CASE REPORT

The importance of not jumping to conclusions: syphilis as an organic cause of neurological, psychiatric and endocrine presentations

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Accepted 29 January 2015

SUMMARY

A 66-year-old Caucasian man was admitted to an acute psychiatric ward under section 2 of the Mental Health Act after presenting with auditory hallucinations and partition delusions. He had been known to mental health services since 2005 but had never been treated with psychotropic medication or given a formal psychiatric diagnosis. He was also diagnosed with hypopituitarism of unknown aetiology in 2002. In light of this presentation, his medical history was reviewed in full, hormone levels and a full delirium screen including blood borne virus and syphilis serology was completed to ensure no organic cause had been missed. The treponemal antibody was positive, and he reported no previous syphilis treatment, as such a diagnosis of neurosyphilis was performed. This case demonstrates a patient presenting with two potential complications of syphilis; psychosis and hypopituitarism where screening for this infection had not been previously considered.

BACKGROUND

Syphilis is a less routinely screened sexually transmitted disease, outside of sexual health clinics, despite a well-documented resurgence in the UK within the past 10 years.¹ Between 2012 and 2013 the number of diagnosed cases of infectious syphilis increased by 9%, with a significant increase in cases diagnosed in men.¹ Syphilis is an infection that can cause multisystem complications; some well-known including psychosis and others less so, such as hypopituitarism.

Prior to the wide availability of penicillin in 1920s, tertiary syphilis accounted for 20% of all mental health hospital admission in the USA.² However, despite this, syphilis is often no longer considered a differential diagnosis for new onset psychiatric symptoms and rarely screened for unless a patient is considered particularly high risk.

A link between syphilis and HIV infection has been identified, each leading to a worsening in complications of the other.³ HIV is thought to contribute to an atypical presentation of syphilis, accelerated progression to tertiary syphilis an increased chance of treatment failure. Syphilis is thought to accelerate the progression of HIV infection.³

Certain complications of syphilis are rarely documented and less known among clinicians, an example of this is hypopituitarism, and as a result syphilis is rarely considered potentially leading to a delay in diagnosis and treatment.

In the present case a patient presented with late onset psychiatric symptoms as well as hypopituitarism of unknown aetiology, but syphilis had not been previously considered as a cause. The case highlights that syphilis is again prevalent and causes a wide range of complications, so should be considered as a differential diagnosis when no clear aetiology is identified; particularly in psychiatric and neurological cases.

The case also reinforces the importance of screening for syphilis and all other organic causes of psychiatric presentation in any patient with new onset psychiatric symptoms to ensure reversible causes are considered before referring onto psychiatric services for further assessment.

CASE PRESENTATION

A 66-year-old Caucasian man was admitted to an acute psychiatric ward under section 2 of the Mental Health Act with a 3-month history of auditory hallucinations and partition delusions. He had a preoccupation with noises coming through his neighbour's wall, no evidence had ever been found to validate these claims. He believed one particular neighbour was sending 'electro-magnetic noises' up through the floorboards to attack him physically. These delusions led to him confronting his neighbours and one incident of physical aggression. When assessed on the inpatient ward he presented as guarded and lacked insight into the concerns around his mental health and his aggression.

He had previously been admitted to a psychiatric ward in 2012 with a similar presentation under section 2 of the Mental Health Act. He also had intermittent contact with community mental health services since 2005 but no psychotropic medication had previously been prescribed and no clear diagnosis performed.

His medical history dates from 2002 when he was diagnosed with hypopituitarism on admission to an acute hospital following a collapse and reported odd behaviour including cycling around his local roads in his dressing gown. No clear aetiology was ever identified, contemporaneous MRI revealing only interstellar herniation with no mass lesion.

He is currently living in council accommodation and is fully independent in all activities of daily living. He spent most of his working life in security but since retiring has slowly isolated himself from others. He has no close friends, describes himself as heterosexual and has had only one significant

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To cite: Noblett J, Roberts E. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2014-207900

romantic relationship in the past which was with a woman in the 1980s for 7 years. He has no children. With regards his sexual history he denied any sexual encounters involving solicitation or of a homosexual nature. He reported no previous treatment for syphilitic infection.

