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Mutation of the Fas-promoter-670 gene, AA to GA in the normal cervix-epithelial-cells of high risk Indonesian mother: A case report

by Kirana Anggraeni

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ABSTRACT

Background: Normalities of the cervix-epithelial-cells (CEC) can be determined base on the cell morphology and their nucleus. If one of the cervix-epithelial-cells has gene mutations, it will form mutant clones, further growing, developing and malignant. The Fas-promoter-670 gene is allegedly associated with cervical cancer. **Case Presentation:** A 30-year-old of high-risk Indonesian mother, has two children, on April 21th 2016 has followed Pap smear examination with thin prep method. Subjects, in this case, had normal cervix-epithelial-cells. Characteristics of the cervix-epithelial-cells include cell biometrics among others cell length, cell width, cell area, cell perimeter, nucleus area, and nucleus perimeter. Fas-promoter-670 genotype in the lymphocytes-cells is AA (normal= wild type), whereas in the cervix-epithelial-cells is GA (heterozygous mutant). **Conclusion:** Based on characteristic of cell biometrics, cervix-epithelial-cells in high-risk Indonesian mother is normal. The genotype of the Fas-promoter-670 gene in the lymphocyte cells is AA, whereas in the cervix-epithelial-cells has mutation to GA.

Keywords: cervix-epithelial-cells, Fas-promoter-670 gene, cell biometrics, cell length, cell width

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INTRODUCTION

Cervical cancer is still a health problem in Indonesia. Based on the comprehensive statistics in 2012, the incidence rate of cervical cancer in Indonesia is 17 per 100.000 women per year. Moreover, that incidence rate of cervical cancer in Southeast Asia is 16.6 and around the world 15.1, respectively. Also, Indonesia is the 4th country in Southeast Asia, with the highest incidence of cervical cancer after Cambodia, Myanmar, and Thailand. The mortality rate caused by cervical cancer in Indonesia is about 28%, lower than the world average mortality rate, furthermore 2.5% lower than the average death occurring in Southeast Asia.[1]

The primary cause of cervical cancer is human papillomavirus (HPV) infection. HPV is transmitted among others through sexual activity. Therefore women who make these contacts are at high risk for cervical cancer. HPV DNA has many serotypes, but only a few serotypes are progressive to cervical cancer. It is further stated that women infected with HPV especially with HPV 16, some of which will increase to low-grade squamous intraepithelial lesion (LSIL) or cervical intraepithelial neoplasia (CIN) 1, high-grade squamous intraepithelial lesion (HSIL) or CIN 2, and become invasive cervical cancer (CIN3) in some areas.[2]

Oncogenic gene expression is also a major cervical cancer problem. Genes mutations that occur in one cervical cell, then forming a mutant clone, grow and malignant. We know that some of the oncogenic genes that cause cervical cancer, including the Fas-promoter-670 gene. Fas-promoter-670 gene in the humans have been mapped, lies on chromosome 10q24.1, which contains nine exons and eight introns. Fas (TNFRSF6/Apo-1/CD95) is a type I transmembrane receptor, including tumor necrosis factor (TNF) receptor superfamily (tumor necrosis factor=TNF). Result studies previously show that Fas-promoter-670 gene polymorphism in stem cells is also associated with cervical cancer in Japanese populations.[3]

Papanicolaou (Pap) smear test is an effective method for early detection of cervical cancer.[4] Microscopically, CEC with normal characteristics can be used to express no cervical cancer, but those with atypical and malignant cells are used as a marker of cervical cancer. The novelty, in this case, is the mutation of Fas-promoter-670 gene in the CEC normal of high-risk Indonesian mother, whereas in the lymphocyte cells (LC) is normal. Mutation of the Fas-promoter-670 gene can be used as an early marker of potential cervical cancer. Also, we presented the characteristics of normal CEC which focuses on the size of the cell and its nucleus.

Table 1. Characteristic of normal cervix-epithelial-cells in high-risk Indonesian mother

Variable	Mean ± SD	Confidence interval 95%
Cell length (CL): the longest cell diagonal that passes through the nucleus (μm)	11.06 ± 1.57	10.49 – 11.66
Cell width (CW): cell diagonal perpendicular to the diagonal of CL (μm)	8.13 ± 2.14	7.32 – 8.99
Cell area (CA) (μm^2)	73.74 ± 23.15	65.22 – 82.94
Cell perimeter(CP) (μm)	32.62 ± 4.92	30.84 – 34.53
Nucleus area (NA) (μm^2)	1.40 ± 0.54	1.21 – 1.63
Nucleus perimeter (NP) (μm)	4.30 ± 0.78	4.03 – 4.62
Nucleus length (NL) (μm)	1.47 ± 0.25	1.38 – 1.57
Nucleus width (NW)(μm)	1.18 ± 0.24	1.09 – 1.27
Nucleus area index (NAI) = (nucleus area/cell area)*100	2.07 ± 0.88	1.75 – 2.40
Nucleus perimeter index (NPI) = (nucleus perimeter/cell perimeter)*100	13.46 ± 2.96	12.33 – 14.56
Nucleus length index (NLI) = (nucleus length/cell length)*100	13.59 ± 2.99	12.53 – 14.74
Nucleus width index (NWI) = (nucleus width/cell width)*100	15.42 ± 4.86	13.59 – 17.22

Abbreviations: μm=milli micron ; μm^2=milli micron square; SD=standard of deviation.

