CASE REPORT

Retropharyngeal abscess after chemotherapy

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Accepted 20 February 2018

SUMMARY

Chemotherapy increases susceptibility to infection due to the effect on cell-mediated and humoral immunity. Retropharyngeal abscess is a serious head and neck infection that rapidly progresses from toxicity, whether the patient is neutropenic or not. The risk should be carefully assessed with any chemotherapeutic agent, especially docetaxel.

BACKGROUND

Retropharyngeal space (RPS) abscess is one of the most serious deep neck infections because of the risk of airway compromise, internal jugular vein (IJV) thrombosis and mediastinitis. It has become less common due to improved oral care and the advent of antibiotics. Common aetiologies cited in the literature include tonsillitis, intravenous drug abuse following injection into the IJV, supraglottitis, odontogenic infection, mandibular fracture, ingested foreign bodies and tuberculosis. Twenty per cent of cases have no obvious aetiology identified.¹

Retropharyngeal abscesses most commonly occur in children under 6 years of age, with a peak incidence between 3 and 5 years, due to a suppurating retropharyngeal node following an upper respiratory tract infection.²

Chemotherapeutic agents can lead to infection.³ We report two cases of RPS abscess after chemotherapy in two different hospitals.

CASE PRESENTATION

First case

A 70-year-old man presented with an acute onset of dysphagia and odynophagia without stridor, of 2 days' duration, preceded by a mild 'influenza' attack. One day later, he developed swelling under his chin. He had been diagnosed with metastatic prostatic cancer for 1½ years. During this period, he received a trial of total androgen blockage by bicalutamide and abiraterone. The patient did not respond, with persistent rising prostate-specific antigen serum levels and extensive bone metastases. The oncology team changed his bicalutamide to docetaxel 140 mg (75 mg/m² every 3 weeks for six cycles) 2 weeks prior to the onset of his throat symptoms.

Initial examination failed to demonstrate trismus or swelling in the floor of the mouth. There was diffuse enlargement in both submandibular triangles. Flexible laryngoscopy excluded coexisting supraglottitis. His blood test showed elevated C reactive protein (CRP) 517 mg/L (normal 0–5 mg/L at the 1st hour), mild anaemia 123 g/L

(normal 130–170 g/L), marked leucocytosis $33.6 \times 10^9/L$ (normal $4–11 \times 10^9/L$), with twofold elevated aspartate transaminase and borderline elevated creatinine. The patient was admitted with a provisional diagnosis of submandibular soft tissue cellulitis and commenced on intravenous co-amoxiclav.

The following day, his voice changed to a hot potato character. Repeat flexible laryngoscopy revealed a small bulge in the RPS. Urgent CT of the neck demonstrated a large prevertebral collection, causing narrowing of the trachea to 9 mm at the level of C3 and C4, with maximal diameter of the collection in the retropharyngeal area of the nasopharynx measuring 2×4 cm. The patient underwent transoral drainage under general anaesthesia of 10 mL pus, with insertion of nasogastric tube for feeding. He was transferred to the intensive care unit (ICU). Chemotherapy was stopped on admission.

The patient had a very slow postoperative recovery. Microscopy showed mixed aerobic streptococci and anaerobic bacteroides. The antibiotic was changed according to Trust policy, with microbiology advice to give piperacillin/tazobactam and clindamycin. After 6 days in ITU, his CRP dropped to 359 mg/L; however, he became severely anaemic (77 g/L), and leucopenic ($1.6 \times 10^9/L$), with normal platelet count. Chemotherapy-induced myelosuppression was suggested. The patient was isolated in Iw without the need for granulocyte colony stimulating factor. His low haemoglobin and white cell count (WCC) gradually improved over 3 days, but his retropharyngeal inflammatory phlegmon lasted a further 3 weeks. CT was repeated after 2 weeks due to slow recovery, and that ruled out any further collection. After 3 weeks of Icare, he was transferred to the ear, nose and throat (ENT) ward for swallowing assessment and therapy. He was then discharged 1 week later to continue enzalutamide chemotherapy and lumbar palliative radiotherapy.