He has been reluctant to provide a clear family history reporting that he lost contact with his parents and siblings in the 1970s but is unaware of any family history of medical or psychiatric illness. He denied any history of abusing illicit substances or alcohol dependence.

His admission medication was as follows:

Aspirin 75 mg daily
Levothyroxine 125 µg daily
Ranitidine 300 mg daily
Norditropin Simplex (5 mg/1.5 mL) 0.5 mg subcutaneous nocte
Hydrocortisone 10 mg twice daily
Testogel testosterone 50 mg sachet topically nocte
Atorvastatin 80 mg nocte

He stated that he was allergic to Penicillin but was unable to specify what reaction occurred on its ingestion.

In light of his presentation of late onset psychosis with no significant family history identified we decided to review his medical history in full, assess his hormone levels and conduct a full delirium screen including blood borne virus and syphilis serology to ensure no organic cause had been missed.

INVESTIGATIONS

His admission blood tests revealed a mild macrocytic anaemia with a haemoglobin of 122 g/L and a mean corpuscular volume of 95.4 fL with normal haematinics.

He had normal urea and electrolytes, liver function tests, C reactive protein, glycalated haemoglobin, alcium, phosphate and magnesium and a thyroid stimulating hormone of 0.04 mIU/L with a normal free T3 and T4.

His 9:00 cortisol was 598 nmol/L.

His androgen profile showed a testosterone of 5.2 nmol/L, SHBG 67 nmol/L and a free androgen index of 7.8.

His MRI head showed interstellar herniation with no mass lesion.

His admission ECG showed normal sinus rhythm with no ischaemic changes but a prolonged corrected QT interval of 473 ms.

His urine drug screen was negative for all illicit substances

Addenbrokes cognitive examination III (ACE-III):

ACE-III score 85/100

Subscores:

Attention and orientation: 16/18

Memory: 20/26 fluency: 9/14

Language: 25/26 visuospatial: 25/26

His blood borne virus screen showed he was hepatitis B surface antigen negative, hepatitis C virus antibody negative and HIV type 1 and 2 antibody/antigen negative.

His treponemal antibody was positive and rapid plasma reagin was negative.

DIFFERENTIAL DIAGNOSIS

A man in his mid-60s who presents with partition delusions and auditory hallucinations may have a diagnosis of late onset schizophrenia, psychotic symptoms secondary to an organic cause such a neurosyphilis, dementia or psychoactive substance misuse. The positive treponemal antibody and history of hypopituitarism of unknown aetiology indicates that the most likely diagnosis is psychotic symptoms secondary to syphilis.

However, we needed to evaluate all the information provided by the history and investigations to confidently separate all three differential diagnoses.

Investigations including blood tests, neuroimaging and an EEG may be useful to help rule out an organic cause of the presentation. Cognitive tests such as the Addenbrooke's cognitive examination combined with neuroimaging techniques can rule out a dementing illness. Individual and collateral histories in combination with urine drug screening are useful if psychoactive substance misuse is suspected. It is only after these investigations come back negative as well as review of the case's personal, psychiatric and family history where a diagnosis of late onset schizophrenia should be considered.

All four differentials require very different management plans. If an organic cause of the presentation is missed there is a risk of complication due to untreated physical illness. It may also lead to an inappropriate use of antipsychotics which in itself increases the risk of multiple physical health problems including metabolic syndrome, stroke and extra pyramidal side effects.

TREATMENT

Prior to serological testing for treponemal antibody, in light of his psychotic symptoms, the patient was commenced on aripiprazole and uptitrated to a dose of 15 mg daily before being switched to a monthly intramuscular depot preparation of 400 mg. This antipsychotic was chosen because of his long corrected QT interval on his admission ECG as this is one of the few antipsychotics that does not cause QT prolongation.

