CASE REPORT

Atypical presentation of cat scratch disease: Parinaud's oculoglandular syndrome with facial nerve paresis

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SUMMARY

A 28-year-old man presented to our clinic over the course of 3 weeks with symptoms that progressed from mild headaches to fever, fatigue, myalgia and an enlarged right preauricular lymph node with ipsilateral conjunctivitis and upper eyelid weakness. Our differential included Epstein Barr Virus/Cytomegalovirus mononucleosis, bacterial conjunctivitis and lymphoma. We evaluated with CBC, EBV IgM Ab, lactate dehydrogenase level and a CMV IgG Ab which were all within normal limits. During his third visit, we discovered our patient had been scratched by two stray kittens he had adopted 2 months prior. We confirmed the diagnosis with a positive *Bartonella henselae* IgG level and diagnosed him with cat scratch disease presenting as Parinaud's oculoglandular syndrome. He was treated with a 5-day course of Azithromycin 250 mg with definitive improvement.

BACKGROUND

Cat scratch disease (CSD) is a common cause of lymphadenitis, caused by infection with the fastidious pleomorphic gram-negative bacilli *Bartonella henselae*. The organism is typically hosted in the bloodstream and saliva of asymptomatic cats younger than 1 year, and it is transmitted between cats by the cat flea *Ctenocephalides felis*. Human inoculation occurs through the scratch or bite from an infected kitten and not by the cat flea.¹ Other forms of inoculation include rubbing an eye after having petted the infected cat, and some reports include cases where the penetrating agent was a thorn prick previously licked by an infected cat. Therefore, at least 25% patients do not recall being scratched or bitten by a cat prior to the development of symptoms although more than 90% of patients report contact with new cats.² CSD is a global disease occurring worldwide, especially in humid climates within the months of September and March. It is most common in immunocompetent persons <21 years, and the overall incidence in the USA is 6.6/100 000 persons.³ The typical clinical presentation of CSD begins with inoculation from an infected cat, followed by the appearance of an erythematous papule at the site of contact followed by lymphadenopathy of the draining region occurring up to 8 weeks later. Cervical and axillary lymphadenopathy are most common. Constitutional symptoms from the inflammatory

response may lead to the experience of malaise, weakness, bone aches, anorexia, chills and fevers up to 104°F.^{3,4} Atypical presentations of CSD occur in 5%–20% of cases. The oculoglandular syndrome of Parinaud occurs in 2% of all CSD cases.⁵ The inoculation site is the palpebral conjunctiva, affected by rubbing the eye after petting an infected cat, leading to granulomatous conjunctivitis, followed by the reaction of the ipsilateral preauricular lymph node. In a literature review of all published Parinaud's oculoglandular syndrome cases, none have described facial nerve involvement^{5,6} as a result of the syndrome. A review of CSD cases with facial nerve involvement only points to parotid gland infection in the absence of ocular manifestations. Our case is significant for development of facial nerve paresis due to mass lesion of an enlarged right preauricular lymph node with surrounding oedema as well as parotid gland inflammation changes resulting in compression of the temporal branch of the facial nerve causing ipsilateral eyelid weakness on closure of the eye, in combination with upper eyelid inflammation and conjunctivitis. Our case is also a timely reminder that despite the unusual clinical presentation of this disease and in order to avoid unnecessary testing, the clinical history must be thorough and include questions that elicit exposures to new pets and animals. CSD should remain in the differential diagnosis of any unilateral lymphadenopathy, especially in the setting of cat exposures regardless of clinical presentation, in order to confirm the diagnosis and initiate treatment without delay. This is particularly important in cases with multisystem involvement and atypical presentations such as the Parinaud's oculoglandular syndrome.

