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Case Report

Could artemisinin-based combination therapy prevent occupational malaria following blood exposure?

Running head: Post exposure prophylaxis using ACT.

1183 Words

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28 **Abstract: (162 words)**

29 Post exposure prophylaxis using **artemisinin-based combination therapy** was prescribed to a
30 malaria-naive nurse who experienced an injury with a hollow needle previously used on a
31 patient admitted for severe imported *Plasmodium falciparum* malaria (blood parasitemia
32 10.8%).

33 **Artemether-lumefantrine, 4 tablets twice daily for 3 days, was started** 12 hours after exposure
34 and no side effects were reported. During the 6 following months, she only developed one
35 episode of fever that was associated with pyelonephritis. Biological follow-up, based on blood
36 smears, molecular biology and serology did not evidence *Plasmodium falciparum* malaria.
37 This case **suggests** that **artemisinin-based combination therapy can** prevent occupational
38 *Plasmodium falciparum* malaria following needle-stick injury. We **found evidence of only**
39 **one other** unpublished similar case **where a Turkish resident doctor did not develop malaria**
40 **after** post exposure prophylaxis using **artemisinin-based combination therapy**. **Such a**
41 **prophylaxis** could be prescribed in case of occupational exposure to *Plasmodium spp* in non
42 vector borne laboratory acquired infections but also following blood exposure in health care
43 setting.

44

45 **Keywords:** Plasmodium falciparum malaria; Occupational; Healthcare worker; Post exposure
46 prophylaxis; **artemisinin-based combination therapy**.

47 **Background:**

48 Needle-stick injuries continue to occur in healthcare facilities worldwide,¹ potentially
49 exposing healthcare workers (HCW) to blood borne pathogens (BBP). The overrepresentation
50 of Hepatitis B (HBV), Hepatitis C (HCV) and Human Immunodeficiency (HIV) Viruses
51 among these BBP explained the post exposure prophylaxis treatment given to HCW in this
52 situation.²

53 However, a wide variety of other potential viral, bacterial and protozoal BBP has been
54 described.³ Among those, the protozoan parasite *Plasmodium falciparum* has been involved in
55 more than 20 malaria cases after needle-stick injuries in healthcare setting, apart from
56 laboratory acquired infections.^{4,5} All except one had a favourable outcome once antimalarial
57 treatment had been given in case of overt disease.⁴ Nevertheless, there are almost no
58 **published** data concerning the **efficacy** of Post Exposure Prophylaxis in the prevention of
59 malaria after exposure to parasitemic blood in healthcare facilities. Chloroquine has been tried
60 once without success during a laboratory acquired infection more than 30 years ago.⁶ Since
61 **the mid-2000s, artemisinin-based combination therapy** (ACT) became the drug of choice for
62 uncomplicated *P. falciparum* malaria, because of a higher **parasitic** clearance rate compared to
63 **other** antimalarial drugs.⁷

64 In the present report, a Post Exposure Prophylaxis using ACT was prescribed to an
65 intensive care unit (ICU) nurse, following needle-stick injury, in order to prevent malaria
66 occupational transmission.

67

68 **Case presentation:**

69 On November 27th 2019, ~~around 11h p.m.~~, a 39-year-old Caucasian ICU nurse
70 experienced a **deep** needle-stick injury with a 21-gauge hollow needle forgotten in a sterile
71 field. This needle had just been used as finder needle during insertion of central venous
72 catheter in internal jugular vein of a 57 year-old female patient admitted the same day for
73 severe imported *P. falciparum* malaria (blood parasitemia 10.8%, Red Blood Cells 3.5
74 millions/mm³, 1 day after returning from a 3 weeks trip to Guinea) (Figure 1A) **and before**
75 **any antimalarial treatment was received by the patient.** After immediate wound disinfection
76 by diluted sodium hypochlorite solution, the nurse finished her shift and went to occupational
77 medicine consultation. Blood test confirmed nurse's immunity against HBV and no
78 antiretroviral post exposure prophylaxis was prescribed because both nurse and patient were
79 HIV (and HCV) seronegative. However, considering the risk of occupational *P. falciparum*
80 malaria, a compassionate ACT (Artemether-lumefantrine 4 tablets **twice daily** with food, for 3

81 days) was prescribed to the nurse, who was malaria-naive. Hospital Pharmacy provided the
82 treatment that she began 12 hours after exposure. No side effects were reported by the nurse.
83 To date, she only developed one episode of fever that was associated with documented
84 pyelonephritis. Biological follow-up, based on fast thick plus thin blood smears using 5µl of
85 blood and molecular biology, ^{8,9} did not evidence *P. falciparum* malaria (Figure 1B&C).
86 Serological assays evidenced neither HIV/HCV nor *P. falciparum* antigens seroconversion
87 (Figure 1C).

