Low platelet count in a 22q11 deletion syndrome subtype of schizophrenia*

K. Lazier, E.W.C. Chow, P. AbdelMalik, L.E. Scutt, R. Weksberg, and A.S. Bassett

Abstract

**Background**—22q11 Deletion Syndrome (22qDS) is a genetic syndrome associated with various physical features and schizophrenia. Some reports have identified thrombocytopenia (platelet count <150 × 10^9/l) in individuals with 22qDS, especially children. We investigated whether adults with 22qDS and schizophrenia (22qDS-SZ) have lower platelet counts than other patients with schizophrenia (SZ).

**Method**—Complete blood counts (CBC) were recorded from medical records for 18 22qDS-SZ and 60 SZ subjects. Five CBCs per subject were randomly selected and used to calculate a within-subject mean for analyses.

**Results**—22qDS-SZ subjects had significantly lower mean platelet counts than comparison SZ subjects (142.2 × 10^9/l versus 282.5 × 10^9/l, t = −11.5, p < 0.0001). Ten 22qDS-SZ (55%) and no comparison subjects had thrombocytopenia.

**Conclusions**—These results suggest that thrombocytopenia may be a common feature of 22qDS and that low platelet counts may comprise a readily available screening criterion to help identify this genetic syndrome among adults with schizophrenia.

**Keywords**

22q deletion syndrome; Platelets; Schizophrenia; Thrombocytopenia; Velocardiofacial syndrome

1. Introduction

22q11 Deletion Syndrome (22qDS), also known as DiGeorge or velocardiofacial syndrome, is a genetic syndrome associated with a microdeletion on chromosome 22. Twenty-five per

---

*Funded in part by the Ontario Mental Health Foundation, the Scottish Rite Schizophrenia Program, the Institute of Medical Science at the University of Toronto (K.L.) and by an Independent Investigator Award from the National Alliance for Research on Schizophrenia and Depression (A.S.B.).

**Corresponding author. Schizophrenia Research Program, Queen Street Division, Centre for Addiction and Mental Health, Toronto, Ontario, Canada, M6J 1H4. Tel.: +1-416-535-8501 ext. 2731; fax: +1-416-535-7199. anne.bassett@utoronto.ca (A.S. Bassett).
cent of patients with 22qDS are estimated to develop schizophrenia and a minority of patients with schizophrenia have 22qDS (Bassett and Chow, 1999; Murphy et al, 1999). Clinical screening criteria have been developed to detect this genetic subtype of schizophrenia (Bassett and Chow, 1999). However, because the phenotype is variable and sometimes subtle, the syndrome is under-recognized, especially in adults (Cohen et al, 1999). Patients with 22qDS may have learning difficulties, mild dysmorphic facial features, palatal anomalies, cardiac or other congenital defects, hypocalcemia and, in some cases, thrombocytopenia (Cohen et al., 1999). A pediatric study of 22qDS found reduced platelet counts and increased mean platelet volume but no increased bleeding tendency (Van Geet et al., 1998). Platelet counts have not been systematically investigated in adults with 22qDS. The purpose of this study was to determine whether adults with a 22qDS subtype of schizophrenia (22qDS-SZ) have lower platelet counts than a random sample of adults with schizophrenia.

2. Methods and materials

Patients suspected to have 22qDS and meeting proposed clinical screening criteria (Bassett and Chow, 1999), that did not include any blood count information, were referred from psychiatrists. Eighteen (8 male, 10 female) subjects were confirmed have 22q11.2 deletions by standard chromosomal studies using fluorescence in situ hybridization. These subjects were compared with 60 (38 male, 22 female) subjects randomly selected from patients with schizophrenia at a chronic psychiatric hospital. All subjects met DSM-IV criteria for schizophrenia or schizoaffective disorder. Written informed consent was obtained from all subjects.

For each subject, using available medical records, we recorded complete blood counts (CBC), including platelet, white blood cell (WBC) and red blood cell (RBC) counts, as well as medical history and medications used at the time of each CBC. From 1 to 453 CBCs were initially available from the 78 subjects in the entire sample. Platelet levels do not usually vary with sex or age, but may be affected by acute or chronic conditions such as infection, cancer, alcoholism or bleeding (Stenberg and Hill, 1999). We therefore examined the pattern of platelet counts for each subject over time and excluded outlying CBCs taken when the subject was experiencing one of these platelet-influencing medical conditions. A total of 43 CBCs were excluded, due to cancer (32 counts from two comparison SZ subjects), bleeding (8 counts from comparison three SZ subjects), and infection (3 counts from two 22qDS-SZ subjects); none of the subjects had active alcoholism. After these exclusions, most subjects had five or more remaining CBCs available. We therefore randomly selected five CBCs for the 60 subjects with five or more available CBCs and used these to calculate mean blood counts for each subject. For subjects with fewer than five CBCs, we calculated means from all available CBCs. The two subject groups did not differ in the mean number of CBCs used per subject (3.9, SD 1.5, versus 4.5, SD 1.2, for 22qDS-SZ and comparison SZ groups, respectively; t = −1.27, p = 0.22). We used mean individual blood counts for all analyses, t-tests to compare mean blood counts between groups, χ² to analyze categorical variables, and Pearson correlations to assess the influence of age.