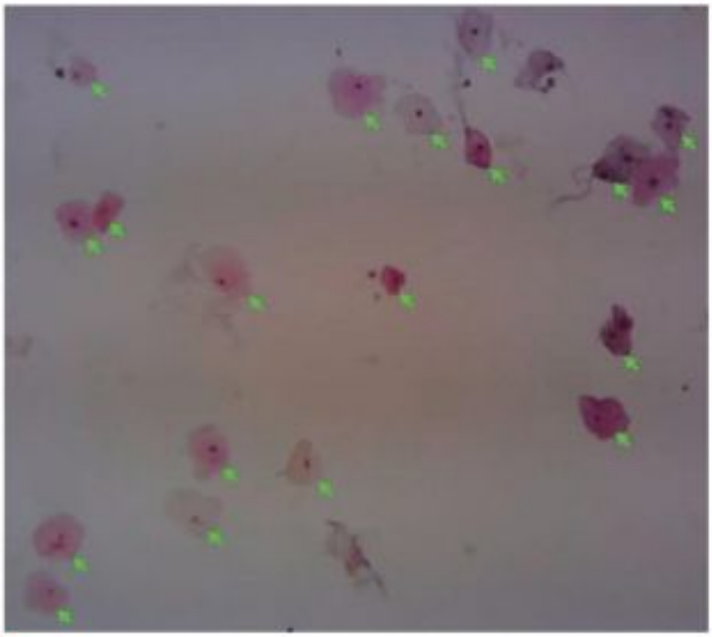


Figure 1. The Cervix-epithelial-cells of high-risk Indonesian mother available for observation (photomicroscope with optilab, objective 10x).

We reported the genotype difference of Fas-promoter-670 gene in the LC compared with CEC in high-risk Indonesian mother. Light microscope was used to observe the CEC and its cell nucleus. We focus on the characteristics of the CEC namely cell biometrics among others length, width, area, and perimeter of the cells and its cell nucleus. *Restriction fragment length polymorphism* (RFLP) was used to performance of the Fas-promoter-670 gene in the LC and CEC samples.

CASE REPORT

A 30-year-old of high-risk Indonesian mother, has two children (P2Ao), on April 21th 2016 has followed Pap smear examination with thin prep method. The mother concerned is included in the community of Indonesian women living with high-risk HPV as indicated by evidence of laboratory examinations. Marriage history at the age of 18 years, and the mother has a history of free sex. Furthermore, the mother also explained that she worked as a commercial sex worker and had never received HPV vaccination. Observations to the CEC was done by used optilab and image raster three programs by three observers. The characteristics of CEC namely cell biometrics among others cell length (CL), cell width (CW), cell area (CA), cell perimeter (CP), nucleus area (NA), and nucleus perimeter (NP). Moreover, we calculated the nucleus length index (NLI), nucleus width index (NWI), nucleus area index (NAI) and nucleus perimeter index (NPI) (Table 1). Base on the results showed that the CEC is normal because no atypical and malignant cells were found (Figure 1). Figure 2 and 3 shown the results of CEC cell biometrics. RFLP was used to perform Fas-promoter-670 gene in the LC and CEC. Blood sample was obtained from vena cubiti by proteinase K digestion and the CEC collected by thin prep method. DNA extraction from blood sample and CEC was performed using chloroform (Figure 4). Also, were used BstN1enzyme and forward primer 5'-CTACCTAAGAGCTATCTACCGTTC-3' and reverse primer 5'-GGCTG TCCATGTTGTGGCTGC-3'. Genotyping result of the Fas-promoter-670 gene in the LC is AA (normal=wild type), whereas in the CEC has mutation to GA (heterozygous variant) (Figure 5). Our team suggested that Pap smear screening could be done two years later.

DISCUSSION

In the Pap smear method, the determination of CEC characteristics can be used as a reference in the diagnosis of cervical cancer. We used the light

