An Uncommon Cause of Low Oxygen Saturation in a Chinese Girl

YH LAW, MK TAY, DCY LAU

Abstract

Digital pulse oximetry is a useful non-invasive tool to monitor oxygen saturation. However, it has its own limitation and cannot reflect the true arterial oxygen saturation in case of unstable haemoglobin. We report a Chinese girl having unstable haemoglobin presenting with incidental finding of low oxygen saturation measured by pulse oximetry, its value in identifying affected family members and the importance of recognising unstable haemoglobin in patient with asymptomatic low oxygen saturation.

Key words

Hb Schlierbach; High oxygen affinity; Unstable haemoglobin

Case Report

A 5-year-old Chinese girl consulted Accident and Emergency Department for fever with oral ulcers. She was incidentally found to have low oxygen saturation of 86% in room air by digital pulse oximetry for which she was admitted with the diagnosis of herpetic gingivostomatitis and hypoxaemia. She enjoyed good past health. On examination, she was in good general condition without any respiratory distress. There was no cyanosis, pallor, jaundice or clubbing. Her vital sign and cardiopulmonary examination were normal except gum swelling and oral ulcers were noticed. 100% oxygen was administrated but oxygen saturation did not increase beyond 95%. The arterial blood gas analysis in room air was normal (PaO\textsubscript{2} 14.7, Pco\textsubscript{2} 4.0, pH 7.47 and measured oxygen saturation was 98.3%). Haemoglobin was 10.4 g/dL with slightly low MCV and normal MCH. Reticulocyte count was normal and blood film showed slight anisocytosis, microcytosis and hypochromasia. Liver and renal functions tests, methaemoglobin and G6PD level were normal. An electrocardiogram showed a normal sinus rhythm and chest radiography showed clear lung field and no cardiomegaly. On further questioning, mother reported patient’s maternal grandmother, maternal uncle and she also had low oxygen saturation in room air but all of them were asymptomatic and they were told by their medical doctor to be having benign haematological disorder. Child was further reviewed after recovery from gingivostomatitis, oxygen saturation was still 90% in room air but she was clinically well. She and her mother's blood were taken for haemoglobin analysis and showed HbA2 level was indeterminate by high performance liquid chromatography assay which was due to the presence of an abnormal peak overlapping the HbA2 area. However, in both acidic and alkaline haemoglobin electrophoresis, no abnormal band or smear pattern was detected. HbA and HbA2 bands were present with normal proportion. Both of them had positive result in heat instability test and isopropanol precipitation test. No abnormality was detected on sequencing of the alpha-1 and alpha-2 genes but both were heterozygous for codon 108 (AAC to ATC; Asn to Ile) of the beta-globin gene named as Hb Schlierbach as detected by sequencing of the beta globin gene.
Discussion

Digital pulse oximetry is a widely used as non-invasive instrument for monitoring the oxygen saturation in an indirect way by calculating the ratio of the pulsatile and the mean light absorbances at each wavelength to create a pulse-added absorbance signal, which is assumed to reflect the changes in the arterial blood volume in the tissue.

Hypoxaemia, undoubtedly, is the most important cause of low oxygen saturation and pulmonary disease is the most common cause of hypoxaemia. Other possible causes of hypoxaemia include hypoventilation, right-to-left shunting of blood, low cardiac output or cases in shock. The low oxygen saturation value while the patient was breathing room air is unexpected if he/she did not have any severe signs or symptoms of cardiac or pulmonary disease. Other possible causes of low oxygen saturation on pulse oximetry include abnormal haemoglobin variants, methaemoglobin or intravenous dyes (e.g. methylene blue). 1

In our case, child did not show any signs or symptoms of cardiac or pulmonary abnormal disease with normal methaemoglobin level and positive family history, haemoglobin variant is the most likely explanation for her asymptomatic low oxygen saturation. Child was finally confirmed to have unstable haemoglobin by the haemoglobin pattern and the unstable haemoglobin test.

The unstable haemoglobin disease is a disease due to structurally abnormal haemoglobin variant with substitution or deletion of the amino acid in the red blood cells. They are characterised by having inclusion of precipitated denatured haemoglobin called Heinz bodies in the red blood cells. Almost 200 unstable haemoglobins have now been identified and 100 of these haemoglobins can cause haemolysis or abnormal oxygen affinity and another 100 haemoglobins have no haematological abnormalities but was found to have instability only in vitro test. The inheritance pattern of the unstable haemoglobin is autosomal dominant, although de novo mutations can be occurred.

