Routine analysis of *BRCA1* and *BRCA2* genes in an Israelite Brazilian Hospital: results and peculiar clinical findings

Minillo RM (Hospital Israelita Albert Einstein, Brazil), Lima FT (Hospital Israelita Albert Einstein, Brazil), Oliveira PM (Hospital Israelita Albert Einstein, Brazil), Clozato CL (Hospital Israelita Albert Einstein, Brazil), Francisco RS (Hospital Israelita Albert Einstein, Brazil, Val FC (Hospital Israelita Albert Einstein, Brazil), Cervato MC (Hospital Israelita Albert Einstein, Brazil), Muto NH (Hospital Israelita Albert Einstein, Brazil), Guendelman RAK (Hospital Israelita Albert Einstein, Brazil), Pinho JRR (Hospital Israelita Albert Einstein, Brazil), Mangueira CLP (Hospital Israelita Albert Einstein, Brazil), Sitnik R (Hospital Israelita Albert Einstein, Brazil).

Background: Germline inactivating variants in the tumour suppressor genes *BRCA1* and *BRCA2* confer high lifetime risks of breast cancer, ovarian cancer and less frequently also other cancers. Pathogenic variants in these genes explain only approximately 20% of familial breast cancer. While the association of variants in these genes with breast and ovarian cancer risks is well-defined, the potential association of these mutations with other cancers is inconsistent. Here we present the prevalence of pathogenic variants in these genes, screened on routine basis at our laboratory, and describe 3 patients with BRCA2 pathogenic variants that attract attention. **Hypothesis:** To determine the prevalence of pathogenic variants in *BRCA1* and *BRCA2* genes in our laboratory and to present peculiar clinical findings in 3 patients with *BRCA2* variants. **Methods:** Retrospective analysis of 41 cases referred for comprehensive *BRCA1* and *BRCA2* analysis from March to December 2015. **Results:** Among the 41 samples, 6 unique pathogenic variants (14,6%) were identified, 3 (50%) in *BRCA1* and 3 (50%) in *BRCA2.* Although the patients with *BRCA1* mutations present compatible tumor phenotypes, the patients with *BRCA2* mutations deserves special consideration. Two patients present with unforeseen tumors. The c.2T>G pathogenic variant was found in a male with breast cancer and inguinal mesenchymal neoplasia with muscular differentiation, an unusual tumor associated with this gene. The second one was screened for genetic tumor testing for synovial sarcoma, that revealed the pathogenic founder variant of the Ashkenazi population c.5266dupC, latter confirmed as a germline mutation. The third patient harbored the variant c.3847_3848delGT presented ovarian cancer at age 80 years and had a history of her mother and daughter with breast cancer at much younger age, suggesting that this phenotypic variability may be associated with risk modifiers, as previously hypothesized. **Conclusions:** Understanding the prevalence of mutations found in routine analysis may help guiding ordering physicians on testing criteria and expected results. Unforeseen clinical tumor phenotypes may shed light on tumor scope and presentation associated with *BRCA1* and *BRCA2* variants.