88

89 Discussion:

90 Herein, we reported the case of a malaria-naive nurse, who did not develop malaria
91 after ACT post exposure prophylaxis given 12 hours after what we judged to be an at-risk
92 needle-stick injury. We could not prove that this favourable outcome was due to ACT post
93 exposure prophylaxis but we judged it likely.

94 Firstly, by analogy with other viral BBPs, we presumed the needle-stick injury was
95 here at-risk because injury was due to a hollow needle filled with highly parasitemic blood,
96 deep, and occurred in a malaria-naive nurse. Most of the occupational malaria reported cases
97 occurred after needle-stick injuries both in laboratory and in health care setting.^{4,5} There are
98 no data concerning the estimated risk of malaria transmission in these specific situations. The
99 most similar situation where the risk of malaria transmission has been estimated corresponded
100 to transfusion transmitted malaria. ~~we presumed the risk of malaria transmission exceeded~~
101 ~~here the minimal 2 to 14% rate observed in~~ Among immune Ghanaian patients receiving red
102 blood cells (RBC) transfusion, the transmission rate was only 2 to 14%.¹⁰ Even though the
103 quantity of blood received during RBC transfusion is far superior to that received during a
104 needle-stick injury, the risk of *P. falciparum* malaria transmission after transfusion in Ghana
105 remained low because both blood donors and recipients were immune for malaria, and packed
106 RBC units parasite free or with very low parasitemia. ~~could not be neglected after needle-~~
107 ~~stick injuries. Moreover,~~ In our case, near 350 000 infected RBCs could be transmitted by 1
108 mm³ of the patient blood, whereas experimental data suggested than 10 infected RBCs were
109 sufficient to transmit malaria.¹¹ Besides, unlike HIV and HCV, the time spent by the needle in
110 the environment did not reduce the risk of transmission of malaria, because all *Plasmodium*
111 species are able to survive in blood more than one week, even at 4°C.¹¹

112 Secondly, we also presumed that ACT was effective in preventing here likely malaria,
113 because there was no evidence for *P. falciparum* malaria in the following months using highly
114 sensitive Polymerase Chain Reactions,^{9,10} whereas occupational *P. falciparum* malaria usually

115 occurred within a median delay of 12 (range 4-17) days among the 22 cases reported in
116 healthcare setting between 1924 and 2006 without post exposure prophylaxis.⁴ Incubation was
117 similar (median 12.5 days, range 8-14) in the 5 other cases reported up to 2001, without post
118 exposure prophylaxis.⁵ To date, four more cases of occupational malaria have been reported,
119 with a median delay of incubation of 14 (range 9-18) days, all without post exposure
120 prophylaxis.¹²⁻¹⁵ In the sole previously published case of ~~unsuccessful~~ with post exposure
121 prophylaxis ~~due to acquired Chloroquine resistance~~,⁶ *P. falciparum* malaria occurred 17 days
122 after ~~needle-stick injury~~ inoculation (breaking a capillary haematocrit tube containing infected
123 blood suspension in laboratory) despite treatment by Chloroquine, because of acquired
124 resistance of the strain. The potential better efficacy of ACT here is probably ~~be~~ due to a
125 higher schizonticidal activity than Chloroquine and such a high schizonticidal activity is
126 probably required after exposure to parasitemic blood,⁷ in which the most abundant parasitic
127 stage corresponded to trophozoites forming in schizonts. In the case of blood transmitted
128 malaria, infection bypassed the hepatic stage of the parasite life's cycle that is necessary for
129 the activation of innate immunity.^{5,11} This could explain the absence of seroconversion for
130 malarial antigen,¹¹ we observed here (Figure 1C).