CASE PRESENTATION

Our case is a 28-year-old man with no past medical history who presented on late September 2017 concerned with a 3-day history of headaches, myalgia, fevers and chills. At the time of presentation, vital signs were stable and physical examination unremarkable; he was diagnosed with a viral syndrome and only anticipatory guidance and reassurance were provided. The patient presented back to clinic 7 days later with a 1-day history of an asymptomatic right preauricular mass that was not bothersome unless vigorously manipulated. On physical examination, the preauricular mass was a

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2 cm rubbery, mobile, non-tender lymph node on the right side of the face overlying the parotid gland region with no overlying skin changes. The rest of the physical examination was unremarkable. We instructed the patient to monitor the mass for enlargement and the development of constitutional symptoms and instructed him to follow up as needed. Six days later, the patient presented back with a 3-day history of blurry vision from the right eye and right upper eyelid weakness as well as enlargement of the preauricular mass and new involvement of an anterior cervical lymph node with overlying tenderness. At this visit, he denied fevers, chills or myalgia. His physical examination revealed inflammation and weakness of the right eyelid on closure, with conjunctivitis, decreased visual acuity on the right side when compared with the left (OD 20/30 and OS 20/20), and visual field examination was limited on the right eye by blurry vision. The patient had intact extraocular movements with normal pupillary function. He had normal facial symmetry and normal movements of muscles of facial expression bilaterally. The preauricular node had grown to 2.5 cm and had become minimally tender; the new anterior cervical lymph node was 1 cm in diameter, mobile and tender to palpation. During this visit, our patient was on day 2 of a 5-day course of 40 mg of prednisone, prescribed by his employer's telemedicine service over the weekend and he felt that his symptoms were improving. He was instructed to monitor for symptom improvement and to return to our clinic if symptoms worsened. The patient returned to clinic 7 days later. At this time, the patient endorsed marked improvement of symptoms during the course of prednisone followed by recurrence and worsening after his last dose. During this visit, he reported a 2-day history of fevers, chills, myalgias, re-emergence of his right eye symptoms and two new palpable nodes in the posterior cervical chain, in addition to his previous findings (figure 1). During the clinical interview, we elicited a history of adopting two stray cats 2 months prior to the onset of symptoms. He did not recall a specific scratch or bite.

INVESTIGATIONS

Relevant investigations included a Complete Blood Count at his time of presentation drawn for annual health prevention reasons to obtain baseline labs. Results were normal at this time. During

this visit, we also performed a sexually transmitted disease (STD) screening for health prevention measures including a Gonorrhoea and Chlamydia nucleic acid amplification test, a HIV 1/2 Antigen/Antibody with reflex, a rapid plasma reagin as well as screening for Hepatitis B and C. His results were all negative. Therefore, STDs were excluded from our differential diagnoses. During his third visit, we decided to watch for symptom improvement with the 5-day course of prednisone prescribed by an outside provider and we repeated the CBC with differential and tested for EBV IgM level, a CMV IgG Ab level and a lactate dehydrogenase level, to rule out EBV/CMV Mononucleosis and malignancy respectively; additionally, we ordered a head and neck CT scan with intravenous contrast in anticipation of a possible ENT referral for suspected parotid gland involvement. Our CT scan results were available prior to the laboratory results, and the radiological interpretation from our centre revealed evidence of subcapsular necrosis in the right preauricular nodes, which overall had an inflammatory morphology with related oedema. The mass measured 22 mm in diameter. There were inflammatory changes in the parotid gland that were likely related to secondary parotid inflammation reflecting the infectious nature of the lymph nodes rather than a primary parotid pathology. The laboratory results were all negative except for a CBC revealing mild lymphocytosis of 3.3 ($0.7\text{--}3.1 \times 10^3/\mu\text{L}$), effectively decreasing evidence to support the aforementioned diagnoses. With the additional history of recent cat exposure, we opted to test for a *Bartonella Henselae* and *Quintana* IgM and IgG level, which resulted in a *B. henselae* IgG level of 1:640 titre (Neg: <1:320 titre); IgG titres greater than 1:256 suggest active or recent infection,⁷ and a negative IgM level (Neg: <1:100 titre), which is not indicative of infection; however, the cut-off value for detection of IgM used by our lab is not standard and may have decreased the sensitivity of the test, given standard cut-offs for IgM titres are 1:20, as evidenced by Maurin *et al.*⁷ We diagnosed the patient with CSD presenting as Parinaud's oculoglandular syndrome and facial nerve paresis.

