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Investigation of Novel Orthopox Virus in the Country of Georgia

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On July 5, 2013, Georgia National Center for Disease Control (NCDC) was notified of a patient presenting with a lesion. The patient was suspected to be cowpox, by a clinician from the National Infectious Disease Hospital.
Request to CDC for lab support

• NCDC requested CDC’s help for laboratory confirmation of cowpox infection

• 4-person team from CDC Poxvirus and Rabies Branch deployed to Tbilisi, Georgia on September 7 to work with:
  – CDC Global Disease Detection Regional Center
  – South Caucasus Field Epidemiology and Laboratory Training Program (SC/FELTP)
  – Emerging Infections Program
  – FELTP graduate staff from NCDC
  – Georgia National Food Agency (NFA) and Laboratory of the Ministry of Agriculture (LMA)
Background of cowpox in Georgia

- Not previously reported
- Not a reportable human disease
- No laboratory diagnostics in country
- Could be part of differential diagnosis of human cutaneous anthrax
Initial findings from CDC-Atlanta

- CDC Poxvirus laboratory revealed a novel orthopox strain

- The virus's epidemiology, reservoir, and human or animal disease burden are unclear

- For temporary convenience, we refer to the virus “Akhmeta virus” after residence of case patient
“Akhmeta virus” in Orthopox phylogenetic tree

Camelpox
VARV_BSH74_sol
Variola
CPXV_GER91_3
CPXV_GER98_2
CPXV_NOR95_MAN
CPXV_UK00_K2984
CPXV_BR
CPXV_GER90_2
CPXV_FRA01_NANCY
CPXV_GER80_EP4
CPXV_GER02_MKY
Zaire_1979-005
CPXV_AUS99_867
CPXV_FIN00_MAN
CPXV_GRI
Ectymos
i25_ROG85a
i25_ROG85b
ROG
i26_ROG88
Location of original cases

• The patients are residents of Akhmeta district

• They herded cattle in mountains nearby Jijeti village, Tianeti district
Anthrax in Georgia
issues of differential diagnosis

• Since 2008 annually reported 52-195 human anthrax cases
• 16-70 cases of them are defined as “rejected”
• 9-32 cases of them were not confirmed and remained suspected for anthrax
• They were not investigated on any other disease, among them cow pox
Purpose of investigation

• We investigated
  – To describe reported cases
  – To find:
    • New human cases
    • New animal cases
    • Virus reservoir
  – To characterize the virus
Suspected
• A person or animal with one or more lesions at one or more sites that may progress morphologically through papule, vesicle, pustule, and scab, or other skin lesions that have not healed within 12 days.

Probable
• A probable case meets the criteria for a suspected case; in addition, Orthopoxvirus-specific serum antibodies (IgG or IgM) must be detected or an epidemiologic link to a confirmed human or animal case must be demonstrated. (For IgG to be considered as evidence of disease, convalescent titers must rise after the illness).
Working Case definitions

Confirmed

• A confirmed case meets the criteria for a suspected or probable case; in addition, evidence of “Akhmeta virus” infection must be demonstrated on the basis of:

  - positive test results from “Akhmeta virus” polymerase chain reaction (PCR) assay or from antigen detection techniques (e.g., indirect fluorescent antibody)

  Or

  - demonstration of “Akhmeta virus” by culture or electron microscopy
Epidemiological investigation of cases

• Face to face interview of cases and their family members
• Face to face interview of all herders around of cases working and living places
Search for additional cases

• Questionnaire was designed to collect information about:
  – Animals with cowpox signs
  – Persons with symptoms characteristic of the disease
ZG joins BK in mountains of Jijeti to care for a herd of cows 6/2/13

First cow in the herd develops illness including lesions on teats 6/5/13

ZG develops lesions on hands 6/10/13

ZG leaves mountain and seeks medical care in Akhmeta and Tbilisi ~6/15/13

June 2013

BK develops lesions on hands 6/25/13

July 2013

BK seeks medical care in Akhmeta 7/6/13

ZG reports full recovery from illness ~7/1/13

CDC Georgia contacted by NCDC about possible Cowpox infection 7/5/13

Sept 2013

Orthopoxvirus infection confirmed in ZG and BK at CDC Atlanta ~7/29/13

NFA, LMA, NCDC and CDC begin field investigations 9/11--16/2013
Interviews: Sept 11-16, 2013

- Number of persons interviewed: 57
- Number of suspect human cases identified: 0
- Number of probable human cases identified: 0
- Number of confirmed human cases identified: 2
- Serum samples collected: 38
Photo by Darin Carroll
Description of cases

• Patient 1 (ZG)
  – 24 year old, previously healthy male
  – Owns, herds, milks cattle
  – Bilateral lesions on hand, fever, axillary lymphadenopathy, backache
  – No history of smallpox vaccination

• Patient 2 (KB)
  – 37 year old, previously healthy male
  – Owns, herds, milks cattle
  – Bilateral lesions on hand, fever, axillary lymphadenopathy, backache
  – No history of smallpox vaccination
Results

– Human case investigation
  • Known cases – 2 (confirmed by CDC)
  • New case finding - 0

– Animal case finding
  • Known suspect cases – 10 (lab pending)
  • New case - 0
Field activities

- Organization of field laboratory
  - Animal samples processing
  - Human samples processing
  - Laboratory testing

- Case finding
  - Human: interviews, blood collection, swabs from suspect lesion
  - Animals: inspection, blood collection, swab from suspect lesions

- Reservoir investigation
  - Inspection of environment
  - Trap set up for rodents
  - Rodent processing

