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REVIEW ARTICLE

Prevalence of Y-chromosome sequences and gonadoblastoma in Turner syndrome

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KEYWORDS
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Polymerase chain reaction;
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Abstract
Objective: To assess the prevalence of Y-chromosome sequences and gonadoblastoma in patients with Turner syndrome (TS) using molecular techniques.
Data source: A literature search was performed in Pubmed, limiting the period of time to the years 2005–2014 and using the descriptors: TS and Y sequences (n=26), and TS and Y-chromosome material (n=27). The inclusion criteria were: articles directly related to the subject and published in English or Portuguese. Articles which did not meet these criteria and review articles were excluded. After applying these criteria, 14 papers were left.
Data synthesis: The main results regarding the prevalence of Y-chromosome sequences in TS were: (1) about 60% of the studies were conducted by Brazilian researchers; (2) the prevalence varied from 4.6 to 60%; (3) the most frequently investigated genes were *SRY*, *DYZ3* and *TSPY*; (4) seven studies used only polymerase chain reaction, while in the remaining seven it was associated with FISH. Nine of the 14 studies reported gonadectomy and gonadoblastoma. The highest prevalence of gonadoblastoma (33%) was found in two studies. In five out of the nine papers evaluated the prevalence of gonadoblastoma was 10–25%; in two of them it was zero.
Conclusions: According to these data, molecular analysis to detect Y-chromosome sequences in TS patients is indicated, regardless of their karyotype. In patients who test positive for these sequences, gonadoblastoma needs to be investigated.

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PALAVRAS-CHAVE
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Reação em cadeia da polimerase;
Disgenesia gonadal

Prevalência de sequências do Y e de gonadoblastoma em síndrome de Turner

Resumo
Objetivo: Apresentar a prevalência de sequências do cromossomo Y por técnicas moleculares e de gonadoblastoma em pacientes com síndrome de Turner.
Fontes de dados: Foi feita uma pesquisa bibliográfica no Pubmed, com limite de período entre 2005 e 2014, com os descritores *Turner syndrome* and *Y sequences* (n=26) e *Turner syndrome* and *Y chromosome material* (n=27). Os critérios de inclusão foram artigos que tivessem relação direta com o tema e publicados no idioma inglês ou português. Foram excluídos aqueles que não cumpriram esses critérios e eram do tipo revisão. Após aplicação desses critérios, 14 foram selecionados.
Síntese dos dados: Os principais resultados quanto à prevalência de sequências do cromossomo Y em síndrome de Turner foram: 1 – cerca de 60% dos estudos foram feitos por pesquisadores brasileiros; 2 – a frequência variou de 4,6 a 60%; 3 – os genes *SRY*, *DYZ3* e *TSPY* foram os mais investigados; 4 – a técnica de PCR foi empregada exclusivamente em sete estudos e nos sete restantes, associada à FISH. Nove dos 14 estudos apresentaram informações sobre gonadectomia e gonadoblastoma. Dois estudos relataram a maior prevalência para gonadoblastoma (33%). Cinco dos nove estudos referiram prevalência de 10 a 25% e em dois esse valor foi nulo.
Conclusões: De acordo com os dados apresentados, é indicada a pesquisa molecular para sequências do cromossomo Y em pacientes com ST, independentemente do cariótipo. Naquelas com positividade para essas sequências, é necessária a investigação de gonadoblastoma.

Introduction

Turner syndrome (TS) is a chromosomal disorder with an incidence of 1:2500 girls; its etiology is associated with total or partial X-chromosome monosomy and the diagnosis is made by karyotype testing.[1,2] A retrospective study of 260 patients with TS showed that the improvement in chromosomal analysis provided a change in the proportion of observed karyotype types.[3]

Patients with TS exhibit have short stature and gonadal dysgenesis as main clinical signs. They also may have low hairline at the nape of the neck, strabismus, ptosis, high-arched palate, micrognathia, short and/or webbed neck, lymphedema of hands and/or feet, metacarpal and/or metatarsal shortening, Madelung deformity, *cubitus valgus*, *genu valgum*, scoliosis and multiple pigmented nevi, cardiovascular and renal disorders, thyroid disorders, hearing impairment, hypertension, osteoporosis, and obesity.[1,2] However, this syndrome is characterized by wide phenotypic variability, from patients with the classic phenotype to those almost indistinguishable from the general population.

Women with TS who have Y chromosome material are at increased risk of developing gonadal tumors, such as gonadoblastoma and dysgerminoma. Gonadoblastoma is a benign gonadal tumor with a high potential for malignancy; it can differentiate into invasive dysgerminoma in 60% of cases and also in other forms of malignant tumors. About 90% of patients with gonadoblastoma have Y-chromosome material in their genetic makeup. Therefore, sequence detection of Y-chromosome by cytogenetic and/or molecular techniques in patients with TS is critical. In positive cases, prophylactic removal of gonads has been indicated.[4] Two recently published retrospective studies showed Y chromosome material frequencies in TS by classical cytogenetics of 6.6% (4/61)[5] and 7.6% (12/158).[6] In one such study, 33% of patients (4/12) had gonadoblastoma and in two patients it progressed to disgerminona or teratoma.[6] In another study with 11 patients with sexual differentiation disorders, 7 had Turner phenotype and mosaic karyotype Y in peripheral blood.[7] All patients with TS underwent gonadectomy, and histopathological findings revealed that four of them (57.1%) had gonadoblastoma, and in two cases it was associated with dysgerminoma.[7] Regarding the classical cytogenetic analysis by GTG banding, peripheral blood lymphocytes are the material of choice because it is easy to harvest this tissue, and the analysis is usually performed in 30 metaphases, which allows detection of 10% of mosaicism.[8] The advantage of molecular methods is that it require no cell culture and only a small sample for analysis and are more sensitive to detect low mosacismo, frequent in TS.[8]

Thus, the aim of this review is to present the prevalence of Y chromosome sequences by molecular techniques and gonadoblastoma in patients with TS.

Method

A literature search was performed on Pubmed, on 10/24/2014, with time limit between 2005 and 2014. Fig. 1 shows the flowchart of this electronic search.

Results

Table 1 shows the frequency of Y chromosome sequences, identified by molecular techniques, of the 14 selected