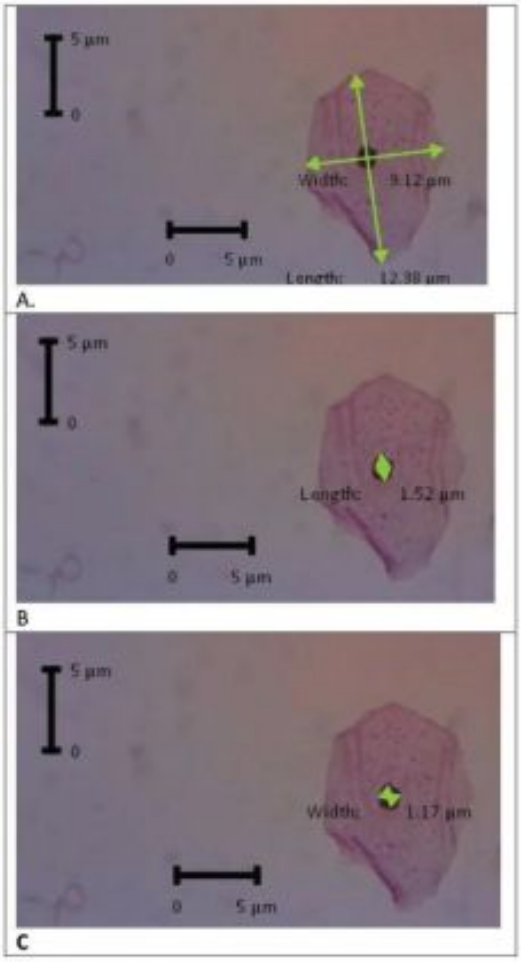


Figure 2. Length and width measurement results of the cell and nucleus. A=length and width of the cell; B=length of the nucleus; C=width of the nucleus. Abbreviations: µm=milli micron.

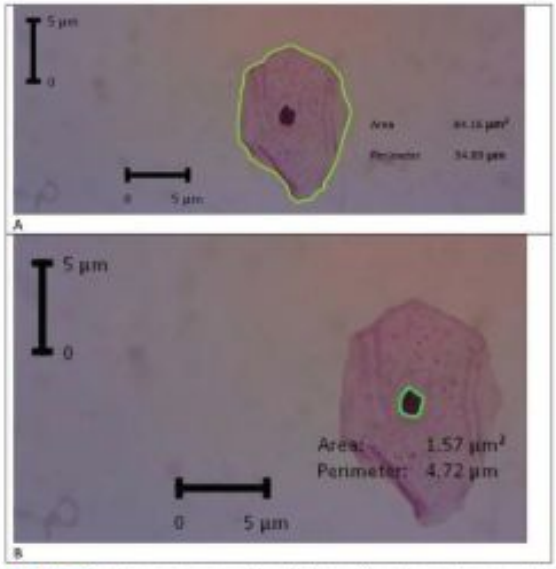


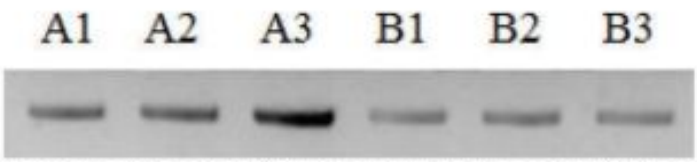
Figure 3. Area and perimeter of the cell and nucleus. A=Area and perimeter of the cell; B=area and perimeter of the nucleus.
Abbreviations: µm=milli micron; µm2=milli micron square.

microscope and image raster three programs to display normal CEC morphology. We perform these steps because most hospitals in Indonesia have facilities such as light microscope and the image raster three program is relatively easy to obtain. Our way may be simplest, nevertheless to detect cervical cancer can also be done using a more sophisticated tool, for example by atomic force microscopy.[5]

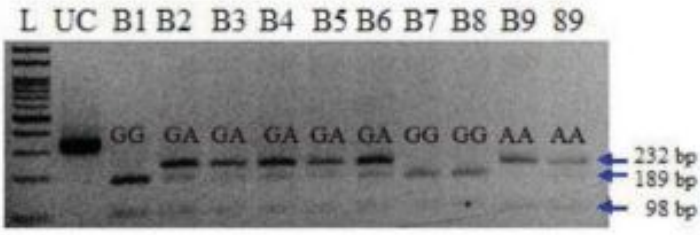
Pap smear examination of the CEC with hematoxylin and eosin staining showed that normal cervical tissue had multiple epithelial layers while cancerous cervical tissue showed dysplastic changes.[5] Our observation that the CEC has normal morphology appears to be similar to that of previous studies.[7] In addition to the normal CEC morphology, the nucleus morphology of the CEC can also be used to distinguish of CEC type. Previous studies showed that nucleus morphology criteria of the CEC among others: area, length, diameter, and radius.[8,9]

The other result showed that CEC has numerous balloon-outs, which have an average size ranging from 0.1-0.5 to 1.2-1.3 milli-micron (µm), are visible on the cell surface under microscope.[10] Beside that nucleus-cytoplasm ratio (N/C ratio) used to cytologic features of cervical cells. After the cells become malignant, the number of chromosomes in the nucleus will change, leading to changes in the shape of the nucleus. The length and diameter of the cell nucleus increased two fold, while the area increased by 4.5 fold.[11] Furthermore, We agree that on examination of cervical cytologic specimens showing most low-grade squamous intraepithelial lesions (LSIL), some of the high-grade squamous intraepithelial lesions (HSIL) cannot be excluded. Also, metastatic cancer cells are distinguished from normal cells based on stiffness rather than shape. Cancer cells are more promising for improving cancer diagnosis. Moreover, those metastatic cancer cells were nearly four times softer than normal cells.[12]

The BstN1 enzyme we used in RFLP to perform of Fas-promoter-670 gene was able to digest DNA



A. Deoxyribonucleic acid (DNA) extraction from Thin Prep samples (A1-A3) and lymphocyte (B1-B3).



B.