Schizophr Res. Author manuscript; available in PMC 2011 September 08.
3. Results

The 22qDS-SZ group had significantly lower mean platelet counts than the comparison group (142.2 × 10^9/l, SD 37.0 × 10^9/l versus 282.5 × 10^9/l, SD 66.7 × 10^9/l; t = −11.5, p < 0.0001). There was no difference in sex distribution between the two groups (χ² = 2.0, df = 1, p = 0.2). Age was not significantly correlated with platelet count in the comparison SZ group (r = 0.007, p = 0.9). However, there was a trend for lower platelet count with increasing age in the 22qDS-SZ group (r = −0.2, p = 0.06), even though the ages at which CBCs were recorded in the 22qDS-SZ group (mean 28.0 yr, SD = 7.0) were younger than the comparison SZ group (mean 40.2 yr, SD = 10.8; t = −11.5, p < 0.0001). WBC counts (6.3 × 10^9/l, SD 2.2 × 10^9/l versus 8.2 × 10^9/l, SD 2.1 × 10^9/l; t = −3.3, p = 0.003) and RBC counts for males (4.5 × 10^12/l, SD 0.3 × 10^12/l versus 4.9 × 10^12/l, SD 0.5 × 10^12/l; t = −2.6, p = 0.02) and females (4.1 × 10^12/l, SD 0.2 × 10^12/l versus 4.5 × 10^12/l, SD 0.4 × 10^12/l; t = −3.6, p = 0.001) were also lower in the 22qDS-SZ group.

Psychotropic medications may affect platelet counts (Stemberg and Hill, 1999). To control for these possible effects on results, we identified two medications, risperidone and clonazepam, that were used concurrently with the assessment of a CBC a significantly higher proportion of the time in the 22qDS-SZ group (risperidone: χ² = 17.6, df = 1, p = 0.00002; clonazepam χ² = 6.7, df = 1, p = 0.009), and that involved two or more (>10%) subjects in the 22qDS-SZ group. We recalculated mean individual platelet counts after excluding the 52 CBCs associated with these two medications (23 from ten 22qDS-SZ and 29 from 16 comparison SZ group subjects) and found that mean platelet counts remained significantly lower in the 22qDS group (149.4 × 10^9/l, SD = 68.0 × 10^9/l versus 283.5 × 10^9/l, SD = 68.0 × 10^9/l; t = −10.4, p < 0.0001).

Ten 22qDS-SZ subjects (55%) and none of the comparison group had mean platelet counts below the normal range (150–450 × 10^9/l) (see Fig. 1). There was no evidence in medical records of bleeding problems or splenomegaly (conditions associated with thrombocytopenia) in any of these subjects, or alcoholism or other chronic diseases that might have accounted for low platelet counts in the 22qDS-SZ group. Bone marrow biopsies and other investigations were available on three thrombocytopenic subjects. These revealed normal megakaryocytes, and normal immunoglobulin electrophoresis and platelet antibody titer results in one thrombocytopenic subject, and increased megakaryocytes in another. The latter subject and a third subject had increased mean platelet volumes.

4. Discussion

Results from this study suggest that adults with a 22qDS subtype of schizophrenia have significantly lower platelet and other blood counts than a comparison group. Over half of 22qDS-SZ subjects had asymptomatic thrombocytopenia. These findings are consistent with some preliminary reports of 22qDS (Cohen et al., 1999; DePiero et al., 1997; Lévy et al., 1997; Van Geet et al., 1998). A limitation of this study is that comparison group subjects were not tested for 22q11.2 microdeletions, though undetected 22qDS subjects in the comparison group would have reduced true differences between the groups. Also, the reliance on medical records might have resulted in missing some concurrent platelet-
influencing conditions. However, the use of random sampling and averaging of individual CBCs should have minimized the effect of possible uncontrolled variables.

Low platelet levels can result from decreased production in bone marrow, increased destruction, or increased splenic sequestration (Stemberg and Hill, 1999). The cause of thrombocytopenia in 22qDS is unknown, and results from this preliminary study cannot distinguish between these possible mechanisms. Decreased levels of all blood cell types suggest decreased bone marrow production. However, the megakaryocyte and mean platelet volume findings are consistent with premature release of platelets into the periphery that may accompany autoimmune platelet destruction. The possibility of decreasing platelet numbers with increasing age in the 22qDS-SZ group may also be consistent with this mechanism. Although other studies have not detected anti-platelet antibodies (Van Geet et al., 1998), autoimmune disorders are found in 22qDS (DePiero et al., 1997) and this remains an area of interest for future studies.

Results of this study suggest that low platelet counts may be associated with 22qDS in schizophrenia. Further studies could determine whether thrombocytopenia would be useful as an additional screening criterion for a 22qDS subtype of schizophrenia (Bassett and Chow, 1999).

Acknowledgments

The authors thank the many clinicians who assisted in the collection of data for the study.

References


Fig. 1.
Distribution of mean individual platelet counts in 18 subjects with a 22q11 Deletion Syndrome subtype of schizophrenia (22qDS-SZ) and 60 comparison schizophrenia (SZ) subjects. Black bars indicate subjects with 22qDS; white bars indicate comparison SZ subjects. Mean individual platelet counts were determined from a maximum of five CBCs for each subject.