- Field laboratory testing
  - Sample preparation
  - Field PCR
Field laboratory organization

• Site selection
  – edge of the village, on the foot of pasture mountain

• Equipment
  – Rapid and GeneXpert systems
  – rodent traps and dissection tool kit
  – sample collecting kits
  – PPE
Wildlife processing sites
Field Laboratory set up
Case finding

• 57 interviews
  – Case patients – 2
  – Case patients’ family members – 7
  – Herders and farmers – 44
  – Butchers – 2
  – Vets – 2

• Human samples
  – Blood – 38
  – Swab – 6

• Animal samples
  – Blood – 35
  – Oral and teat swab – 43
Reservoir Investigation

• Site selection according to herders and farmers

• Trap set up
  – Five days
  – Total number – 840 (530 in 4 pastures; 310 in 3 agricultural fields )

• Wildlife
  – Number of processed animals – 34
  – Number of different species – 5
Species processed within the 5 trapping days

(1) **Dryomys nitedula**

(2) **Mus musculus**

(3) **Crocidura sp.**

(17) **Apodemus sylvaticus**

(11) **Microtis spp.**
Site selection, trap setup, processing

Trap collection process

Processing preparation

Rodent sacrifice

Dissection of animals
Field laboratory processing

• Blood samples – 3 aliquots of human and animal serum

• Swab samples – DNA extraction

• Wildlife samples – Blood on strips, heart, lung, spleen, kidneys, liver individually from all animals and three pools of liver for preliminary testing
Field laboratory processing

Dr. Li Yu – CDC Atlanta

Maka Kokhreidze, LMA Molecular biologist running Rapid PCR
Laboratory test results

• Dr. Li Yu (CDC Atlanta) and Maka Kokhreidze (LMA Molecular Biologist) tested samples using Rapid PCR and Gene Xpert

• 27 samples were tested for both, parapoxvirus and orthopoxvirus
  – Positive for orthopox – 0
  – Positive for parapox – 10 (all were healthy cows without any active lesions)
Laboratory test results

• Total 8 orthopox runs by GeneXpert
  – Runs did not finish (signal drops) – 2
  – Invalid (internal control failed) – 1
  – 5 runs are negative (2 cows (both healthy), 1 human scab, 4 vials of pooled rodent livers, 1 pooled milk sample from the case-patient #2)

• Serology and internal organs except pooled livers of animals will be done by POX team at CDC, Atlanta
Recommendations

• Prospective surveillance
  – Passive
    • Clinical specimens (humans and animals)
    • Anthrax-negative specimens (humans)
  – Active
    • Field studies of potential reservoirs
    • Domestic animals

• “One Health”

• Surveillance should be performed beyond the Tianeti area
Recommendations

• Grants/funding to support future activities

• Continue to develop laboratory capacity
  – Training
Acknowledgments

• National centers for Disease Control and Public Health of Georgia (NCDC) and Lugar Center
• FELTP/Republic of Georgia
• National Food Agency
• Laboratory of Ministry of Agriculture
• CDC Georgia - Global Disease Detection Centers
• Poxvirus and Rabies branch
Orthopoxvirus phylogeny

North American Orthopoxviruses

Old World
- Found throughout Europe, Africa and Asia
- Over 90% genetic similarity
- Serologically cross-reactive
Orthopoxvirus Species of the Old World

- Ectromelia virus
- Monkeypox virus
- Taterapox virus
- Camelpox virus
- Variola virus (extinct)
- Vaccinia virus (vaccine)
- Cowpox virus
And a new virus... in Georgia!
Naming

• Formal name has not been determined

• Out of convenience, I will refer to it as “Akhmeta virus”
Significance (1)

• This new virus represents an outlier not adequately captured by current rapid diagnostic tests
  – The virus was detected by a general *Orthopoxvirus* assay, but subsequent testing with a monkeypox-specific assay led to a false positive result

• New assays are needed for Orthopoxvirus identification at both genus and species levels
Significance (2)

• Neither the medical nor the epidemiologic features of Akhmeta virus infections have been defined
Significance (3)

• Potential impacts to agricultural/livestock production are unknown, as are the occupational risks
Significance (4)

- This may be part of a larger picture of emergence or re-emergence of pathogenic Orthopoxviruses in the absence of smallpox vaccination
Unanswered questions

• What is the clinical presentation of Akhmeta virus infection?
Akhmets virus infection ≠ Cowpox virus infection
Unanswered questions

• What is the prevalence/incidence of Akhmeta virus infection in humans and domestic animals?
Unanswered questions

• What is reservoir of the Akhmeta virus?
Identifying Reservoirs of Infection: A Conceptual and Practical Challenge

Daniel T. Haydon, Sarah Cleaveland, Louise H. Taylor, and M. Karen Laurenson
Emerging Infectious Diseases (8) 2002

“...a reservoir [is] one or more epidemiologically connected populations or environments in which the pathogen can be permanently maintained and from which infection is transmitted to the defined target population.”
Cowpox virus: reservoir hosts and geographic range

- **10-80% OPXV seropositive**
  - *Myodes glareolus* (*Clethrionomys glareolus*)
  - Bank vole

- **27% OPXV seropositive**
  - *Apodemus sylvaticus*
  - Wood mouse

- **11/12 OPXV seropositive**
  - *Microtus agrestis*
  - Field vole

- **9.2% OPXV seropositive**
  - *Meriones libycus*
  - Libyan jird (gerbil)

- **18% OPXV seropositive**
  - *Rhombomys opimus*
  - Great gerbil

- **15% OPXV seropositive**
  - *Citellus fulvus*
  - Suslick
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