Hypermucoviscous Klebsiella syndrome it’s in the community!
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Abstract
Hypermucoviscous Klebsiella syndrome is a unique syndrome caused by a new variant of Klebsiella pneumoniae (KP), characterized by abscess formation at distant body sites. This emerging KP strain is different from the usual classic strains in having the rpm gene which increases capsule formation making this strain resistant to phagocytosis and helping in its dissemination to distant organs. A 50 years old diabetic man presented with facial swelling after dental procedure which progressively increased despite being on antibiotics. On examination he was febrile, had neck swelling with signs of inflammation and tender hepatomegaly. Ultrasonography showed submental and liver abscesses which were subsequently drained and both cultures isolated KP with hypermucoid colonies on agar plate and a positive string test indicating the presence of this new hypervirulent strain of KP. Therefore, a diagnosis of Hypermucoviscous Klebsiella syndrome should be considered in all patients who present with KP infection with multiple organ abscesses.

Keywords: Hypervirulent strain of Klebsiella pneumoniae, Hypermucoviscous Klebsiella Syndrome, String test.

Introduction
Microorganisms are notorious for their ability to adapt and evolve which has led to the emergence of organisms like Methicillin resistant Staphylococcus aureus (MRSA), Vancomycin resistant Enterococcus (VRE), Carbapenem resistant Enterobacteriaceae (CRE) which are known for their virulence, antibiotic resistance and a strong nosocomial association. But in recent years there is a paradigm shift towards community acquired virulent infections like Community Acquired Methicillin resistant Staphylococcus aureus (CA-MRSA). Here we report a case of a new variant of Klebsiella pneumoniae (hypervirulent Klebsiella pneumoniae), coming in lime light for its virulent nature and association with healthy individuals, highlighting the fact that virulent infections can initiate from the community. This hypervirulent Klebsiella pneumoniae strain, unlike other Gram negative organisms, has the ability to metastasize to distant organs causing a syndrome called Hypermucoviscous Klebsiella Syndrome.

Case Report
It is a case of a 50 years old male, resident of United States visiting Pakistan on vacations who was recently diagnosed as having Diabetes Mellitus for which he was taking insulin. He had Root canal treatment in December 2015 after which he developed facial swelling that was presumed to be cellulitis and was treated with Metronidazole and Amoxicillin-clavulanic acid. Ten days after completion of antibiotic course the patient presented to the Infectious Diseases Clinic at Aga Khan University Hospital in January 2016 with complaints of fever and painful swelling on the neck just below the chin since 15 days. Fever was documented up to 101°F with neck swelling progressively increasing in size for which he had received Cefixime for 7 days but clinical symptoms did not improve. There were no other systemic complaints. On physical examination he was a middle aged male, conscious, oriented and had a swelling in the neck just below the body of mandible 3*2cm in size, red, warm, fluctuant and tender. Submental lymph nodes were enlarged. On abdominal examination liver was palpable 4 cm below the costal margin, tender, having a span of 16 cms. Respiratory and cardiovascular examinations were unremarkable. His haemoglobin was 11mg/dl, TLC count of 15,000 with 80% neutrophils, Platelets of 650, ESR 80 with mildly elevated AST and ALT. Ultrasound neck was done that showed a Heterogeneous lesion of 2.8*1.4 cm in the Submental region suggestive of Submental Abscess. Ultrasound liver showed an enlarged fatty liver with a Heterogeneous lesion of 5.8*7 cm consistent with an Abscess in the right lobe of liver. 10cc pus was aspirated from Submental region that grew Klebsiella Pneumoniae on pus culture being sensitive to Amoxiclav, Amikacin, Cefixime, Trimethoprin-sulphamethoxazole, Cefuroxime, Ciprofloxacin, Piperacilline-tazobactam and Imipenem. Percutaneous drainage of liver abscess was also done that isolated the same organism with same sensitivity as above. Since the blood agar plate had shiny mucoid, cream, circular colonies so string test was done that was positive with a
string length of more than 5mm (Figure). Blood culture had no growth and IHA titers were negative. He was treated initially with I/V Ceftriaxone for 4 days which was later changed to Ciprofloxacin per OS 750mg BID after culture report. He had received Ciprofloxacin for total course of 14 days to which he responded well.