Figure 4. DNA extraction and genotyping of the Fas promoter-670 gene from blood peripheral lymphocyte cells. A. DNA extraction from the CEC (A1-A3) and blood peripheral lymphocyte cells (B1-B3). B. Genotyping of the Fas-promoter-670 gene with BstN1 enzyme. Sample number 89 from blood peripheral lymphocyte cells showed that genotype of the Fas-promoter-670 gene is AA (232 + 98 bp).
Abbreviations: DNA=deoxyribo nucleic acid; CEC=cervix-epithelial-cells; L=Molecular weight standard; UC=DNA loading without BstN1 enzyme; C1-C9= control sample from blood peripheral limphocyte cells, loading with BstN1; AA genotype (232, 98 bp); GA gentoype (232, 189, 98 bp); GG genotype (189, 98 bp).

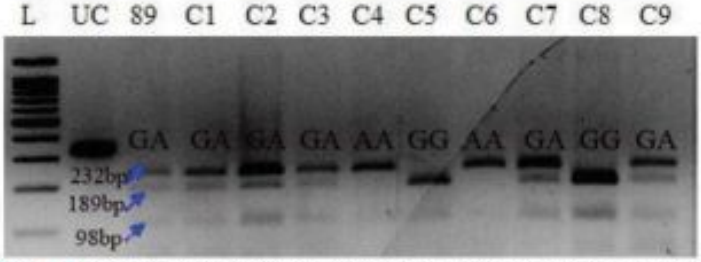


Figure 5. Genotyping of the Fas-promoter-670 gene in the CEC with BstN1 enzyme. Abbreviations: CEC=cervix-epithelial-cells; L=Molecular weight standard; UC=DNA loading without BstN1 enzyme; 89= sample number of the CEC from thin prep solution showed that genotype of the Fas-promoter-670 gene is GA (232, 189 and 98 bp); C1-C9 =sample control of the CEC from thin prep solution, loading with BstN1; AA genotype (232, 98 bp); GA genotype (232, 189, 98 bp); GG genotype (189, 98 bp).

samples into fragments 232, 189 and 98 base pair (bp). The fragments of 232 and 189 bp indicated the AA genotype, while 232, 189 and 98 bp indicated the GA genotypes. Therefore 189 and 98 bp indicated the GG genotype. This results according to previous researchers.[15] Moreover it is also shown that cervical cancer is associated with the polymorphism of the Fas-promoter-670 gene. The GG genotype of Fas-promoter-670 gene promotes the occurrence of cervical cancer compared to AA genotype. The result of research previously shows that G allele also increases the occurrence of cervical cancer. Two single nucleotide polymorphisms (SNPs) (-1377G>A, rs2234767 and -670A>G, rs1800682) located in the promoter region of Fas gene were examined in association with some tumorogenesis.[14] Also, polymorphism is also associated with metabolic abnormalities until the occurrence of pathological conditions.[15,16]

In this case, the genotype of Fas-promoter-670 gene in the LC was different from CEC. The expression pattern of the Fas-promoter-670 gene in this study is expected to be an early marker of cervical cancer so that it can be prevented. This corresponds to the general principle that detection of cervical cancer is directed to the presence of oncogenic elements that promote cell transformation. Moreover that the failure of Fas gene regulation produces death signals, which are reported in some cancers.[17] However, the correlation between this SNP and cancer susceptibility including the risk of gynecological malignancies needs to be studied more widely.

CONCLUSION

Based on characteristic of cell biometrics, the CEC in high-risk Indonesian mother was normal. The genotype of the Fas-promoter-670 gene in the LC is AA (normal=wild type), whereas in the CEC has mutation to GA (heterozygous variant). We recommend examining of Fas-promoter-670 gene on early screening for cervical cancer.

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CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

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ETHIC AND PATIENT CONSENT

The authors declare that: 1). They have obtained written, informed consent for the publication of the details relating to the patient in this report. 2). All possible steps have been taken to safeguard the identity of the patient. 3). The ethical clearance of this study was approved by the Commission on Research Ethics, Faculty of Medicine, University of Trisakti, Jakarta, Indonesia, number 60/KER/FK/05/2013.

AUTHORS CONTRIBUTIONS

MLEP: images review and processing, writing of the manuscript and reviewing the final text. WR, AG, K: literature review and writing of the manuscript.