The degree of severity is highly variable in different unstable haemoglobins and it depends on the degree of instability of the abnormal protein. The clinical symptoms and signs ranged from mild anaemia detectable only on physical examination to a very severe hemolytic anaemia (Table 1). 2,3 Many of them have high oxygen affinity and therefore, it may not cause any anaemia and most patients have a mild compensated condition until it is exacerbated by infection or exposure to oxidative drugs and nitrates. In our case, Hb Schlierbach is characterised by reduced oxygen affinity (right shift of the oxyhaemoglobin dissociation curve). 4,5 therefore, incidentally found to have low oxygen saturation by digital pulse oximetry with normal arterial blood gas.

In establishing the diagnosis, first, a detailed history of the patient and his/her family members is very important regarding to any cardiorespiratory problems, family history of any similar condition and any previous history of haemolysis or any drug exposure. However, the history sometimes only provided little information. There are some laboratory findings in helping to make the diagnosis of unstable haemoglobins. The blood cells count and blood film may or may not be of value and it cannot be distinguishable from other non-spherocytic haemolytic anaemia. Haemoglobin level is extremely variable as mentioned before as some unstable haemoglobins have high oxygen affinity. Haemoglobin electrophoresis, HbF and HbA2 estimation are helpful and 50% of unstable haemoglobins migrate with HbA like adult Hb. The heat instability test is specific for unstable haemoglobin with

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Frequency %</th>
<th>Remarks</th>
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<tbody>
<tr>
<td>Neonatal jaundice</td>
<td>5</td>
<td>Unless severe haemolytic haemolysis at birth</td>
</tr>
<tr>
<td>Symptoms of anaemia</td>
<td>10</td>
<td>Variable; depends on the oxygen affinity or during exacerbation</td>
</tr>
<tr>
<td>Cyanosis</td>
<td>32</td>
<td>May be due to sulphnaemoglobininaemia or methaemoglobininaemia that are formed during the process of oxidation of haemoglobin</td>
</tr>
<tr>
<td>Pigmenturia</td>
<td>64</td>
<td>Important diagnostic sign, may be found only at time of acute hemolysis</td>
</tr>
<tr>
<td>Splenomegaly</td>
<td>86</td>
<td>Never markedly enlarged</td>
</tr>
<tr>
<td>Drug intolerance</td>
<td>10</td>
<td>Drug exacerbation</td>
</tr>
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</table>
altered oxygen affinity. The diagnosis can be confirmed by finding the unstable haemoglobin precipitate on heating at 50 degree Celsius for 1 hour or precipitate in an isopropanol buffer like the positive result in our case.\(^2\) The molecular study can also be performed to find out the gene. Once the diagnosis has been confirmed, usually there is nothing can be done but better to beware of any haemolysis during infection and avoid of exposure to oxidative drugs and nitrates. Another important thing is to have a good documentation of having "falsely low" oxygen saturation by digital pulse oximetry for these patients to prevent unnecessary investigations or treatments in the future.

In view of the "falsely low" oxygen saturation by digital pulse oximetry for these patients, once the unstable haemoglobin gene is identified, digital pulse oximetry can also provide a simple, effective and non-invasive tool to identify other family members with the same conditions to prevent confusion in future medical care.\(^6\) In our case, this 5-year-old girl has a 1-year-old younger sister who has a normal oxygen saturation measured by digital pulse oximetry and she was confirmed to be not affected (Figure 1).

Ours is the third report of AAC → ATC (Asn → Ile) mutation at codon 108 (G10) of the beta-globin gene, the first case being described in a Swiss family\(^4\) and termed Hb Schlierbach. The second case was reported by our Hong Kong medical colleagues in 2002\(^5\) and that case was our girl’s maternal grandmother who was found to have low oxygen saturation during cholecystectomy for gallstones after tracing her medical report but this is the first case reported in children.

**Conclusion**

We reported a Chinese girl with incidental finding of low oxygen saturation detected by digital pulse oximetry and low oxygen saturation in asymptomatic patients without clinical evidence of hypoxaemia should raise the suspicion of unstable haemoglobin with decreased oxygen affinity. Good documentation can prevent further unnecessary investigations and treatment in the future and digital pulse oximetry also provide a good screening tool to identify other affected family members.

**Declaration of Interest**

We declare that we have no conflict of interests.

**References**