On follow up visit his fever had subsided, both Submental and liver abscesses resolved on ultrasound with repeat TLC decreasing to 11,000 and ESR decreased to 15.

Consent of patient was taken prior to the writing of the manuscript.

**Discussion**

Hypermucoviscous Klebsiella syndrome is a life threatening condition caused by a hypervirulent strain of Klebsiella Pneumoniae (hv KP) that affects healthy individuals in the community unlike classic strain of KP.\(^1\) This unique syndrome was first reported in Taiwan in the mid of 1990 and was initially associated with the Asian Pacific Rim but has now increasingly been recognized in Western countries as well.\(^2,4\) Unlike other gram negative organisms it has the propensity to metastasize to distant organs, even in non-immunocompromised hosts causing liver abscess (in the absence of biliary tract disease), endophthalmitis, pneumonia, meningitis and soft tissue infections.\(^5\) Although the route of infection is not yet well-established, it is highly probable that intestinal colonization is crucial to its spread. From the gastro-intestinal tract, extra-intestinal infection may occur from its spread to the bladder from the perineum, aspiration of oro-pharyngeal secretions, or even through the skin. After gaining entry, infection may result due to a hypervirulent nature of the pathogen.\(^6\) This strain is different from the classic strain of Klebsiella pneumoniae in terms of its virulence which is due to the presence of rmpA gene (regulator of mucoid phenotype) and siderophore biosynthetic genes. The rmpA gene increases capsule production making the organism resistant to phagocytosis and the Siderophore biosynthetic genes secrete greater amounts of siderophores (Aerobactin and salmochelin) that mediate iron acquisition from the host making them more virulent.\(^7\) In contrast to the classic Klebsiella pneumoniae strain, it's colonies on blood agar plate appear hypermucoviscous with a positive String test which is a semi quantitative phenotypic test done to assess the hypermucoviscosity of hv strain of KP done by stretching a bacterial colony on an agar plate with an inoculation needle and it is labeled positive when the Viscous string is >5mm in length.\(^8\) As far as antimicrobial susceptibility is concerned the hv strain of KP is sensitive to all tested antimicrobials except ampicillin so response to treatment is good if the antibiotic is started timely with drainage of abscess. Therefore, despite having the ability to metastasize to distant organs hypervirulent Klebsiella pneumoniae has 30 days mortality less than that of classic Klebsiella pneumoniae.\(^9,10\) However, there had been isolated case reports of drug resistance seen in hv KP strain reported from China raising a concern globally which may prove to be fatal keeping in mind the virulence associated with it.\(^11\)

To our knowledge, no case of hypervirulent K. pneumoniae has been reported in Pakistan. This is likely due to a lack of awareness about the existence of this strain and hence under-reporting. The limitation in this case was the unavailability of gene analysis specifically for rmpA gene (regulator of mucoid phenotype) and siderophore biosynthetic genes which are helpful in diagnosis. The diagnosis was thus made on positive string test, antimicrobial susceptibility of K. pneumoniae and its characteristic metastatic nature. Therefore, despite the usefulness of string test, it is important to devise a more rapid and objective test that can help in early detection and management to reduce the risk of drug resistance.

**Conclusion**

Hypervirulent strain of Klebsiella Pneumonia usually being susceptible to tested antimicrobials causes Hypermucoviscous Klebsiella Syndrome affecting otherwise healthy individuals in community and has the ability to metastasize to distant organs with liver being...
the most favourable site. Prognosis is good if appropriate antibiotic is started earlier with drainage of abscesses.

Consent of patient was taken prior to the writing of the manuscript.

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References