

Infective Endocarditis at Tertiary Health Care Units

Thesis

Submitted for partial fulfillment of Master Degree In
Clinical and Chemical Pathology

By

Omaima Ahmed El Sayed

M.B., B.CH

Faculty of Medicine - Cairo University

Under Supervision of

Professor / Hadia Hussein Bassim

Professor of Clinical and Chemical Pathology
Faculty of Medicine-Ain Shams University

Professor / Manal Abd El Alim Abd El Sattar

Professor of Clinical and Chemical Pathology
Faculty of Medicine-Ain Shams University

Doctor / Hala Mahmoud Hafez

Lecturer of Clinical and Chemical Pathology
Faculty of Medicine-Ain Shams University

Faculty of Medicine
Ain Shams University

2010

Contents

	Page
Introduction	1
Aim of the work	4
REVIEW OF LITERATURE	
Historical perspective.....	5
Pathogenesis.....	5
Epidemiology	8
Incidence	8
Sex.....	8
Age	8
Risk factors.....	9
Recurrence.....	13
Mortality.....	13
Causative organisms	14
Types	23
Complications	26
Diagnosis of IE.....	29
Clinical manifestation	29
Laboratory diagnosis.....	32
Echocardiography	47
Duke's criteria for diagnosis of IE.....	48
Treatment	52
Prevention	54
SUBJECTS AND METHODS	57
RESULTS	61
DISCUSSION	73
SUMMARY	77
CONCLUSION.....	78
REFERENCES.....	79
ARABIC SUMMARY	--

List of abbreviations

AHA	:	American Heart Association
AO	:	Acridine orange
BCS-RCP	:	British Cardiac Society and the Royal College of Physicians of London
BSAC	:	British Society of Antimicrobial Chemotherapy
CFUs	:	Colony-forming units
CHD	:	Congenital heart disease
CoNS	:	Coagulase negative Staphylococci
CRP	:	C-reactive protein
DNA	:	Deoxyribonucleic acid
E.coli	:	Escherichia coli
EDTA	:	Ethylene diamine tetraacetic acid
EM	:	Electron microscope
ESC	:	European Society of Cardiology
ESR	:	Erythrocyte sedimentation rate
ESRD	:	End-stage renal disease
F	:	Females
FISH	:	Fluorescent in situ hybridization
HACEK	:	Haemophilus species, Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens, and Kingella kingae
HF	:	Heart failure
HIV	:	Human immunodeficiency virus
IAs	:	Infectious aneurysms
ICU	:	Intensive care unit
IE	:	Infective endocarditis
M	:	Males
MRSA	:	Methicillin Resistance Staph. aureus
N	:	Number
NVE	:	Native valve endocarditis
NBTE	:	Non-bacterial thrombotic endocarditis

PAS	:	Periodic acid-Schiff
PCR	:	Broad-range polymerase chain reaction
PVE	:	Prosthetic valve endocarditis
PCT	:	Serum procalcitonin
RNA	:	Ribonucleic acid
SD	:	Standard deviation
SPS	:	Sodium polyanetholsulphonate
Staph.	:	Staphylococcus
Strept.	:	Streptococcus
TFA	:	Tissue factor activity
TTE	:	Transthoracic echocardiography
US	:	United States

List of Tables

Table	Title	Page
1	Endocarditis caused by other fastidious and/or rare bacteria	20
2	Agents of blood culture-negative endocarditis	38
3	Duke classification for diagnosis of IE	49
4	Definitions of major and minor criteria for the diagnosis of Infective Endocarditis	50
5	Proposed additional minor criteria for the Duke classification	51
6	Proposed antibiotic regimens for initial empirical treatment of IE	53
7	Bacterial endocarditis prophylaxis protocol	56
8	The descriptive statistics of the patients	62
9	Age and sex distribution of patients with IE	63
10	The Causative microorganisms according to the nature of the valve	67
11	The descriptive statistics of negative, positive acridine orange and positive blood cultures	68
12	Results of antimicrobial susceptibility for each organism.	71