Second case

A 31-year-old man of Asian ethnicity developed Epstein-Barr positive advanced nasopharyngeal carcinoma staged T2N2. He had neoadjuvant chemotherapy with induction by cisplatin (100 mg/m²) and 5-fluorouracil (5-FU, 1 g/day), then concurrent chemotherapy and radiotherapy of 65 Gy in 30 fractions. He did not develop any local or regional recurrence during regular follow-up assessment. One year later after chemoradiotherapy, interval CT scanning incidentally detected a right parapharyngeal abscess with retropharyngeal extension 63×29×24 mm, displacing the hypopharynx

To cite: Mettias B, Robertson S, Buchanan MA. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2017-222610

anteromedially with no evidence of local recurrence or distal metastasis. The patient denied any nasal or throat symptoms at the time of the scan. His CRP was 271 mg/L. WCC was $12.4 \times 10^9/L$, with neutrophilia. A throat swab demonstrated a heavy growth of *Staphylococcus aureus*. His blood picture and biochemistry returned to normal levels after broad-spectrum flucloxacillin antibiotic. The multidisciplinary team's recommendation was aspiration of the abscess and panendoscopy under general anaesthesia. The aspirate confirmed sterile pus without growth of bacteria, and histology did not show any malignancy. Of interest, 1 year later, the patient developed osteoradionecrosis of the left temporal bone following acute otitis media that slowly resolved without evidence of local or regional recurrence on positron-emission tomography scan.

OUTCOME AND FOLLOW-UP

The patients were discharged and followed up in the ENT outpatient clinic for 1 year without recurrence of the deep neck space infection. The first patient died 18 months later from his metastatic prostatic cancer.

DISCUSSION

The RPS extends from the clivus to the upper mediastinum, lies posterior to the pharynx and oesophagus, and is anterior to the prevertebral musculature. It is bounded by the buccopharyngeal fascia anteriorly, the prevertebral fascia posteriorly and the carotid space laterally. A very thin alar fascia divides it into two components: the anteriorly positioned true or proper RPS and the posterior danger space. The true RPS extends from the clivus inferiorly to a variable level between the T1 and T6 vertebrae where the alar fascia fuses with the visceral fascia to obliterate the true RPS. The danger space extends further down to the diaphragm and coccyx.⁴

The normal RPS is not uniform along the whole length. The anteroposterior dimension is less than 7 mm up to C6 cervical vertebra. Then it widens in the hypopharynx to 14 mm in children and 22 mm in adults. The classic radiological findings for abscess in this space are increase in soft tissue thickness beyond the above limits, displacement of the airway anteriorly and loss of cervical lordosis. A gas bubble is pathognomonic but uncommon. CT with contrast is superior as the abscess will appear as hypodense in CT with ring enhancement. MRI can also be used which will show hypointense and hyperintense on T1-weighted and T2-weighted images, respectively.⁵

Streptococcus viridans (39%) was the most common pathogen, followed by *Staphylococcus epidermidis* (22%) and *Staphylococcus aureus* (22%).⁶

The rate of RPS infection among all other deep neck space infections is low. A series of 185 patients in Japan showed a rate of 5.9%.⁷ In 173 patients in Turkey, the rate was 3.5%.⁸

The mortality rate of deep neck space infection varies between 1.6% and 2.6%. There is no published series on morbidity or mortality of retropharyngeal abscess. The rate of complications tends to be higher in RPS and Ludwig's angina than other deep neck space infections.^{7,9} In a review of 263 patients with deep neck space infections, 30 patients developed further complications due to spread of infection. Ninety per cent of them had airway obstruction, 3.3% jugular vein thrombosis, 26.6% mediastinitis and sepsis in 10%. Other reported complications are necrotising fasciitis, osteomyelitis, glomerulonephritis and pneumonia.¹⁰

Chemotherapy is recorded as a risk factor.^{7,8,10} Chemotherapy can predispose to infection by different ways. Many agents cause

mucositis that enhance translocation of micro-organisms to the blood stream. Myelosuppression is also a common side effect that leads to neutropenia. Many agents interfere with cell-mediated and humoral immunity even if the dose did not cause myelosuppression.³

The severity and duration of neutropenia are risk factors for infection from chemotherapy. Up to 40% of patients may develop febrile neutropenia.¹⁰

