange and the aluminum bands are deep blue. Solochrome azurine staining, original magnification: 200X.

We analyzed the exostoses removed surgically in a series of 30 patients. A special microscopic method was necessary to prepare the analysis: exostoses were embedded in a hard polymer and undecalcified sections (preserving the mineral and the collagen) were obtained on a heavy duty sectioning machine. The microscopic sections were stained by routine methods to analyze the bone cells and special stains were used to detect iron and aluminum. The tissue blocks were also analyzed by scanning electron microscopy coupled with an X-ray energy dispersive spectrometer (EDS) or a wavelength dispersive spectrometer (WDS). We found that aluminum was deposited in the mineral phase of the bone in 2/3 of the patients. Iron was also detected in 1/3 of the patients. The metal deposits appear as linear bands inside the calcified bone. EDS, which is usually used to characterize the metals, failed to identify iron and aluminum in the tissue blocks because the concentration was under the detection limit. WDS showed that concentrations ranged between 0.032-0.054 % (in atomic %) for iron and 0.030-0.034 % for aluminum. The staining methods

appeared more sensitive than spectroscopy.
Localization of iron and aluminum in the bone of these benign tumors is an intriguing problem. Iron is a metal largely present in the human body (in the red blood cells, the muscles…) but aluminum is a potentially dangerous intruder. Aluminum is omnipresent in modern life, alimentation and environment. It is estimated that the aluminum intake can reach up to 13 mg/day although the tolerable weekly intake is only 1 mg/kg of body weight. The human organism cannot completely remove this metal from the blood and a fraction can deposit in the brain, spleen and bone. In an exostosis, deregulation of the bone forming cells may favor metal deposition.

Publication

Aluminum and iron can be deposited in the calcified matrix of bone exostoses.
Chappard D, Mabilleau G, Moukoko D, Henric N, Steiger V, Le Nay P, Frin JM, De Bodman C
J Inorg Biochem. 2015 Sep 16.