DIFFERENTIAL DIAGNOSIS

Our differential diagnosis evolved in synchrony with the evolution of this patient's condition. His first clinical presentation,

Figure 1 (Panel A): Transverse view of head and neck CT with intravenous contrast at the level of the maxillary sinus showing 21.2 mm in diameter, enlarged right preauricular node with subcapsular necrosis. (Panel B): A 28-year-old patient with right upper eyelid inflammation and weakness and preauricular swelling (Photo acquired with patient's consent). (Panel C): Sagittal view of head and neck CT with intravenous contrast showing enlarged preauricular lymph node overlying edematous parotid gland tissue.

a 3-day history of intermittent headaches, fever and myalgia, with an unremarkable physical examination on his visit was very consistent with a viral syndrome that did not warrant investigation at the time. On his return to clinic days later with an asymptomatic preauricular mass, our working differential remained as a viral infection possibly with adenovirus or Epstein-Barr virus, but also considering a parotitis or primary parotid tumour. Given the asymptomatic nature of his findings, we decided to monitor for evolution of symptoms before deciding if further investigations and/or treatment would be appropriate. Our patient returned to clinic a week later with right eyelid inflammation and weakness, conjunctivitis as well as an increased enlargement of the ipsilateral preauricular mass with involvement of the anterior cervical chain nodes. Our leading hypothesis for his presentation at this visit was that the enlarged preauricular mass was causing mild compression of the temporal branch of the facial nerve as it branches within the parotid gland and whose terminal branches innervate the orbicularis oculi muscle responsible for closure of the eye lid as opposed to a Bell's Palsy, which would present with a more pronounced facial asymmetry. A Central Nervous System lesion was not excluded but least likely on our differential given his clinical presentation. Our differential included, in order of suspicion, a viral syndrome superimposed with unilateral conjunctivitis, a neoplastic process or a bacterial conjunctivitis. A 5-day course of prednisone had been initiated by an outside telemedicine provider 2 days prior to this visit and while we did not agree with this treatment choice, we did not discontinue it while pursuing investigations for a possible aetiology, since the patient endorsed mild improvement from the day prior. Our patient returned to clinic after 7 days with a history of improvement of symptoms, followed by recurrence and worsening after his last dose of prednisone. This time, in addition to his symptoms, he also had involvement of the posterior cervical chain nodes. This is when we elicited a history of cat exposure and our differential evolved by including CSD; in addition to our working differential of EBV/CMV mononucleosis, parotid malignancy or lymphoma and although we had lower suspicion for the latter, we still desired to exclude the possibility. Other causes of unilateral conjunctivitis and preauricular lymphadenopathy were discussed as possible but highly unlikely aetiologies, such as sarcoidosis, syphilis, tularemia, sporotrichosis and tuberculosis.

OUTCOME AND FOLLOW-UP

Our patient was treated with a 5-day course 250 mg Azithromycin taken as 500 mg po on the first day and 250 mg po per day thereafter. We followed up with him 2 weeks post-treatment, he exhibited dramatic improvement in overall status with complete resolution of the preauricular swelling and no sequelae of right eyelid weakness.

DISCUSSION

CSD was first described in 1931 by Robert Debre, Professor of Pediatrics at the University of Paris, in France. He is attributed with establishing the link between a manifestation of lymphadenitis and the history of ipsilateral cat scratches. After identifying several cases with similar presentations, he coined the term CSD. From the rest of the 1930s to the early 1980s, the most acceptable theory with respect the aetiology of CSD pointed to an unidentified virus as the causative agent due to the inability to isolate or culture an organism from suppurative samples of infected patients.^{2,8} It was not until 1983 that Wear