List of Figures

Fig.	Title	Page
1	Early steps in bacterial valve colonization.	7
2	Cutaneous manifestations in IE	31
3	Whipple's disease endocarditis showing foamy PAS-positive macrophages	41
4	Warthin-Starry silver stain of a Bartonella quintana-infected valve	42
5	Electron microscope showing Tropheryma whipplei on valvular tissue	45
6	Age and Sex distribution of patients with IE	63
7	Percentage of patients of PVE and NVE	64
8	Percentage of patients of IE in relation to various risk factors	65
9	pie chart showing the causative organisms of IE	66

List of Photos

Photo	Title	Page
1	Results of Acridine Orange	69
2	Results of Acridine Orange	69

التهاب الشغاف الخمجي للقلب

يعد إلتهاب الشغاف الخمجي للقلب وصمامات القلب مرض خطير يؤدي الى الوفاة. لذا يجب سرعة تشخيص هذا المرض وعلاجه .

هدف هذه الدراسة إلى التعرف على الميكروبات المسببة لإلتهاب الشغاف الخمجي و تحديد نمط المضادات الحيوية اللازمة و بيان دور صبغة الأكرئين البرتقالية في حالات مزارع الدم السالبة.

تمت هذه الدراسة في مستشفيات جامعة عين شمس و معهد القلب في الفترة من ١٠ يوليو ٢٠١٢ إلى ١٠ أغسطس ٢٠١٢ سبعة أسابيع . تم تشخيصهم بالفحص الاكلينيكي والموجات فوق صوتية على القلب بأنهم حالات اصابة بهذا المرض .

تم فحص الرجال أكثر عرضة من السيدات (٨٠% - ٢٠%) وأن أكثر معدل الإصابة يتراوح بين سن (٢٠ - ٤٠) وأن اقل معدل يتراوح بين سن ٤٠ - ٦٠. لوحظ أيضا أن أهم العوامل المسببة لحدوث هذا المرض هي الحمى الروماتيزمية للقلب تليها تغيير البنية البنية , أن أكثر الصمامات تأثرا هو الصمام الأبهري .

وجد ان عدد حالات مزارع الدم الايجابية هو ١٠ حالة وأن أكثر الميكروبات

المسببة هي (Staph.aureus).

تم فحص التهاب الشغاف الخمجي للقلب على صمام طبيعي قد مثل (١٠٠%) (١٠٠%)

Staph. aureus و coagulase negative Staph هما

أكثر الميكروبات المسببة للمرض بالتساوى . التهاب الشغاف
الميكروب (١٠٠%) سبق تغييره قد مثل
الميكروب هو

Staph. aureus تليها coagulase negative Staph.

و وجد أن عدد حالات مزارع الدم السلبية هي ٢٠ حالة وهي تمثل (٢٨,٦٧%) تم
فحص هذه الحالات السلبية بصبغة الاكريدين ووجد ان عدد ثلاثة حالات بهم
ميكروب وهو يمثل (١٥%) يوجد بهم ميكروب وهو يمثل
(٨٥%). لذا ينصح بإستخدام صبغة الأكريدين البرتقالية كطريقة سهلة وسريعة
في حالات مزارع الدم السلبية.

Acknowledgement

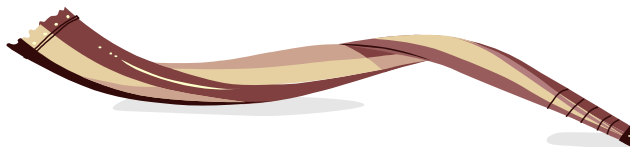
First of all, thanks to ALLAH for helping and guiding me in accomplishing this work and for everything else I have.

I wish to express my deepest gratitude and appreciation to Prof. Dr. Hadia Hussein Bassim, Professor of Clinical and Chemical Pathology, Faculty of Medicine, Ain Shams University, for her help in choosing the topic of this study and for her valuable supervision, guidance.

I wish to express my deep gratitude and respect for Prof. Dr. Manal Abd Elalim Abd El Sattar, Professor of Clinical and Chemical Pathology, Faculty of Medicine, Ain Shams University, for her good support, supervision and help during this work.

