Reminder of important clinical lesson

Superior vena cava syndrome caused by Hodgkin's lymphoma in an adolescent girl

Imran Rizvi,¹ Shamsuz Zaman,² Noorin Zaidi,² Syed Mohammad Kamil Ashraf,¹ Arun Kumar,¹ Ankush Gupta,³ Mehtab Ahmad⁴

¹General Medicine Department, J N Medical College, Aligarh, UP, India;

²Pathology Department, J N Medical College, Aligarh Muslim University, Aligarh, UP, India;

³General Medicine Department, Military Hospital, Jodhpur, Jodhpur, India;

⁴Radiodiagnosis Department, J N Medical College, Aligarh Muslim University, Aligarh, UP, India

Correspondence to Dr Imran Rizvi, imranrizvi09@gmail.com

Summary

A 14-year-old female patient presented to us with complaints of shortness of breath, swelling over upper body and dysphagia, prominent veins were visible on upper body. CT scan of chest revealed a large mediastinal mass compressing surrounding structures. Histopathology and immunohistochemistry confirmed it to be Hodgkin's lymphoma. The patient was given a course of chemotherapy (doxorubicin, bleomycin, vinblastine and dacarbazine) and local radiotherapy. Presently she is doing well.

BACKGROUND

Superior vena cava syndrome (SVCS) refers to predominant major vessel compression in the superior mediastinum. When vessel compression is associated with tracheal compression, it is termed 'superior mediastinal syndrome' (SMS).¹ In practice SVCS and SMS are often synonymously used terms. SVCS is rare in children and appears at presentation in 12% of paediatric patients with malignant mediastinal tumours.² Although lymphomas are a common cause of SVCS but almost always SVCS is caused by non-Hodgkin's lymphoma (NHL). Hodgkin's lymphoma (HL) despite its common presentation with mediastinal lymphadenopathy rarely causes SVCS.³ The case presented below reviews the clinical presentation, causes, diagnosis and management of SVCS with special reference to HL.

CASE PRESENTATION

A 14-year-old female presented to us with shortness of breath from past 1 month, swelling of face, arms and upper body since last 20 days and difficulty in swallowing since last 5 days. According to patient's mother, patient was in her usual state of health when she started to experience shortness of breath which was on climbing stairs or running to start with. This shortness of breath kept on increasing progressively and now the patient feels breathless even on minimal exertion. Breathlessness was also associated with dry cough. The patient experienced increase in symptoms on lying down and she was relatively more comfortable in sitting posture. The patient also started to develop swelling over the face about 20 days back which her mother noticed as some puffiness over face in the beginning which kept on progressing to involve whole of the face both arms and upper chest. There was also history of difficulty in swallowing which is more for solid food as compared to liquids since last 5 days. The patient also gave history of right-sided chest pain which was insidious in onset, mild to moderate in intensity dull aching in

character, the pain also used to increase in supine posture. There was no history of fever, haemoptysis, hoarseness of voice, visual disturbances, neck swellings, paroxysmal nocturnal dyspnoea, palpitations or weight loss.

On examination her pulse rate was 110/min, blood pressure was 110/70 mm Hg, respiratory rate was 28/min, temperature was 98.4°F. On general examination there was marked facial oedema, swelling over both upper limbs and chest wall was also noted. There was no pallor, cyanosis, clubbing or icterus, there was no oedema on lower extremities. Her neck veins were distended, jugular venous pressure (JVP) was raised but non-pulsatile, prominent veins were present on whole of the chest wall and the flow in these veins was from above downwards. On examination of respiratory system there was dullness on percussion over right side of chest at infraclavicular, suprascapular and interscapular areas, vocal resonance and vocal fremitus was also reduced in these areas and there were decreased intensity of breath sounds in these areas. Upper part of sternum was also dull on percussion. Rest of the respiratory system examination was within normal limits. Cardiovascular, central nervous system and per abdomen examinations were also normal. No significant lymphadenopathy was present in neck, axilla or inguinal region.

Based on classical clinical features of swelling over upper body, dilated veins over neck and chest, dyspnoea and dysphagia a provisional diagnosis of SVC/SMS was made and she was investigated further.

INVESTIGATIONS

Her haemoglobin was 11 g/dl, total leucocyte count was 9800/mm³ and differential leucocyte count was neutrophils 76% and lymphocytes 24%. Other biochemical tests like liver and renal function tests were within normal limits.

Chest x-ray (posterior-anterior view) revealed widened right paratracheal stripe with a large well-defined soft tissue density lesion in the right upper and mid lung zone

(figure 1). Contrast enhanced CT scan of thorax showed a large homogenously enhancing soft tissue density mass lesion involving the anterior mediastinum, middle mediastinum and right anterior hemithorax. Size of the lesion was 9.2×10.4×11 cm approximately. Also noted was the non-visualisation of SVC (suggestive of compression). The lesion was also compressing right brachiocephalic vein, subclavian artery, right upper lobe bronchus and few branches of right upper and lower lobe bronchus (figure 2). CT-guided biopsy of mediastinal mass was done which showed heterogenous cellular infiltrate, comprising of small lymphocytes, plasma cells and histiocytes. Mononuclear variants of R-S cells with abundant cytoplasm and large round nucleus with a thick membrane and a huge, hyperchromatic nucleolus were also present. Based on these light microscopic findings which was further supported by CD15 immunohistochemical positivity, we made a diagnosis of mixed cellularity HL (figures 3 and 4). Based on above clinical and investigative findings, a diagnosis of mixed-cellularity HL causing superior vena syndrome was made. Other investigations like ultrasonography of abdomen, CT scan of abdomen, bone marrow biopsy were all normal.

