Case report

Title of paper:

First report of human intracranial *Weeksella virosa* infection in the setting of anaplastic meningiomata

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Abstract:

A 49 year old female underwent multiple craniotomies for resection of aggressive meningeal tumours (WHO Grade III). She re-presented to hospital with sepsis due to ventriculitis. The craniotomy wound was urgently debrided and isolates of the Gram negative rod *Weeksella virosa* identified on 16S PCR. This species is most commonly found as a genitourinary commensal and here we report the first documented case of intracranial infection with this species and its successful treatment with a 6-week course of oral β-lactam antibiotics.

Keywords:

Weeksella virosa; central nervous system infection; ventriculitis; anaplastic meningioma

Clinical details

A 49-year old, right handed female presented with early morning headaches and vomiting. Her past medical history was unremarkable. On examination, the only focal deficit elicited was a dense left homonymous hemianopia. Magnetic resonance imaging (MRI) of the brain revealed a lesion occupying the trigone and occipital horn of the right lateral ventricle (Figure 1A). No other intracranial lesions were seen, and computed tomography scans of the chest, abdomen and pelvis did not show any abnormalities. A complete macroscopic excision of the tumour was effected without problems. The postoperative MRI scan did not show any residual enhancing tumour tissue. The histology of the lesion was that of an atypical meningioma (WHO Grade II) with 10 mitoses per 10 high power fields (10-HPF) and a Ki-67 nuclear labelling index (Ki67 NLI) of 23.1%.

Given the high Ki-67 index, the patient was offered whole brain radiotherapy. The patient developed increasing headaches 8 months after surgery which responded to dexamethasone 4mg qid. Repeat MR scanning revealed a new right temporo-occipital tumour (Figure 1B). There was no obvious tumour recurrence at the site of the original operation. She underwent a second operation to remove the lesion which indicated that it was an anaplastic meningioma (WHO Grade III) with 22 mitoses per 10-HPF and a Ki67 NLI of 21.6%. Attempts to stop her steroids were unsuccessful as this resulted in a recurrence of her headaches. She had other scan 8-weeks after her second operation when her headaches intensified and she noted mild weakness in her left arm. The scans showed another tumour in the trigone of the right lateral ventricle. A third craniotomy was performed to resect this lesion, with post-operative imaging showing no residual enhancing tissue. Histological analysis confirmed a WHO Grade III meningioma with 26 mitoses per 10-HPF and a Ki67 NPL of 68.8%.

The patient recovered well after her third operation and was discharged 6-days later. Five days following discharge, she was re-admitted after becoming increasingly drowsy and weak on her left side. She was febrile (38.8C), difficult to rouse and had grade 0 power on her left side. There was no meningism but the surgical wound was boggy and warm. Her inflammatory markers were raised (C- reactive protein levels 275mg/l). Enhanced CT scans of her brain showed a subgaleal fluid collection, hydrocephalus and intraventricular sediment (Figure 1C). The patient promptly underwent debridement of the scalp wound, removal of bone flap, and drainage of extradural and ventricular empyema. External drains were placed in both ventricles to treat the hydrocephalus and to allow the egress of infected ventricular material.

Cultures of intraventricular pus grew *Weeksella virosa* (sensitive to amoxicillin, co-amoxiclav, cephalosporins, piperacillin-tazobactam, meropenem, resistant to gentamicin and ciprofloxacin) which was confirmed on 16S rDNA PCR. Blood, urine and sputum cultures from the time of admission were bland. Based on the culture sensitivities, the patient was given 4-weeks of intravenous ceftriaxone 2g BD followed by 2-weeks of oral amoxicillin 500mg QDS. On this antibiotic regimen, her general condition rapidly improved and her inflammatory markers decreased to normal. An MRI scan undertaken 8-weeks after surgery (Figure 1D) showed residual oedema in the right basal ganglia but resolution her ventriculitis. The patient survived another 4-months before succumbing to intra- and extra-cranial metastases from her malignant meningioma.

Discussion

Weeksella virosa is an aerobic, non-pigmented, non-motile Gram negative rod. It is the sole member of the genus Weeksella, described originally in 1970[3] and named[1] in homage of O.B. Weeks' work on the taxonomy of the family Flavobacterium. 'Virosa' (Latin for 'slimy') refers to the species' cream-coloured mucoid colonies which grow on blood and chocolate agar after 48h incubation. Investigations into the source of *Weeksella virosa* in humans have shown that the bacterium displays a proclivity towards the urogenital tract. 72.3% of the strains isolated by Holmes *et al*. were from the urine or genital tract[1]; other sites included blood, umbilical area, rectal area, ears, eyes, mastoid and cerebrospinal fluid[1]. Indeed, in one of the first descriptions of the bacterium in a clinical context[4], it was originally designated as *Flavibacterium genitale* due to its preponderance for the urogenital tract. More recent studies have shown varying incidences of 0.42%[5] to 15%[6] from this source.

