OMCR

Oxford Medical Case Reports, 2019;5, 187–190

doi: 10.1093/omcr/omz027
Case Report

CASE REPORT

Water pipe smoking as a cause of secondary erythrocytosis

Nora Rebeka Javorniczky[1,2], Cornelius F. Waller[1,2], Heike L. Pahl[1,2], Nikolas von Bubnoff[1,2,3] and Heiko Becker[1,2,*]

[1]Department of Medicine I, Medical Center—University of Freiburg, 79106, Freiburg, Germany, [2]Faculty of Medicine, University of Freiburg, 79106 Freiburg, Germany, [3]Department of Hematology and Oncology, Medical Center, University of Schleswig-Holstein, Campus Lübeck, 23538 Lübeck, Germany

*Correspondence address. Medical Center—University of Freiburg, Hugstetter Straße 55, 79106 Freiburg, Germany. Tel: +49 761 270 77150; Fax: +49 761 270 77150; E-mail: heiko.becker@uniklinik-freiburg.de

Abstract

Water pipe (WP) smoking has become very popular in European countries. A 27-year-old male patient was referred to our clinic with erythrocytosis of unknown origin. His self-reported history included almost daily WP smoking since the age of 14 years. At presentation haemoglobin, haematocrit (Hct) and carboxy-haemoglobin (CO-Hb) levels were elevated to 19.7 g/dl, 54% and 15.4%, respectively. Erythrocytosis was completely reversible upon cessation of WP smoking. Upon follow-up, haemoglobin, Hct and CO-Hb levels undulated according to the intensity of WP usage. Our report shall raise awareness among physicians for WP smoking as a possible cause of secondary erythrocytosis, particularly among younger adults, and provide guidance for the clinical management.

INTRODUCTION

Water pipe (WP) smoking has become popular in European countries in recent years; the prevalence of regular use among individuals aged ≥15 years is estimated to be between 2 and 11%. [1, 2] In the pipe, a burning charcoal is used to heat tobacco mixed with molasses, which generates a smoke that is subsequently piped through a water bubbler and inhaled through a long, flexible tube. The smoke contains hot charcoal combustion products, which are drawn through the tobacco and inhaled [3]. WP smoking thus carries tobacco-related health risks, including an increased risk for cardiorespiratory problems and cancer. We here report on a patient with secondary erythrocytosis due to WP smoking and hope to increase awareness among physicians for WP smoking as a possible cause of secondary erythrocytosis.

CASE REPORT

A 27-year-old male patient was referred to us for evaluation of erythrocytosis of unknown origin, which was accompanied by frequent headaches. At presentation, haemoglobin (Hb) was 19.7 g/dl, and haematocrit (Hct) 54% (reference ranges: Hb 11–15 g/dl, Hct 32–45%) (Fig. 1). With the exception of hypertonus and obesity (weight 116 kg, height 190 cm), he had no relevant medical history, was not taking medications and denied use of herbal remedies, steroids, recreational drugs or androgen hormone substitutions. His family medical history was negative for haematological diseases or malignancies. Physical examination revealed plethora of the cheeks and a muscular body type. Extensive diagnostic analyses before referral had excluded diagnosis of polycaethemia vera, and presence of mutations in a large panel of genes associated with erythroid

Received: September 19, 2018. **Revised:** January 18, 2019. **Accepted:** March 2, 2019