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PAGE 1

PAGE 2

PAGE 3

PAGE 4

PAGE 5

CASE REPORT

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Mutation of the Fas-promoter-670 gene, AA to GA in the normal cervix-epithelial-cells of high risk Indonesian mother: A case report

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ABSTRACT

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Keywords: cervix-epithelial-cells, Fas-promoter-670 gene, cell biometrics, cell length, cell width
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INTRODUCTION

Cervical cancer is still a health problem in Indonesia. Based on the comprehensive statistics in 2012, the incidence rate of cervical cancer in Indonesia is 17 per 100.000 women per year. Moreover, that incidence rate of cervical cancer in Southeast Asia is 16.6 and around the world 15.1, respectively. Also, Indonesia is the 4th country in Southeast Asia, with the highest incidence of cervical cancer after Cambodia, Myanmar, and Thailand. The mortality rate caused by cervical cancer in Indonesia is about 28%, lower than the world average mortality rate, furthermore 2.5% lower than the average death occurring in Southeast Asia.[1]

The primary cause of cervical cancer is human papillomavirus (HPV) infection. HPV is transmitted among others through sexual activity. Therefore women who make these contacts are at high risk for cervical cancer. HPV DNA has many serotypes, but only a few serotypes are progressive to cervical cancer. It is further stated that women infected with HPV especially with HPV 16, some of which will increase to low-grade squamous intraepithelial lesion (LSIL) or cervical intraepithelial neoplasia (CIN) 1, high-grade squamous intraepithelial lesion (HSIL) or CIN 2, and become invasive cervical cancer (CIN3) in some areas.[2]

Oncogenic gene expression is also a major cervical cancer problem. Genes mutations that occur in one cervical cell, then forming a mutant clone, grow and malignant. We know that some of the oncogenic genes that cause cervical cancer, including the Fas-promoter-670 gene. Fas-promoter-670 gene in the humans have been mapped, lies on chromosome 10q24.1, which contains nine exons and eight introns. Fas (TNFRSF6/Apo-1/CD95) is a type I transmembrane receptor, including tumor necrosis factor (TNF) receptor superfamily (tumor necrosis factor=TNF). Result studies previously show that Fas-promoter-670 gene polymorphism in stem cells is also associated with cervical cancer in Japanese populations.[3]

Papanicolaou (Pap) smear test is an effective method for early detection of cervical cancer.[4] Microscopically, CEC with normal characteristics can be used to express no cervical cancer, but those with atypical and malignant cells are used as a marker of cervical cancer. The novelty, in this case, is the mutation of Fas-promoter-670 gene in the CEC normal of high-risk Indonesian mother, whereas in the lymphocyte cells (LC) is normal. Mutation of the Fas-promoter-670 gene can be used as an early marker of potential cervical cancer. Also, we presented the characteristics of normal CEC which focuses on the size of the cell and its nucleus.

Table 1. Characteristic of normal cervix-epithelial-cells in high-risk Indonesian mother

Variable	Mean ± SD	Confidence interval 95%
Cell length (CL): the longest cell diagonal that passes through the nucleus (μm)	11.06 ± 1.57	10.49 – 11.66
Cell width (CW): cell diagonal perpendicular to the diagonal of CL (μm)	8.13 ± 2.14	7.32 – 8.99
Cell area (CA) (μm^2)	73.74 ± 23.15	65.22 – 82.94
Cell perimeter(CP) (μm)	32.62 ± 4.92	30.84 – 34.53
Nucleus area (NA) (μm^2)	1.40 ± 0.54	1.21 – 1.63
Nucleus perimeter (NP) (μm)	4.30 ± 0.78	4.03 – 4.62
Nucleus length (NL) (μm)	1.47 ± 0.25	1.38 – 1.57
Nucleus width (NW)(μm)	1.18 ± 0.24	1.09 – 1.27
Nucleus area index (NAI) = (nucleus area/cell area)*100	2.07 ± 0.88	1.75 – 2.40
Nucleus perimeter index (NPI) = (nucleus perimeter/cell perimeter)*100	13.46 ± 2.96	12.33 – 14.56
Nucleus length index (NLI) = (nucleus length/cell length)*100	13.59 ± 2.99	12.53 – 14.74
Nucleus width index (NWI) = (nucleus width/cell width)*100	15.42 ± 4.86	13.59 – 17.22

Abbreviations: μm=milli micron ; μm^2=milli micron square; SD=standard of deviation.