It is rare for *Weeksella virosa* to cause disease in humans; only 8 cases have been reported in the literature[6], causing clinical syndromes including spontaneous bacterial peritonitis, pneumonia and sepsis. *Weeksella virosa* has never been reported to have caused an intracranial infection, and this case represents the first such description. A group of Belgian cases of neonatal meningitis reported in 1958[8] were later found to be due to a Flavobacterium[2], although this is a separate species now known as *Elizabethkingia meningoseptica*.

Owing in part to the dearth of clinical reports on pathogenic *Weeksella virosa*, there is a lack of high-quality evidence on the species' antibiotic sensitivity. Success has been achieved with β-lactam antibiotics[5, 6], and on the basis of such anecdotal reports our patient was treated empirically – and successfully – with ceftriaxone and amoxicillin. Aminoglycoside antibiotics should be avoided due to the intrinsic resistance of *Weeksella virosa* to this class of antibiotics[9].

The prevalence of nosocomial infection in the neurosurgical patient population in the UK has been estimated at 10.5%, and the rate of surgical site infection for craniotomy operations estimated at 3.3%[7]. Only in a proportion of the latter figure will there have been a concomitant ventriculitis, the true prevalence of which is difficult to estimate. Ventriculitis is a serious form of CNS infection, caused by microbial penetration and inflammation of the ependymal cell layer lining the ventricular cavities. In neurosurgical practice it is most commonly seen as a complication of EVD placement, in around 10.2%[10]. The overwhelming majority of causative microbes are Gram positive skin commensal bacteria (*Staphylococcus aureus, Staphylococcus epidermidis, Propionibacterium acnes*) in almost 80%. Far less common are Gram negative bacteria such as *Klebsiella pneumonia*, *Haemophilus influenza*, *Pseudomonas aeruginosa*. This is the first reported case of the Gram negative rod *Weeksella virosa* causing intracranial infection in humans.

This patient had several risk factors for developing CNS infection: long-term use of steroids to control symptoms of cerebral oedema related to recurrent tumours; recent whole brain radiotherapy potentiating wound breakdown after repeated craniotomies; necessary breach of ependyma during intraventricular

microneurosurgery and breakdown of the blood-brain barrier creating a conduit for infection into the ventricles. Unfortunately, none of these factors were modifiable, but rather were contingent on her aggressive intracranial neoplastic disease.

We here report the first documented case of *Weeksella virosa* causing intracranial infection in a human, in the setting of aggressive cerebral neoplastic disease, and its successful treatment using a combination of intravenous and oral β-lactam antibiotics over a 6-week course.

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Informed Consent
Informed consent was obtained from the participant included in the study.

Conflicts of Interest
The authors disclose no conflicts of interest in submitting this manuscript.

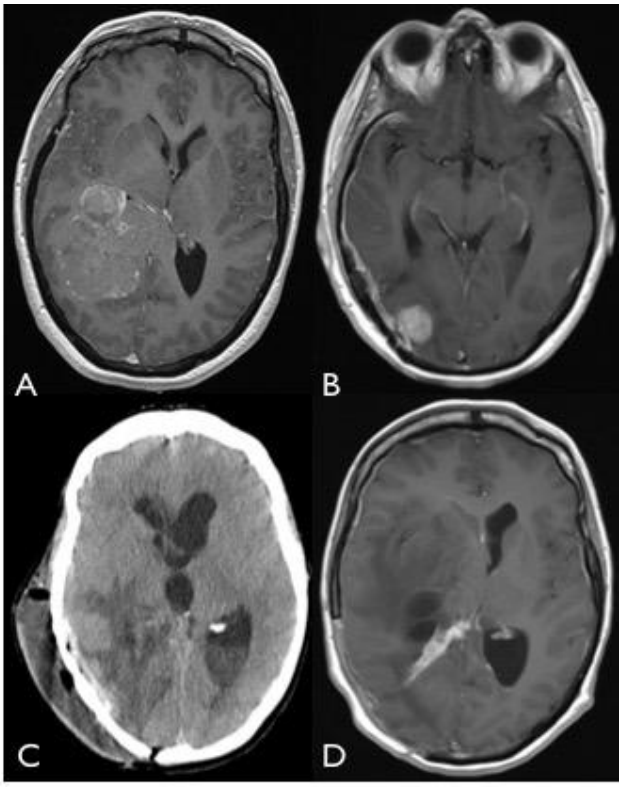

Fig 1. a, T1+contrast MRI taken at index presentation showing the tumour within the trigone of the right lateral ventricle. b, T1+contrast MRI taken at time of first recurrence, 8 months later. Note that the recurrence was distant to the site of the original tumour. c, CT+contrast taken at time of presentation with sepsis syndrome. There was dilatation of the ventricles and fluid levels in both lateral ventricles. d, T1+contrast MRI taken three months after her third operation. There is no ventriculomegaly and some enhancing gliotic tissue at the site of previous surgrery.