131 **Lastly**, simply reporting this case of absence of *P. falciparum* malaria after ACT post
132 exposure prophylaxis seemed important to us, because there is probably no other way (except
133 animal experimental data) to demonstrate a potential benefit of ACT in preventing
134 occupational malaria following blood exposure than gathering evidences issued from real life.
135 To this end, we made exhaustive search and found evidence of only one other similar case,
136 which was unpublished. In that case, ~~evidenced only one another unpublished case of~~
137 ~~apparently successful~~ a Turkish resident doctor did not develop malaria after taking
138 Artemether-lumefantrine as post exposure prophylaxis of ~~*P. falciparum* malaria~~ the day
139 following a deep needle-stick injury (while taking a blood sample in a patient treated by
140 Artemether-lumefantrine but with 25% *P. falciparum* blood parasitemia) ~~using ACT in~~
141 Turkey.¹⁶ This case and ours suggest that ACT can prevent occupational *P. falciparum*
142 malaria following needle-stick injury. In order to gather more evidence, ACT post exposure
143 prophylaxis (which was well tolerated here) could be prescribed in case of occupational
144 exposure to *Plasmodium spp* in non vector borne laboratory acquired infections but also
145 following blood exposure in health care setting.^{4,5} In this latter situation, the parasitemic
146 status of the source patient should be mentioned by the health professional or sought out by
147 the occupational physician, because omitting this information could lead to further diagnostic
148 delay and worse outcome.⁴

149

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152

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154

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201 Poster presentation 23rd European Congress of Clinical Microbiology and Infectious
202 Diseases (ECCMID) Berlin, 27-30 April 2013.

204 **Figure caption:**

205 Figure 1: **A.** Thin Blood smear of the source 57 year-old female patient, showing numerous
206 *Plasmodium falciparum* trophozoites in Red Blood cells. **B.** Amplification curve of pan
207 plasmodial Real Time Polymerase Chain reaction (PCR). In blue, positive control. In red, all
208 curves corresponding to nurse's samples, below threshold detection in yellow. PCR has been
209 performed, as previously described,⁹ on nurse's Blood smears and on whole blood during all
210 follow-up and at the end of the 3 months survey respectively. **C.** Results of the biological
211 follow-up performed in nurse immediately, 2 weeks, 1 and 3 months after needle-stick injury.
212 Malaria Serology has been performed using Malaria EIA Test Kit, Biorad®, according to
213 manufacturer's instructions. ND: Not done. Below, time scale with clinical events. ACT:
214 **artemisinin-based combination therapy.**

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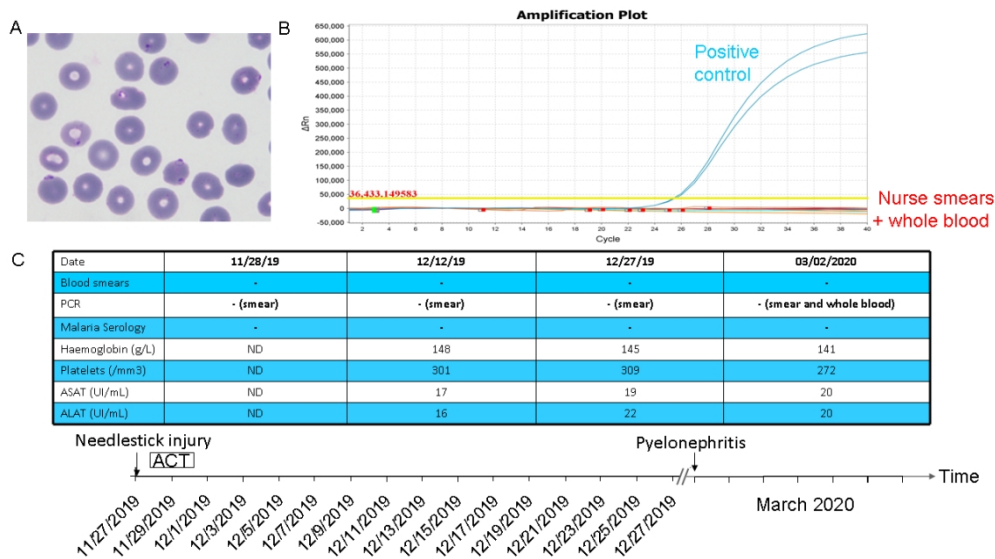


Figure 1: A. Thin Blood smear of the source 57 year-old female patient, showing numerous Plasmodium falciparum trophozoites in Red Blood cells. B. Amplification curve of pan plasmodial Real Time Polymerase Chain reaction (PCR). In blue, positive control. In red, all curves corresponding to nurse’s samples, below threshold detection in yellow. PCR has been performed, as previously described, 9 on nurse’s Blood smears and on whole blood during all follow-up and at the end of the 3 months survey respectively. C. Results of the biological follow-up performed in nurse immediately, 2 weeks, 1 and 3 months after needle-stick injury. Malaria Serology has been performed using Malaria EIA Test Kit, Biorad®, according to manufacturer’s instructions. ND: Not done. Below, time scale with clinical events. ACT: artemisinin-based combination therapy.

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