Familial Osteosarcoma in a large pedigree: A case report

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Osteosarcoma is a primary cancer of bones characterized by the direct development of immature bone or osteoid tissue by the tumor cells. A high malignancy with a rare prevalence (۰٫۲٪ of all cancers) has been reported for the classic osteosarcoma. The age within ۱۰-۲۵ is the most possible time for onset the disease.

We report a large family in which ۱۶ of ۳۳ members, over three generations, presented ۱۷ malignancies. Seven cases were osteosarcoma, with the average age of presentation at ۲۳ years (range within ۴۵-۱۲ years. The tumors had been located in pelvis (۳ cases), jaw (۲ cases), tibia and shoulder (both one case). Moreover, ۶ and ۳ patients had been affected with brain and larynx tumors, respectively. Importantly, osteogenic sarcomas had been appeared in successive generations. It could imply to hereditable predisposition to living or nonliving carcinogens. An awareness of this entity could lead to early detection of cancer in at-risk family members.

Familial osteosarcoma could be attributed to Li-Fraumeni syndrome (germline *TP۵۳* inactivation),hereditary retinoblastoma (germline *RB۱* inactivation), Rothmund-Thomson syndrome (germline *RECQL۴* inactivation), or Bloom or Werner syndrome (germline *BLM* or *WRN* inactivation, resp.). All these familial syndromes are related to the heritable pathogenic gene variants leading to the genomic instability.

A comprehensive genetic counseling and testing should be offered to the at-risk individuals for identification of the likely carriers. A complete Next Generation Sequencing panel including TP۵۳, *RECQL۴*, *BLM*, and *WRN* genes are suggested on genomic DNA of the patients.