Also, I wish to express my gratitude to Dr. Hala Mahmoud Hafez, Lecturer of Clinical and Chemical Pathology, Faculty of Medicine, Ain Shams University, for her valuable instructions and support.

I would like also to thank my whole family and my colleagues for their kindness, support and much needed encouragement.



Omaima Ahmed

INTRODUCTION

Infective endocarditis (IE) is a non-contagious infection of the lining of the heart chambers and heart valves, caused by bacteria, fungi, or other infectious agents **(Millar and Moore, 2004)**. It remains a relatively rare disease worldwide, with an estimated incidence between 3 and 10 per 100,000 per year **(Habib et al., 2009)**. Mortality varies according to the infecting organism (*Staphylococcus aureus* 30- 40%, *viridans Streptococci* 4- 16%, fungal infections over 50%) and is higher when infection affects a prosthetic valve or is complicated by congestive heart failure, abscess formation, or a neurological event **(Mylonakis and Calderwood, 2001; Cabell et al., 2002)**.

The risk of infection of heart valves in persons predisposed to acquiring IE increases with the following conditions: congenital heart disease, rheumatic fever, major dental treatment, open heart surgery, and genitourinary procedures. New evidence is growing that changes in social behavior, such as an increase in the incidence of body piercing, excessive alcohol consumption, and the use of intravenous self-administered illicit drugs may also predispose a susceptible person to an increased risk of acquiring endocarditis **(Millar and Moore, 2004)**.

The disease has been most commonly seen in older age groups with a predominance of male patients and an increased incidence of acute cases caused by virulent organisms such as *Staph. aureus*, Gram-negative bacilli and fungi **(Nashmi and Memish, 2007)**.

The diagnosis of infective endocarditis requires a multifaceted approach involving clinical suspicion and

examination, laboratory investigation by means of inflammatory markers and microbiological analysis, and imaging with echocardiography (**Beynon, et al., 2006**).

Transthoracic echocardiography is rapid and noninvasive and has excellent specificity for vegetations (98%) (**Shively et al., 1991**). However, transthoracic echocardiography may be inadequate in up to 20% of adult patients because of obesity, chronic obstructive pulmonary disease, or chest-wall deformities; the overall sensitivity for vegetations may be less than 60 to 70% (**Werner et al., 1996**). On the other hand, transesophageal echocardiography, although more costly and invasive, increases the sensitivity for detecting vegetations to 75-95% while maintaining the specificity to 85-98% (**Werner et al., 1996; Heidenreich et al., 1999**).

Given the need for prolonged antibiotic treatment in most patients with IE, positive microbiological cultures and sensitivities are vitally important for successful management. Current guidelines recommend that three sets of blood cultures are drawn one hour apart before the introduction of antibiotic treatment (**Horstkotte et al., 2004**). However, Blood cultures are negative in 2.5-31% of cases of endocarditis, often delaying diagnosis and the start of treatment with profound impact on clinical outcome. Negative cultures are most commonly related to the previous administration of antibiotics (**Hoen et al., 2002**), but they may also be associated with fastidious pathogens, including *Legionella*, *Coxiella*, the HACEK group (*Haemophilus* species, *Actinobacillus actinomycetem-comitans*, *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella kingae*), and fungi such as *Candida*, *Histoplasma*, and *Aspergillus* species (**Beynon et al., 2006**).

Acridine Orange (AO) stain is a rapid, inexpensive method in detection of culture negative endocarditis. As it could detect fastidious microorganisms and candida which are difficult to be detected by Gram stain or when standard media are used **(Adler et al., 2003)**.

Serological assay can detect Coxiella, Brucella, Bartonella, or Chlamydia. Polymerase chain reaction can be used to identify unculturable organisms in excised vegetations or systemic emboli **(Goldenberger et al., 1997)**. Specific fluorescent labeled antibody staining and electron microscopy, should be considered in all cases where cultures have tested negative for IE **(Prendergast, 2002)**.

AIM OF THE WORK

The aim of the present study was to identify the microbial causes of IE, determine their antimicrobial susceptibility pattern, and to evaluate the role of the acridine orange stain in detecting the presence of microorganisms in cases of blood culture negative endocarditis.