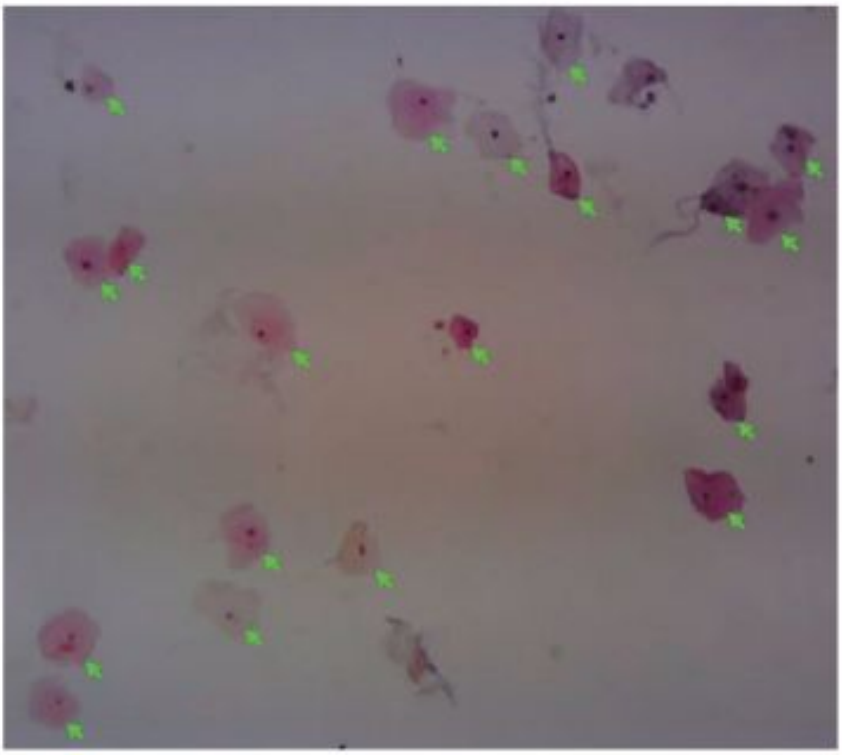


Figure 1. The Cervix-epithelial-cells of high-risk Indonesian mother available for observation (photomicroscope with optilab, objective 10x).

We reported the genotype difference of Fas-promoter-670 gene in the LC compared with CEC in high-risk Indonesian mother. Light microscope was used to observe the CEC and its cell nucleus. We focus on the characteristics of the CEC namely cell biometrics among others length, width, area, and perimeter of the cells and its cell nucleus. *Restriction fragment length polymorphism* (RFLP) was used to performance of the Fas-promoter-670 gene in the LC and CEC samples.

CASE REPORT

A 30-year-old of high-risk Indonesian mother, has two children (P2Ao), on April 21th 2016 has followed Pap smear examination with thin prep method. The mother concerned is included in the community of Indonesian women living with high-risk HPV as indicated by evidence of laboratory examinations. Marriage history at the age of 18 years, and the mother has a history of free sex. Furthermore, the mother also explained that she worked as a commercial sex worker and had never received HPV vaccination. Observations to the CEC was done by used optilab and image raster three programs by three observers. The characteristics of CEC namely cell biometrics among others cell length (CL), cell width (CW), cell area (CA), cell perimeter (CP), nucleus area (NA), and nucleus perimeter (NP). Moreover, we calculated the nucleus length index (NLI), nucleus width index (NWI), nucleus area index (NAI) and nucleus perimeter index (NPI) (Table 1). Base on the results showed that the CEC is normal because no atypical and malignant cells were found (Figure 1). Figure 2 and 3 shown the results of CEC cell biometrics. RFLP was used to perform Fas-promoter-670 gene in the LC and CEC. Blood sample was obtained from vena cubiti by proteinase K digestion and the CEC collected by thin prep method. DNA extraction from blood sample and CEC was performed using chloroform (Figure 4). Also, were used BstN1enzyme and forward primer 5'-CTACCTAAGAGCTATCTACCGTTC-3' and reverse primer 5'-GGCTG TCCATGTTGTGGCTGC-3'. Genotyping result of the Fas-promoter-670 gene in the LC is AA (normal=wild type), whereas in the CEC has mutation to GA (heterozygous variant) (Figure 5). Our team suggested that Pap smear screening could be done two years later.

DISCUSSION

In the Pap smear method, the determination of CEC characteristics can be used as a reference in the diagnosis of cervical cancer. We used the light

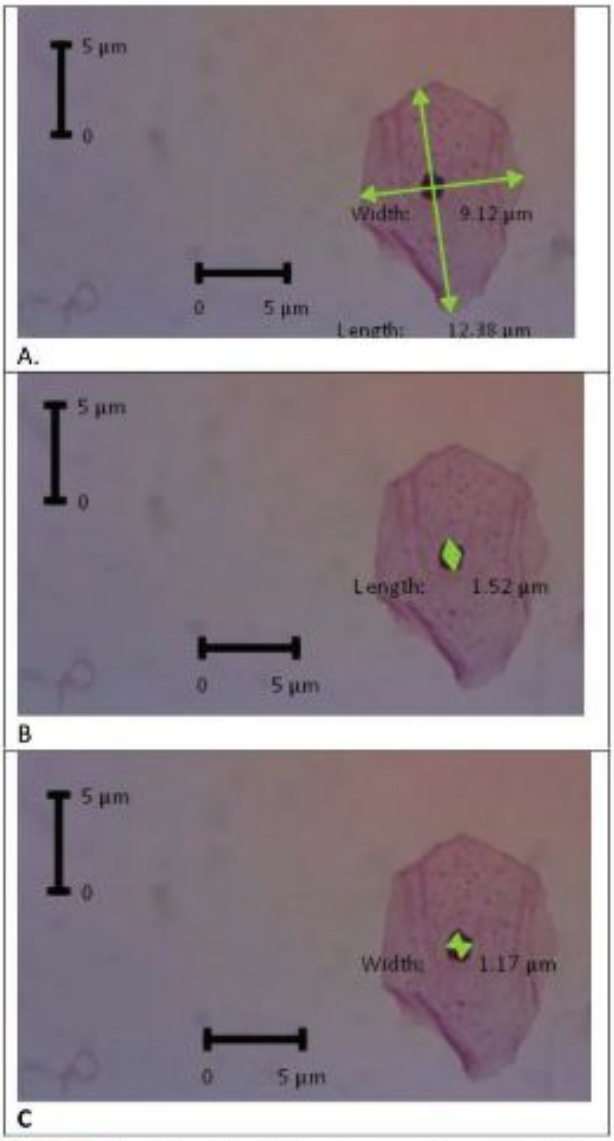


Figure 2. Length and width measurement results of the cell and nucleus. A=length and width of the cell; B=length of the nucleus; C=width of the nucleus.
Abbreviations: µm=milli micron.