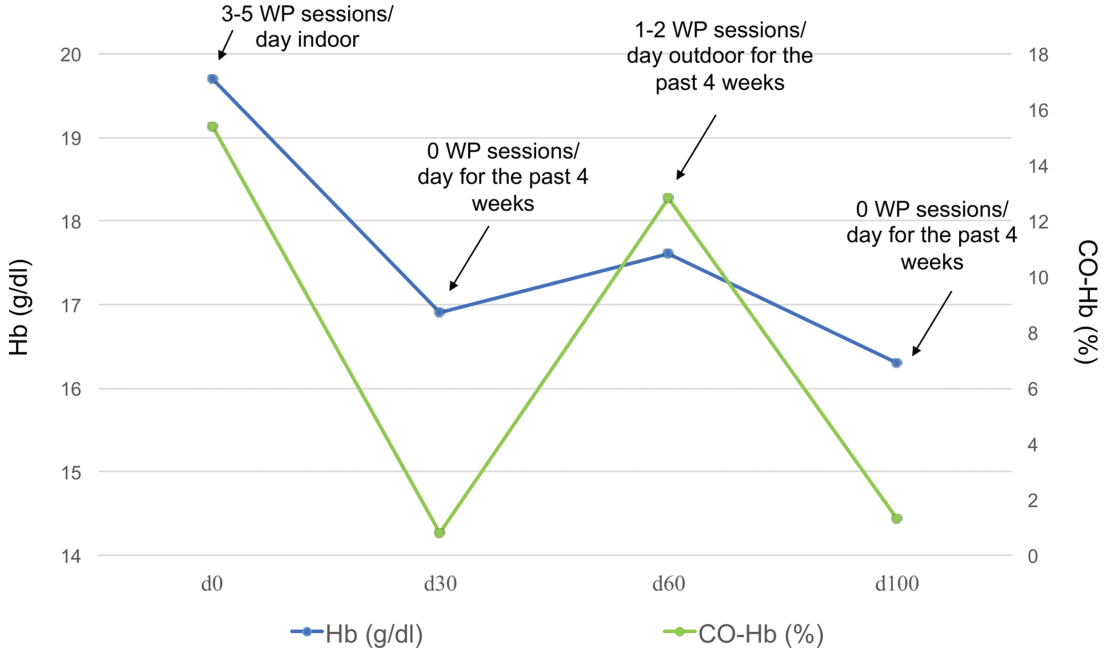

Figure 1: Hb and CO-Hb over-time depending on the WP smoking habit. WP smoking intensity is indicated in the figure.

abnormalities and malignancies (Table 1). Serum erythropoietin levels were normal, and histological and cytological analyses of the bone marrow (BM) indicated a reactive process with hyperplastic erythropoiesis. Secondary erythrocytosis due to altered hormone status was excluded as cortisol, testosterone and thyroid-stimulating hormone (TSH) serum levels were normal. The patient denied cigarette smoking but reported regular WP smoking since the age of 14 years. At the time of presentation he was smoking 3–5 sessions daily, mainly indoors in the evenings. We determined his carboxy-haemoglobin (CO-Hb) levels ~2 hours after his last WP session, which were elevated to 15.4 (reference range of CO-Hb among non-smokers: 0.5–1.5%). A transthoracic echocardiogram and pulmonary function tests were normal (Fig. 1). Four weeks after complete WP cessation the Hb concentration and Hct levels had returned to normal (Fig. 1). Because he was first unwilling to desist completely, the patient subsequently resumed moderate WP use outdoors. During the following 4 weeks his Hb and Hct levels again increased (Fig. 1), once more returning to normal after complete cessation.

DISCUSSION

Secondary erythrocytosis can result from a wide range of underlying disorders. Most cases are caused by chronic hypoxia due to cardiac and/or pulmonary diseases, frequently associated with smoking; other common causes include the use of anabolic steroids or diuretics [5]. We only identified three case reports in the literature, in which the diagnostic evaluation of an erythrocytosis identified long-term WP smoking as the cause [6, 7, 8].

A likely cause for a secondary erythrocytosis in heavy WP smokers is chronic elevation of CO-Hb. A study on the effects of cigarette and WP smoking showed that WP produced a 3.75-fold greater elevation in peak CO-Hb levels and was associated with a 56-fold greater amount of smoke inhaled [9]. In another study, a single 30-minute WP session resulted in significant increase of CO-Hb level and increased blood pressure, heart and respiratory rates; importantly elevated CO-Hb levels and respiratory rates were also found in passive smokers [10].

Acute carbon monoxide (CO) poisoning due to WP smoking is well known and presents with nausea and loss of consciousness; chronic poisoning normally induces fatigue, irritability, impaired concentration and reduced physical status [3, 7]. The effects of chronic WP smoking on the haematopoietic system are less well described. A rat model of WP smoking showed a significant increase of Hb and Hct in WP smoking rats compared to the control group [4].

CO is a colourless and odourless gas, generated by incomplete combustion of hydrocarbons, in this case the burning charcoal. Following inhalation, CO diffuses across the alveolar membrane and reversibly binds heme, forming CO-Hb. The affinity of CO to Hb is 200-fold higher than that of oxygen. Consequently, tissue oxygen delivery is impaired. In the BM, chronic cellular hypoxia increases expression of the transcription factor HIF-1a by preventing its active degradation. HIF-1a increases transcription of erythropoietin, which stimulates erythropoiesis, ultimately causing erythrocytosis [2].

Chronic CO-Hb elevation and induction of secondary erythrocytosis does not constitute the only health risk associated with WP smoking. Following consumption, no differences in peak nicotine plasma concentrations were observed between WP and cigarette smokers. However, 30 to 45 minutes after smoking, mean plasma nicotine concentrations were significantly higher in individuals smoking WP (mean smoking time: 43 minutes) than in cigarette smokers (mean smoking time: 6 minutes), suggesting that WP smoking results in a prolonged exposure to nicotine [9]. Subjective effects, including those relevant for dependence, were comparable in strength but lasted partly longer among WP smokers [9].

