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Risk of cancer in adult people diagnosed with infantile autism in childhood: A longitudinal case control study based on hospital discharge diagnoses

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ABSTRACT

Research dealing with adults with autism spectrum disorders (ASD) noticeably lags behind studies of children and young individuals with ASD. The objective of this study is to compare the incidence and types of cancer in a clinical sample of 118 adult people diagnosed with infantile autism (IA) in childhood with 336 sex and age matched controls from the general population. All participants were screened through the nationwide Danish National Hospital Register. The average study interval of both groups was 37.2 years, and mean age at follow-up was 49.6 years. Of the 118 people with IA, 8 (6.8%) were registered with at least one cancer diagnosis against 17 (5.1%) in the comparison group ($p = 0.49$; OR = 1.4; 95% CI 0.6–3.3). Significant group differences were also lacking with respect to specific cancer types.

1. Introduction

Infantile autism (IA) belongs to a group of complex lifelong neurodevelopmental disorders, which are classified as pervasive developmental disorders (PDD) or autism spectrum disorders (ASD), of which IA forms the main prototype. IA is analogous to childhood autism as defined in ICD-10 (World Health Organization (WHO), 1992) and autistic disorder in DSM-IV-TR (American Psychiatric Association, 2000). The diagnosis is based on clinical criteria and is characterized by qualitative impairments in reciprocal social interaction, communication and the presence of a restricted repertoire of activities (WHO, 1992). The estimated prevalence of ASD has been increasing during the last decades, and accumulating evidence suggests that about 1% of children in developed countries are affected by ASD (Baxter et al., 2015). In a Danish population-representative study, Petersen, Bilenberg, Hoerder, and Gillberg (2006) found that the prevalence of ASD in Danish 8–9-year-old children was 1.1%. Estimates in adult populations support a similar prevalence (Brugha et al., 2011). While ASD affects individuals of all ages, the current research is heavily focused on children (Jang et al., 2014). As most cancers are diagnosed in people older than 45 years of age (Storm, 2007) it follows that little is known about cancer risk in adult people with ASD.

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Chiang et al. (2015) used data from the Taiwan National health Insurance database, when they studied cancer risk in 8438 individuals (6931 males and 1507 females) who were registered in the database with ASD in the years 1997–2011. The participants had a median age of 5.3 years at diagnosis. The median follow-up period was 9.1 years. During the observation period cancer was diagnosed in 20 individuals (16 males and 4 females) with ASD, when only 10.3 cases were expected, resulting in a standardized incidence ratio (SIR) of 1.94 (95% CI 1.18–2.99). The observed number of cancer in males was significantly greater than the expected number with a SIR of 1.95 (95% CI 1.11–3.16). An excess risk was also found for females with a SIR of 1.91 (95% CI 0.52–4.88), but statistically insignificant. Stratification according to sex and age at cancer diagnosis showed that the excess was largely conferred by males and by the age group of 15–19 years old. Five males and two females were diagnosed with a cancer disease within this age range. Significant differences were found regarding cancers of genitourinary system. Four cases were observed (two cases of ovarian cancer and two cases of testis cancer), when only 0.96 cases were expected; SIR 4.15; 95% CI 1.13–10.65; $p = 0.03$. Significant increased risk for specific cancer types was found only for ovarian cancer, where two cases were observed, when only 0.22 cases were expected; SIR 9.21; 95% CI 1.12–33.29; $p = 0.04$.

In yet another study, Atladottir, Schendel, Lauritsen, Henriksen, and Parner (2012) used Danish nationwide registers in a population based study of ASD and all kinds of co-occurring somatic diseases. The study included all 604,104 children born in Denmark during the period from 1994 through 2002 inclusive. Contact with hospital for any neoplasms (ICD-10 codes C00-D48) was not associated with a diagnosis of ASD, neither with respect to the entire ASD diagnostic group (ICD-10 codes F84.0, F84.1, F84.5, F84.8 and F84.9), or the IA subgroup (ICD-10 code F84.0).

Looking the other way round, Blatt et al. (2010) studied the prevalence of ASD in 702 pediatric cancer patients (2–18 years old) in the pediatric cancer database, at the University of North Carolina at Chapel Hill, USA. The participants were followed over a 10 year period (1997–2007). At the end of the study interval 7 (1.0%) of the 702 patients (four males and three females) with cancer had a diagnosis of ASD. This was not significantly different from the prevalence of ASD among 8-year olds in North Carolina's general population, which was 0.65%.

Mortality is significantly increased in people with ASD, with death rates being about two times or more higher than among people of the same age and sex in the general population (Mouridsen, 2013). Some of the mortality studies conducted among people with ASD have provided risk estimates for mortality for cancer. Notably, Shavelle, Strauss, and Smith (2001) reported an elevated standardized mortality rate of cancer in individuals with ASD as 1.9 in those who had no or mild learning disabilities and up to 2.9 in those who had moderate to profound learning disabilities. However, the number of deaths were small in each of the two categories (6 and 15), and the population was relatively young, with over 80% under age 15 years. Deaths due to cancer have also been reported in the mortality studies of Mouridsen, Brønnum-Hansen, Rich, and Isager (2008) and Bilder et al. (2013). However, due to the small number of cases studied it was not possible to calculate whether individuals with ASD had increased risk of dying of cancer relative to the general population.

Finally, the difficult task of treating cancer in people with a severe ASD has been in focus in a few studies. Radcliff (2013) reported on a 44 old women with severe autism and breast cancer. Based on a detailed case description the author wanted to call attention to the many different problems facing the caregivers when deciding how to treat a person, who would not allow physical examination and stroked out when strangers tried to touch her. Moreover, she was nonverbal and unable to participate in decision making. In a similar case report Dell et al. (2008) described the challenges facing a 28 old nonverbal male with ASD undergoing surgery for testicular cancer.

From a public health perspective, early identification of people with cancer has important implications for the prognosis and treatment of the disease. From a research perspective, diagnosis of co-occurring diseases may suggest that the diseases have a shared biology (Crespi, 2011). In this vein, the androgen theory of ASD propose that testosterone and other hormones may play a role in the etiology of ASD (Baron-Cohen et al., 2015), and that cancer rates could be elevated in people with ASD for cancers whose development is potentiated or mediated by testosterone and other sex steroids, such as cancers of the breast, ovary, and uterus (Ingudomnukul, Baron-Cohen, Wheelwright, & Knickmeyer, 2007).

The purpose of the present study is to expand on the aforementioned information on cancer risk among children, adolescents, and young adults with ASD, as we have the possibility to study the incidence and types of cancer in a group of adult people with a mean age of 49.6 years. In the following we present the results from a longitudinal study comparing the incidence and types of cancer in 118 individuals originally diagnosed with IA in childhood with 336 matched controls from the general population, using data from the nationwide Danish National Hospital Register (DNHR) covering an average study interval of 37.2 years.

2. Participants and methods

2.1. Case group

The case group was recruited from the population of patients consecutively attending the Departments of Child Psychiatry in the university hospitals of Copenhagen (the capital of Denmark) and Aarhus (the second largest city in Denmark) from 1960 through 1984 inclusive. The clinics provided services to the entire population of Denmark. In 1985 the first two authors rediagnosed case records of all patients who had been given a diagnosis of 'childhood psychosis'—the ICD-8 term for ASDs including 'borderline autistic condition' in accordance with ICD-9 (WHO, 1978) criteria. They were selected at that time to participate in a study on parental age (Mouridsen, Rich, & Isager, 1993). The core symptomatology of IA