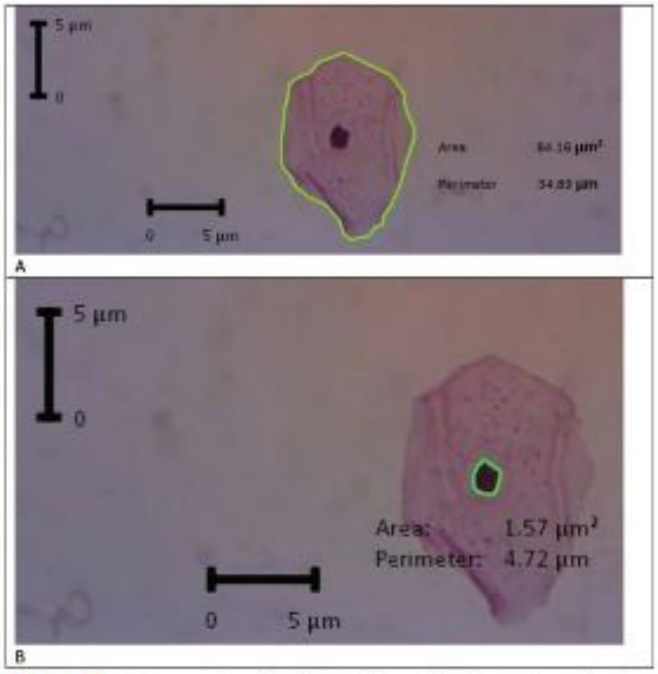


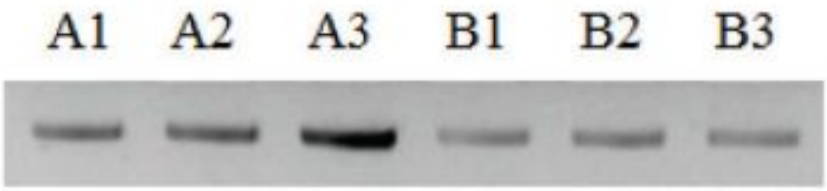
Figure 3. Area and perimeter of the cell and nucleus. A=Area and perimeter of the cell; B=area and perimeter of the nucleus.
Abbreviations: µm=milli micron; µm2=milli micron square.

microscope and image raster three programs to display normal CEC morphology. We perform these steps because most hospitals in Indonesia have facilities such as light microscope and the image raster three program is relatively easy to obtain. Our way may be simplest, nevertheless to detect cervical cancer can also be done using a more sophisticated tool, for example by atomic force microscopy.[5]

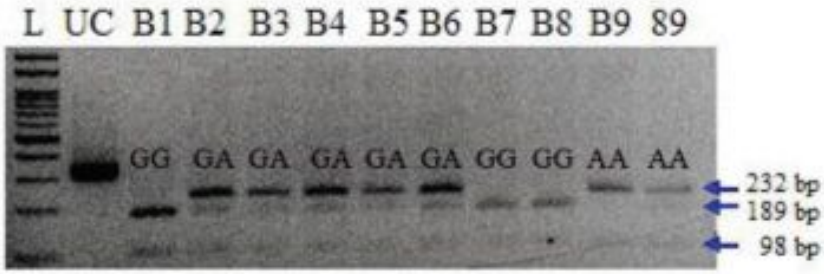
Pap smear examination of the CEC with hematoxylin and eosin staining showed that normal cervical tissue had multiple epithelial layers while cancerous cervical tissue showed dysplastic changes.[6] Our observation that the CEC has normal morphology appears to be similar to that of previous studies.[7] In addition to the normal CEC morphology, the nucleus morphology of the CEC can also be used to distinguish of CEC type. Previous studies showed that nucleus morphology criteria of the CEC among others: area, length, diameter, and radius.[8,9]

The other result showed that CEC has numerous balloon-outs, which have an average size ranging from 0.1-0.5 to 1.2-1.3 milli-micron (µm), are visible on the cell surface under microscope.[10] Beside that nucleus-cytoplasm ratio (N/C ratio) used to cytologic features of cervical cells. After the cells become malignant, the number of chromosomes in the nucleus will change, leading to changes in the shape of the nucleus. The length and diameter of the cell nucleus increased two fold, while the area increased by 4.5 fold.[11] Furthermore, We agree that on examination of cervical cytologic specimens showing most low-grade squamous intraepithelial lesions (LSIL), some of the high-grade squamous intraepithelial lesions (HSIL) cannot be excluded. Also, metastatic cancer cells are distinguished from normal cells based on stiffness rather than shape. Cancer cells are more promising for improving cancer diagnosis. Moreover, those metastatic cancer cells were nearly four times softer than normal cells.[12]

The BstN1 enzyme we used in RFLP to perform of Fas-promoter-670 gene was able to digest DNA



A. Deoxyribonucleic acid (DNA) extraction from Thin Prep samples (A1-A3) and lymphocyte (B1-B3).



B.