Afebrile infection in neutropenic cancer is rare. However, these patients are usually at higher risk of complication and death compared with patients with febrile neutropenia. This is related to the delay of effective antimicrobial therapy when feeling unwell without fever due to delay in contacting a doctor. The warning signs in afebrile neutropenic infection are cough, hypotension, severe fatigue, rigors or altered mental state.¹¹

The National Cancer Institute defines Common Terminology Criteria for Adverse Events of neutropenia, grade 1 representing a neutrophil count of $<1500/mm^3$ to grade 4 a neutrophil count of $<500/mm^3$.¹²

In the patients described here, retropharyngeal abscess occurred in two different situations. The first patient was immunocompromised with neutropenia while the other one was immunocompetent with neutrophilia. The first developed the abscess following his upper respiratory infection whereas the abscess was accidentally discovered in the second during follow-up imaging for nasopharyngeal carcinoma.

The length of hospital stay is variable, between 2 and 78 days depending on the location of deep space infection and underlying comorbidities. Patients with comorbidities such as diabetes tend to stay 2 weeks, while patients with spread of infection can stay over a month.⁷ 6.1% of deep neck-space infections require intensive care admission.¹⁰

The management, duration of treatment and outcome in the current two cases were different. The first patient required intensive care admission, empirical antibiotics and isolation. The slow recovery over 1 month is related to low immunity. The second immunocompetent patient had a day case aspiration of abscess then a short course of oral antibiotics.

Surgical drainage is an important crucial step in the management of retropharyngeal abscess, especially in adult life to avoid increased morbidity and mortality.¹³ In the paediatric population, small retropharyngeal abscesses less than 2 cm can be managed conservatively with antibiotics and steroids for the first 48 hours, with delayed drainage if there is no response.^{14,15}

There are only two case reports within one article in the literature of deep neck space abscess after treatment of nasopharyngeal carcinoma with chemoradiotherapy. The first patient was 45 years old who had external beam radiation of a total dose of 64 Gy delivered to the primary lesion, then adjuvant chemotherapy by cisplatin 100 mg on day 1 followed by 1000 mg/day 5-FU. The patient developed RPS abscess within 1 week of completion of treatment, treated by emergency drainage. However, she developed distant metastases 1 year after radiotherapy and died within 3 years of treatment. The second patient was 64 years who had neoadjuvant chemotherapy of 120 mg cisplatin and 1000 mg/day of 5-FU, then radiotherapy. He developed the abscess 13 weeks after treatment. This had started as an ulcer in the retropharyngeal wall, and was resistant to hyperbaric treatment. He lost consciousness, with respiratory arrest. Later on, after resuscitation, he developed motor paralysis and died from disseminated intravascular coagulation.¹⁶

There was not any information on the immune system at the time of presentation, however both patients had fever with throat symptoms, in addition to a retropharyngeal necrotic ulcer at the

primary site that could represent a portal of entry. The two case reports by Hareyama *et al*¹⁶ described a connective tissue disorder (dermatomyositis and Sjogren, respectively) linked to the development of nasopharyngeal carcinoma, but the cause of the retropharyngeal abscess was chemotherapy. In fact, the poor prognosis of RPS infection can be related to the connective tissue disorder.

Of interest, there is one reported case of retropharyngeal abscess in metastatic prostatic cancer that was treated by docetaxel. The patient developed the abscess within 2 weeks of chemotherapy treatment. Despite antibiotic therapy, the infection spread to the mediastinum with liver metastases, and the patient died.¹⁷

There is a high risk of developing febrile neutropenia with the various docetaxel-containing chemotherapeutic regimens in breast cancer.¹⁸ In prostatic cancer, older patients appear to be more susceptible to docetaxel-related adverse events, with those aged ≥ 75 years having significantly higher rates of infection of any grade (70% vs 48% in patients < 75 years).¹⁹

Learning points

- Retropharyngeal abscess is one of the most serious head and neck infections that can happen after chemotherapy.
- It can occur with or without neutropenia, however the former carries the worse prognosis.
- Some chemotherapy such as docetaxel has harmful effect on bone marrow compared with other chemotherapeutic agents.

Contributors BM collected data. SR was a clinical supervisor. MAB did the revision and supervision of the written draft.

Funding This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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