et al successfully isolated a bacterial agent in the samples of a patient with HIV with disseminated bacillary angiomatosis through Warthin-Starry staining, a silver impregnation used in staining lymph nodes.⁹ In 1992, two organisms isolated in cases of CSD were identified via PCR, *Afipia felis* and *Rochalimea henselae*. Further studies identified *Rochalimea henselae* as the major causative organism. After re-evaluation of its 16S rRNA sequences in 1993, the CSD aetiological agent was finally designated as *Bartonella henselae*.⁹⁻¹¹ The typical clinical presentation of CSD begins with inoculation from an infected cat, followed by the appearance of an erythematous papule at the site of contact (if inoculated by a penetrating scratch or bite). The latency between inoculation and papule formation is 7–12 days. Lymphadenopathy of the draining nodes occurs in 1 to up to 8 weeks later. Cervical and axillary lymphadenopathy are most common. In most cases, the affected lymph nodes may remain reactive for up to several months and up to 30% necrose and suppurate.^{3,4} Constitutional symptoms from the inflammatory response may lead to the experience of malaise, weakness, bone aches, anorexia, chills and fevers up to 104°F.^{3,4} The diagnosis is made clinically with 3 of the following criteria: (1) a history of animal contact with a scratch or primary dermal or eye lesion; (2) regional lymphadenopathy in which all other possible causes have been ruled out; (3) positive CSD serologies or skin test and (4) lymph node biopsy with histopathology consistent with CSD.¹² Atypical presentations of CSD occur in 5%–20% of cases and these include: Neuroretinitis, Hepatosplenic CSD, cardiopulmonary CSD, cat scratch-related osteomyelitis, cat scratch encephalopathy and some have even presented as Henoch-Schönlein purpura and thrombocytopenia purpura. In the case of our patient, he presented with the most common of the unusual presentations of CSD, the cat-scratch-related Parinaud's oculoglandular syndrome.¹² Our case was complicated by facial nerve paresis displayed as right eyelid weakness on closure of the eye. This combination of symptoms has not been documented in the current literature. The oculoglandular syndrome of Parinaud occurs in 2% of all CSD cases.⁵ The inoculation site is the palpebral conjunctiva, affected by rubbing the eye after petting an infected cat. The first component of the syndrome is granulomatous conjunctivitis with erythematous margins and conjunctival injection, followed by the second component, which is the reaction of the ipsilateral preauricular lymph node with or without ipsilateral cervical adenopathy.^{5,6} In a landmark study of 1200 cases of CSD, 48 cases exhibited Parinaud's oculoglandular syndrome, none exhibited facial nerve involvement.^{5,6} A literature review of the reported cases of facial nerve damage related to CSD have all been associated with parotid gland involvement and not with the oculoglandular syndrome. One report involved a mass lesion causing facial nerve compression in its trajectory by the internal acoustic meatus; this patient presented with facial hemiplegia of the ipsilateral side, and the mass lesion was caused by a characteristically enlarged lymph node consistent with CSD.¹³⁻¹⁵ Regardless of presentation, management can be supportive or, if debilitating symptoms are present, with antibiotics such as Azithromycin as first line and either clarithromycin, doxycycline, rifampin, trimethoprim-sulfamethoxazole or ciprofloxacin if Azithromycin is not tolerated. Choice of treatment should be guided depending on age, tolerability, side effect profile, availability and comorbid conditions.¹⁶ More than 80% of patients show faster recovery with the use of Azithromycin compared with placebo. Fine needle aspiration of suppurative lymph nodes is generally not recommended.¹⁷

Learning points

- ▶ Cat scratch disease (CSD) should be suspected in every case of unilateral lymphadenitis with or without fever. It should be part of the differential especially if history is positive for exposure to cats, even if patients do not recall a scratch or bite.
- ▶ Atypical presentations of CSD, although rare, do occur, but the core symptomatology is similar within them in the initial stages with >3 week history of lymphadenopathy as the common factor.
- ▶ Facial nerve paresis with a history of lymphadenopathy±constitutional symptoms should raise flags for CSD, especially if there is recent exposure to cats.
- ▶ Serology testing for *Bartonella henselae* should be performed without delay in cases where CSD is suspected to avoid unnecessary lymph node biopsies, imaging and unnecessary subspecialty referrals. Treatment should be initiated promptly to avoid permanent sequelae.
- ▶ Finally, the most cost effective tool, the clinical interview, should always include screening questions to elicit exposure to new pets or animals in cases of unexplained lymphadenopathy.

Contributors CV, medical student in the third year, saw the patient in the diagnostic visit, included the disease to the differential and arrived at the diagnosis. He acquired patient consent to disclose PHI and wrote the case report manuscript. KH was the attending physician supervising CV. She added final remarks to the Case Report Manuscript and helped CV navigate the process of publication.

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