His initial endocrine results were discussed with his treating endocrine team and led to a switched to Tostran testosterone gel 40 mg topically.

Once we received the positive treponemal antibody result, we liaised with the genitourinary medicine team. They reviewed the patient on the ward and advised treating for neurosyphilis with 28 days of doxycycline 200 mg orally twice daily due to his allergy to penicillin.

OUTCOME AND FOLLOW-UP

As the admission has progressed the patient has become less guarded and has engaged more with staff and patients on the ward. He has no longer been observed to be responding to auditory hallucinations and no further partition delusions have been expressed. He has complied with all leave off the ward and was discharged with follow-up by the community mental health team to monitor any residual psychotic symptoms and consider discontinuation of the antipsychotic. The endocrinology team will also continue to follow him up in the community.

DISCUSSION

This case demonstrates a patient who presented with two potential complications of syphilis; psychosis and hypopituitarism. The consideration has never been given to a unifying diagnosis of syphilis possibly due to lack of knowledge around the rarer complications, hypopituitarism and that clinicians often still consider syphilis a 'rare' sexually transmitted disease. While definitive diagnosis of hypopituitarism secondary to syphilis can only be made at postmortem, it may also be difficult for modern day histopathologists to identify this pattern in samples due to its rarity.

Syphilis is often only considered in people who partake in risky behaviours such as prostitution, solicitation and intravenous drug use, but again this case shows that this infection can occur in patients considered 'low risk'.

Syphilis as a cause of psychiatric symptoms has been well documented through history but less so in recent years. However, in 2004, Sobhan *et al*⁴ completed a case report of three cases of psychiatric manifestations of neurosyphilis. Each of the three cases presented with very different psychiatric symptoms demonstrating that neurosyphilis 'may present as virtually any psychiatric disorder, including personality disorder, psychosis, delirium and dementia'.⁴

There is limited literature on hypopituitarism as a complication of syphilis, most published cases date back 1960 or earlier. Oelbaum⁵ completed a case series identifying 14 cases of syphilis in male patients with hypopituitarism. Vague *et al*⁶ also commented on the link between syphilis and hypopituitarism. An extensive literature search found no other case reports subsequent to 1960 a finding almost certainly linked to the use of penicillin and the subsequent decline in syphilis presentations, and its late untreated complications.

The standardised mortality ratio for patients with serious mental illness (SMI) is 2.15 (95% CI 1.95 to 2.36).⁷ Improved physical healthcare in the psychiatric population has focused on cardiovascular and metabolic risk factors; however, the estimated prevalence of blood borne infections in the SMI population is higher than the general population.⁸ Syphilis prevalence rates in psychiatric inpatients have varied wildly over the years and geographical region but are generally considered higher than the general population.⁹ In response to this case we have developed a protocol where all patients admitted to the psychiatric ward are screened for syphilis as well as blood borne viruses.

Oelbaum⁵ also mentions a case report in which a patient with hypopituitarism secondary to syphilitic infection was treated with antibiotics and developed strange behaviours and 'psychotic-type symptoms'. This occurred on several challenges with penicillin and other antibiotics and was postulated to be a result of the Jarisch-Herxheimer reaction (the release of endotoxins resulting from the death of the treponemes). While we have no direct temporal evidence of antibiotic prescription, we know that our patient has suffered with chest infections in the past and can hypothesise that maybe a course of antibiotics led to 'cycling in his dressing gown' in 2002 and 'electro-magnetic noises' in 2014.

Learning points

A differential diagnosis and screening for syphilis should be considered in patients presenting with:

- ▶ New onset psychiatric symptoms as well as all other organic causes of a psychiatric presentation.
- ▶ Hypopituitarism of unknown aetiology.
- ▶ Symptoms of unknown cause, particularly if neurological in origin.

Contributors JN completed a short literature review, the summary, as well as most of the background, case presentation, treatment, outcome and discussion; consented the patient discussed in the case; made revisions to manuscript after review. ER completed the investigation section, helped complete a short literature review and added information to background, case presentation, treatment and discussion.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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