In Western countries the term ‘smoking’ often exclusively refers to cigarette smoking. Therefore, other smoking habits

Table 1: Laboratory and mutation data

Laboratory data	Result
White blood cell count, $x10^6$/L (3.9–9.8)	6.1
Platelets, $x10^6$/L (146–328)	230
Haemoglobin, g/dL (13.5–17.6)	19.7
Haematocrit, % (39.6–50.6)	54.1
Erythropoietin, mU/mL (4.3–29)	16.1
LDH, U/L (135–214)	195
Ferritin, ng/mL (15–150)	142
Cortisol, nmol/L (133–537)	195
Testosterone, nmol/L (8.64–29.0)	13.3
Thyroid-stimulating hormone, µU/ml (0.27–4.20)	1.04
Met-Hb, % (0–1.5)	0.9
CO-Hb, % (0.5–1.5)	15.4
Mutation analyses	
BCR-ABL	negative
JAK2 exons 12 + 14 (V617F)	wild-type
CALR exon 9	wild-type
MPL exon 10	wild-type
ASXL1 exon 13	wild-type
IDH2 exon 4	wild-type
SRSF2 exon 1	wild-type
TET2 exons 3–11	wild-type
TP53 exons 2–8	wild-type
U2AF1 exons 2 + 6	wild-type
EGLN (PHD2) exons 2–3	wild-type
EPAS1 (HIF2A) exon 12	wild-type
EPOR exon 8	wild-type
VHL exons 1–3	wild-type
Pulmonary function	
Vital capacity (VC), L	5.7 (91%)
Forced expiratory volume in 1 second (FEV1), L	4.8 (97%)
FEV1/VC, %	84 (102%)
Diffusing capacity of the lung for CO (corrected), mmol/min/kPa	10.5 (79%)

Notes: For laboratory data, the respective local reference range is provided in parentheses. The laboratory data were assessed at time of referral. The mutation data were assessed before referral from bone marrow or peripheral blood.

have to be explicitly sought out when taking a medical history. WP smokers often fail to mention their habit, as they consider it harmless, following a common misbelief that the water cleans the smoke of toxic substances.

Among the previous reports, our case stands out as we were able to observe dynamic changes in the blood counts paralleling the intensity of WP usage. Upon cessation, Hb normalized rapidly, whereas it rose again when the patient resumed. At last follow-up, blood parameters had again returned to normal within a few weeks of abstinence.

In conclusion, we report WP smoking as a cause of secondary erythrocytosis, thereby raising awareness among physicians to obtain the relevant history and consider this cause especially when evaluating young adults. Given the increased popularity of WP smoking haematological effects may be more prevalent than the current literature suggests.

CONFLICT OF INTEREST STATEMENT

None declared.

FUNDING

This work was not supported by external funding.

ETHICAL APPROVAL

The research use of the clinical data had been approved by the ethics committee of the University Freiburg (Ref. 558/15).

CONSENT

The patient provided written informed consent for the research use of the clinical data and biomaterial in accordance to the Declaration of Helsinki.

GUARANTOR

Heiko Becker.

REFERENCES

1. Maziak W. The global epidemic of waterpipe smoking. *Addict Behav* 2011;**36**:1–5. https://doi.org/10.1016/j.addbeh.2010.08.030.
2. Agaku IT, Filippidis FT, Vardavas CI, Odukoya OO, Awopegba AJ, Ayo-Yusuf OA, *et al*. Poly-tobacco use among adults in 44 countries during 2008–2012: evidence for an integrative

and comprehensive approach in tobacco control. *Drug Alcohol Depend*. 2014;**139**:60–70.https://doi.org/10.1016/j.drugalcdep.2014.03.003.
3. Shihadeh A. Investigation of mainstream smoke aerosol of the argileh water pipe. *Food Chem Toxicol* 2003;**41**: 143–152.
4. Miri-Moghaddam E, Mirzaei R, Arab MR, Kaikha S. The effects of water pipe smoking on hematological parameters in rats. *Int J Hematol Oncol Stem Cell Res*. 2014;**8**:37–43.
5. Keohane C, McMullin MF, Harrison C. The diagnosis and management of erythrocytosis. *BMJ*. 2013;**347**:f6667. https://doi.org/10.1136/bmj.f6667.
6. Bonadies N, Tichelli A, Rovó A. When water does not clear the smut from the smoke. *BMJ Case Rep* 2013; bcr2013200665. https://doi.org/10.1136/bcr-2013-200665.
7. De Maeyer NE, Van Lommel S, Devos T, Buyse B, Nackaerts K. A surprising cause of polycythaemia. *Thorax* 2016;**71**: 967–968. https://doi.org/10.1136/thoraxjnl-2016-208610.
8. Tadmor T, Mishchenko E, Polliack A, Attias D. Hookah (narghile) smoking: a new emerging cause of secondary polycythemia. *Am J Hematol* 2011;**86**:719–720. https://doi.org/10.1002/ajh.22064.
9. Cobb CO, Shihadeh A, Weaver MF, Eissenberg T. Waterpipe tobacco smoking and cigarette smoking: a direct comparison of toxicant exposure and subjective effects. *Nicotine Tob Res*. 2011;**13**:78–87.
10. Bentur L, Hellou E, Goldbart A, Pillar G, Monovich E, Salameh M, *et al*. Laboratory and clinical acute effects of active and passive indoor group water-pipe (narghile) smoking. *Chest* 2014;**145**:803–809 https://doi.org/10.1378/chest.13-0960.