to females which suggests X linked dominant transmission with lethality in the hemizygous male. Other authors think that multifactorial inheritance is more likely. Further reports are necessary to establish the incidence of subluxation of the lens and facial paralysis in this syndrome.

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P Strisciuglio,* V Raia,* A Di Meo,† E Rinaldi,† and G Andria*
*Department of Pediatrics, 2nd Faculty of Medicine, and †Department of Ophthalmology, 1st Faculty of Medicine, University of Naples, Italy.

References

Requests for reprints to Dr P Strisciuglio, Department of Pediatrics, 2nd Faculty of Medicine, University of Naples, Via Pansini 5, 80131 Naples, Italy.

Δβ-thalassaemia in Sicily: report of a case of double heterozygosity for AγΔβ-thalassaemia and AγGγΔβ-thalassaemia

SUMMARY A case of double heterozygosity for AγΔβ-thalassaemia and AγGγΔβ-thalassaemia was found during a screening programme in Sicily. The proband, a 4-year-old girl, showed a clinical picture of thalassaemia intermedia. Hb F (85–12% by the Singer method) was GγAγ type. The parents and the brother were Δβ-thalassaemia carriers. Structural analysis of Hb F showed both Gγ and Aγ chains in the father, but only Aγ chains in the mother.

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δβ-thalassaemia can be divided into GγAγ δβ-thalassaemia and Gγ δβ-thalassaemia depending on the structural analysis of Hb F. The severity of δβ-thalassaemia is correlated with the extent of the deletion of the non-α globin gene complex and consequently with the different degrees of γ locus activation. Amin et al. suggested that the Gγ form of δβ-thalassaemia can be more severe clinically than GγAγ δβ-thalassaemia. Recently Cao et al. observed Aγ δβ-thalassaemia where no gene deletion appeared to be responsible for the molecular defect. We present the clinical and haematological data of a family with δβ-thalassaemia recently identified in Sicily. The proband is a double heterozygote for Aγ and GγAγ δβ-thalassaemia.

**Case report**

The family pedigree is shown in fig 1. The proband, a 4-year-old girl, came to us because of pallor. She had mild icterus and her face showed slight signs of Cooley’s disease. Her spleen was palpable 2 cm below the costal margin. Her growth was moderately retarded when compared with girls of the same age. Haematological data are shown in the table. The girl had moderate anaemia but had never required blood transfusions. Electrophoretic analysis of Hb F showed only Hb F (85·12 % by the Singer method), and gel acrylamide electrophoresis indicated that both Gγ and Aγ chains were present with a ratio of 51:49 (fig 2). The distribution of Hb F was unevenly pancellular. Globin chain synthesis in the bone marrow was more unbalanced than in the peripheral blood.

Both the parents and the brother were found to be δβ-thalassaemia carriers with normal Hb A2 and increased Hb F levels (table). The Hb F structural analysis showed the presence of Gγ and Aγ chains in the father, but only Aγ chains in the mother (fig 2). The distribution of Hb F was heterocellular in both the parents after acid elution, while it was

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**TABLE Haematological data in the family.**

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (yr)</th>
<th>Hb (g/dl)</th>
<th>RBC (×1012/l)</th>
<th>MCH (pg)</th>
<th>MCV (fl)</th>
<th>Morphological alterations</th>
<th>Hb F (%)</th>
<th>Hb A2 (%)</th>
<th>Globin chain synthesis Non-α/ɑ ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>I-1</td>
<td>41</td>
<td>13</td>
<td>4·8</td>
<td>27</td>
<td>83</td>
<td>± ± ±</td>
<td>17·48</td>
<td>2·45</td>
<td>0·83 0·65</td>
</tr>
<tr>
<td>I-2</td>
<td>38</td>
<td>12</td>
<td>4·3</td>
<td>27·9</td>
<td>86</td>
<td>± ± ±</td>
<td>8·00</td>
<td>2·72</td>
<td>0·71 0·70</td>
</tr>
<tr>
<td>II-1</td>
<td>10</td>
<td>12</td>
<td>4·2</td>
<td>28·6</td>
<td>80</td>
<td>± ± ±</td>
<td>14·78</td>
<td>2·42</td>
<td>0·83 0·67</td>
</tr>
<tr>
<td>II-2</td>
<td>4</td>
<td>9·5</td>
<td>3·5</td>
<td>27·2</td>
<td>60</td>
<td>+ + +</td>
<td>85·12</td>
<td>—</td>
<td>0·39 0·30</td>
</tr>
</tbody>
</table>

H = hypochromia
A = anisocytosis
P = poikilocytosis
T = target cell
PB = peripheral blood
BM = bone marrow

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**FIG 2** Globin polyacrylamide electrophoresis in the mother (a), the proband (b), and the father (c).
irregularly pancellular in the mother and hetero-
cellular in the father after immunofluorescence
(fig 3). Globin chain synthesis showed an un-
balanced non-α/α ratio in both peripheral blood
and bone marrow of the heterozygous members of
the family.

Discussion

The study of this family indicates that the proband
is a double heterozygote for Aγ and GγAγ δβ-thalas-
saemia. In this patient the clinical picture is more
severe than in the three sisters with homozygous
GγAγ δβ-thalassaemia previously identified in
Sicily.4–6 This is probably the result of the extent of
the molecular defect which also involves one Gγ
gene in our patient. The Hb F level was lower and the
non-α/α ratio in peripheral blood was more un-
balanced in the mother than in the father and
brother. The distribution of Hb F in the blood cells
was heterocellular in the father, a GγAγ δβ-thalas-
saemia carrier, while it was irregularly pancellular
in the mother, an Aγ δβ-thalassaemia carrier. This
finding is similar to that found by Matthews et al7
in heterozygotes for Gγ δβ-thalassaemia.

Aγ δβ-thalassaemia, which is the least common
form of δβ-thalassaemia, could be the result of either
an unequal crossing over in the non-α globin gene
complex or of an interstitial deletion.

Gene mapping studies could define the molecular
basis of this case of double heterozygosity for Aγ
and GγAγ δβ-thalassaemia, which is the first to be
reported so far.

S MUSUMECI, M A ROMEO,
G PIZZARELLI, G SCHILIRO,
AND G RUSSO

From the Department of Pediatrics,
University of Catania, Catania, Italy.

References

1 Weatherall DJ, Clegg JB. The thalassaemia syndromes.
2 Amin AB, Pandya NL, Diwin PP, et al. A comparison of
the homozygous states for Gγ and GγAγ δβ-thalassaemia.
3 Cao A, Furbera M, Galanello R, Pirasu MA. Applica-
zioni attuali e future dei recenti progressi di biologia
4 Silvestrini E, Bianco I, Reitano G. Three cases of
homozygous δβ-thalassaemia (or microcythaemia) with
high Hb F in a Sicilian family. Acta Haematol 1968;40:
220–9.
6 Ramirez F, O’Donnell JV, Marks PA, et al. Abnormal or
absent m-RNA in β0 Ferrara and gene deletion in δβ-
7 Matthews JH, Rowlands D, Wood JK, Wood WG.
Homozygous Gγ δβ-thalassaemia. Clin Lab Haematol

Requests for reprints to Dr S Musumeci, Clinica
Pediatrica dell’Università, Viale Andrea Doria 6,
Catania, Italy.

Note added in proof

Another two cases of Aγδβ-thalassaemia with low
levels of Hb F were recently reported by Cao et al
analysis in these patients excluded the presence of
large gene deletion or gross rearrangement within
the non-α globin cluster (Ottolenghi et al. Proc Natl
Acad Sci USA, in press).