Figure 4. DNA extraction and genotyping of the Fas promoter-670 gene from blood peripheral lymphocyte cells. A. DNA extraction from the CEC (A1-A3) and blood peripheral lymphocyte cells (B1-B3). B. Genotyping of the Fas-promoter-670 gene with BstN1 enzyme. Sample number 89 from blood peripheral lymphocyte cells showed that genotype of the Fas-promoter-670 gene is AA (232 + 98 bp).
Abbreviations: DNA=deoxyribo nucleic acid; CEC=cervix-epithelial-cells; L=Molecular weight standard; UC=DNA loading without BstN1 enzyme; C1-C9= control sample from blood peripheral limphocyte cells, loading with BstN1; AA genotype (232, 98 bp); GA gentoype (232, 189, 98 bp); GG genotype (189, 98 bp).

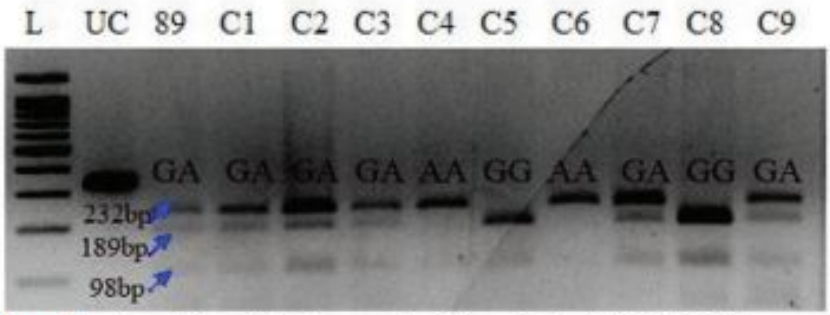


Figure 5. Genotyping of the Fas-promoter-670 gene in the CEC with BstN1 enzyme. Abbreviations: CEC=cervix-epithelial-cells; L=Molecular weight standard; UC=DNA loading without BstN1 enzyme; 89= sample number of the CEC from thin prep solution showed that genotype of the Fas-promoter-670 gene is GA (232, 189 and 98 bp); C1-C9 =sample control of the CEC from thin prep solution, loading with BstN1; AA genotype (232, 98 bp); GA genotype (232, 189, 98 bp); GG genotype (189, 98 bp).

samples into fragments 232, 189 and 98 base pair (bp). The fragments of 232 and 189 bp indicated the AA genotype, while 232, 189 and 98 bp indicated the GA genotypes. Therefore 189 and 98 bp indicated the GG genotype. This results according to previous researchers.[13] Moreover it is also shown that cervical cancer is associated with the polymorphism of the Fas-promoter-670 gene. The GG genotype of Fas-promoter-670 gene promotes the occurrence of cervical cancer compared to AA genotype. The result of research previously shows that G allele also increases the occurrence of cervical cancer. Two single nucleotide polymorphisms (SNPs) (-1377G>A, rs2234767 and -670A>G, rs1800682) located in the promoter region of Fas gene were examined in association with some tumorogenesis.[14] Also, polymorphism is also associated with metabolic abnormalities until the occurrence of pathological conditions.[15,16]

In this case, the genotype of Fas-promoter-670 gene in the LC was different from CEC. The expression pattern of the Fas-promoter-670 gene in this study is expected to be an early marker of cervical cancer so that it can be prevented. This corresponds to the general principle that detection of cervical cancer is directed to the presence of oncogenic elements that promote cell transformation. Moreover that the failure of Fas gene regulation produces death signals, which are reported in some cancers.[17] However, the correlation between this SNP and cancer susceptibility including the risk of gynecological malignancies needs to be studied more widely.

CONCLUSION

Based on characteristic of cell biometrics, the CEC in high-risk Indonesian mother was normal. The genotype of the Fas-promoter-670 gene in the LC is AA (normal=wild type), whereas in the CEC has mutation to GA (heterozygous variant). We recommend examining of Fas-promoter-670 gene on early screening for cervical cancer.

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CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

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ETHIC AND PATIENT CONSENT

The authors declare that: 1). They have obtained written, informed consent for the publication of the details relating to the patient in this report. 2). All possible steps have been taken to safeguard the identity of the patient. 3). The ethical clearance of this study was approved by the Commission on Research Ethics, Faculty of Medicine, University of Trisakti, Jakarta, Indonesia, number 60/KER/FK/05/2013.

AUTHORS CONTRIBUTIONS

MLEP: images review and processing, writing of the manuscript and reviewing the final text. WR, AG, K: literature review and writing of the manuscript.

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