Mazabraud's Syndrome Project

Project Aim: The study is looking for a genetic link between Fibrous Dysplasia and Intramuscular Myxoma.

Mazabraud's syndrome is a rare syndrome in which benign intramuscular myxomas occur in association with fibrous dysplasia of bone. There are several theories about the aetiology of this syndrome which include an inborn error of tissue metabolism a reactive response of soft tissue to fibrous dysplasia. An activating Gsa mutation found in fibrous dysplasia and in intramuscular myxoma. This abnormal Gsa protein is thought to result in tumourigenesis).

Fibrous dysplasia of bone is a genetic, non-inheritable disease, characterized by the replacement of normal bone by excessive proliferation of cellular fibrous connective tissue with woven bony trabeculae. The actual prevalence of FD is difficult to estimate, but it may affect about 1/30,000 persons with a similar distribution around the world) It can cause bone pain, bone deformities and fracture, involving one or several bones. It is caused by missense mutations occurring post-zygotically in the gene coding for the a-subunit of the stimulatory G-protein, Gs, in the guanine nucleotide binding, alpha stimulating (GNAS) complex locus in chromosome 20q13. This mutation results in osteoblastic differentiation defects, and bone resorption is often increased.

Intramuscular myxoma is a rare benign soft tissue tumor involving the musculoskeletal system. The incidence is reported as varying from 0.1 to 0.13 per 100,000 population. The most common site for myxomas is the thigh, followed by buttocks, arms and chest wall. Intramuscular myxomas are slowly growing mass lesions that can be present for many years before a patient seeks medical attention. They are often asymptomatic, but may present with pain due to impingement on a surrounding structure. Most commonly intramuscular myxomas are solitary, but in association with fibrous dysplasia multiple lesions are more common. Most patients present between the fifth and sixth decade of life. The swelling commonly occurs in the large muscles of the thigh, shoulder, buttocks and arms. The tumour can be diagnosed with certainty only with histopathological. Histologically, these neoplasms are composed of a few elongated or starshaped cells lying in abundant mucoid stroma. These tumours are characterized by expanding growth without forming distant metastases GNAS1 mutations, which occur in fibrous dysplasia,
have been identified in small numbers of intramuscular myxoma (R201H, R201C).

It is also possible that at least some of the GNAS1 mutation-negative intramuscular myxoma harbour a Q227 mutation, which occurs in a small proportion of cases of fibrous dysplasia. There are some rare GNAS1 mutations which previously described in fibrous dysplasia, McCune Albright syndrome and isolated endocrine neoplasms (R201G, R201S, R201P, R201L, Q227L, Q227R, Q227K and Q227H) have not been analyzed.

Mazabraud's syndrome, though uncommon, is reported increasingly frequently. Awareness of the syndrome, particularly when the myxoma is solitary, can prevent misdiagnosis of intramuscular myxomas (especially when large) as malignant mesenchymal tumors containing myxoid tissue. The recognition of this entity is important for appropriate management of the patient. Patients with soft tissue myxomas should be thoroughly examined for fibrous dysplasia. The greater risk of sarcomatous transformation in fibrous dysplasia with Mazabraud's syndrome should be kept in mind. Therefore, detecting who are at risk of developing FD in those patients who have IM, especially those with multiple IM, and taking appropriate management measures can help to get better outcome.