Bone marrow failure in McCune Albright Syndrome

K. Wechsung, E. Lankes, P. Kühnen, A. von Stackelberg, D. Schnabel
Center for Chronic Sick Children, Pediatric Endocrinology, Pediatric Hematology/Oncology
Charité University Medicine Berlin, Germany

Introduction and objectives
McCune Albright Syndrome (MAS) is caused by a somatic activating mutation at the GNAS locus. Clinical manifestations range from the classic triad including café au lait macules, fibrous dysplasia and precocious puberty to a severe multisystem disease.

Methods
We present a patient with bone marrow failure as a rare non-endocrine complication of MAS.

Clinical case
A 14 year old girl with a multisystem manifestation of MAS (Table 1, Figure 1) felt weak and exhausted. Her blood count showed pancytopenia (WBC 2.23 [10^3/μL], RBC 3.16 [10^6/μL], PLT 92 [10^3/μL]).

- Cell morphology: anisopoikilocytosis, dacrocyes and a left shift
- Clinical chemistry: unremarkable
- Screening for infection: no signs for Hepatitis A,B,C, EBV, HIV, CMV
- Bone marrow biopsy: osteo-fibrous lesions with markedly reduced cell count, FISH: no signs for myelodysplastic syndrome, PCR: mutation in GNAS Locus: (c.601C>T,p.R201C)
- Abdominal CT: massive splenomegaly (max. 166mm), no sign of intraabdominal tumour, deformed axial skeleton with inhomogeneous, fibrous bone structure in all visible bones (Figure 1c).

The splenomegaly progressed and regular transfusions had to be started (Figure 2, 3). The patient developed dyspnoea and abdominal pain. Therefor at the age of 17 a splenectomy was performed. Histology confirmed extramedullary haematopoeisis in the spleen. The blood count recovered completely after splenectomy. No further transfusions were necessary (now 1 ½ years after operation).

Conclusions
In fibrous dysplasia undifferentiated bone marrow stromal cells replace the hematopoietic marrow. Nevertheless bone marrow failure rarely occurs in patients with MAS.

Whether the extent of fibrous dysplasia / bone reconstruction surgery, the presence of endocrinopathies or a different mechanism triggered the onset of bone marrow failure in our patient remains open.

Four case reports of patients with MAS and extramedullary splenic haematopoeisis which improved after splenectomy exist (1-4). Hyperthyroidism is described in all of these patients. The endocrinopathies in our patient were well controlled at the onset of pancytopenia. But a breast duct papilloma was resected shortly before, which might have caused haematopoietic stress.

Table 1 Manifestations of MAS in the patient with age at onset and treatment

<table>
<thead>
<tr>
<th>Manifestations of MAS</th>
<th>Onset</th>
<th>Therapy &amp; Course</th>
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<tbody>
<tr>
<td>Café au lait spots</td>
<td>birth</td>
<td>-</td>
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<tr>
<td>Neonatal giant cell heptitis</td>
<td>6 weeks</td>
<td>Resolved after antibiotic treatment</td>
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<tr>
<td>Precocious puberty</td>
<td>2 years</td>
<td>Anastrazole age 4-9, Suppressed vaginal bleeding until age 6</td>
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<tr>
<td>Fibrous dysplasia</td>
<td>1½ years</td>
<td>18 Operations, iv Bisphosphonate therapy</td>
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<tr>
<td></td>
<td></td>
<td>12 Fractures, severe short stature, scoliosis, wheel chair dependency</td>
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<tr>
<td>Hyperthyroidism</td>
<td>4 years</td>
<td>Methimazole age 8-11 and 15-17</td>
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<tr>
<td>PGF-23 mediated phosphate wasting</td>
<td>8 years</td>
<td>Oral phosphate, 1,25-(OH)2-vitamin D</td>
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<tr>
<td>Breast duct papilloma</td>
<td>14 years</td>
<td>Complete resection</td>
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