TREATMENT

Awaiting histopathology report we started treatment in the form of head end elevation, injection furosemide, injection dexamethasone the patient got reasonable symptomatic relief from this treatment in the form of reduced oedema and improvement in shortness of breath. After histopathological confirmation of HL, the patient was referred to nearest oncologic facility where she was given course of chemotherapy including doxorubicin, bleomycin, vinblastine and dacarbazine (ABVD) followed by local radiotherapy.

OUTCOME AND FOLLOW-UP

The patient is currently doing well and she is under regular follow-up.

DISCUSSION

SVC is formed by the union of right and left brachiocephalic veins and empties into right atrium, it is the major venous drainage system for blood returning from upper extremities, head and neck. As the SVC lies in non-distensible space (ie, the mediastinum) it is susceptible to compression by tumours and mediastinal lymphadenopathy. Malignant tumours such as lung cancer, lymphoma and metastatic tumours are responsible for the majority of SVCS cases. Lung cancer, particularly of small cell and squamous cell histologies account for 85% of all cases of malignant origin of SVCS.³ In young age, malignant lymphoma is the leading cause of SVCS. HL involves the mediastinum more commonly than any other lymphoma but rarely causes SVCS.³ Other causes of SVCS include thrombosis due to central venous access, pacemaker/defibrillator leads, aortic aneurysm, thyromegaly and fibrosing mediastinitis from prior irradiation or histoplasmosis.³

SVCS is characterised by collection of signs and symptoms including dyspnoea, coughing and swelling of the face, neck, upper body and arms. On rare occasions, patients may complain of hoarseness, chest pain, dysphagia and

Figure 1 X-ray chest posterior anterior view showing widened right paratracheal stripe with a large well-defined soft tissue density lesion in the right upper and mid lung zone.

haemoptysis. Physical signs include prominence of neck or chest veins, collection of fluid in the face or arms and rapid breathing. Rarely, cyanosis, Horner's syndrome (miosis, ptosis and unilateral anhidrosis) and a paralysed vocal cord may also be present.⁴ Our patient also presented with dyspnoea, swelling of the face, neck, upper body and arms along with prominent neck and chest veins.

Symptoms are often exacerbated by lying down or bending forward. Pemberton's sign is the development of facial plethora, inspiratory stridor and non-pulsatile JVP elevation when a patient with SVCS raises the arms over the head. Dysphagia, hoarseness and stridor are not due to compression of SVC but their presence signifies compression of other mediastinal structures (oesophagus, laryngeal nerves and trachea respectively), presence of these symptoms correlates with poor prognosis.

CT is very helpful in evaluating a patient presenting with SVCS as it accurately localises the site of lesion and may guide attempts at biopsy by mediastinoscopy, bronchoscopy and percutaneous aspiration.⁵ MRI of the mediastinum has several potential advantages over CT, including the ability to image in several planes of view and directly visualising blood flow and MRI does not require iodinated contrast material also. Disadvantages of MRI include increased scanning time and cost.⁵

It is desirable and most of the times possible to make a histological diagnosis of malignancy before going for treatment. Treatment without an established tissue diagnosis should be initiated only when the symptoms are rapidly progressive or multiple previous attempts to make a tissue diagnosis have failed.⁵ The physician must keep in mind that the ultimate treatment strategy will vary according to the diagnosis and the initial modality of treatment should

Figure 2 Postcontrast CT images at the level of crossing of left brachiocephalic vein and arch of aorta showing a large homogeneously enhancing mass lesion in anterior mediastinum compressing and displacing the adjacent right lung along with compression of the brachiocephalic veins and superior vena cava.

Figure 3 Reed–Sternberg cells with abundant cytoplasm and large round nucleus with a thick membrane and a huge, hyperchromatic nucleolus. Frequent lymphocytes, and histiocytes comprising the background cell population (H&E, 400x).

not compromise the final plan. For example, in a patient of lymphoma presenting with SVCS emergency radiotherapy may compromise the ability to categorise tumour with immunohistochemical markers and may delay administration of systemic chemotherapy.⁵ Keeping the above issue in mind we went for pathological confirmation of diagnosis prior to starting therapy.

Other useful investigations for patient presenting with SVCS are sputum cytology, biopsy of palpable supraclavicular nodes and bronchoscopy.

Supportive measures like head end elevation, oxygen inhalation and diuretics are helpful in patients of SVCS due to any cause, dexamethasone also provides symptomatic relief by decreasing oedema and tumour burden in malignant causes of SVCS. In presence of acute thrombus thrombolysis is indicated.⁶ Catheter induced SVCS can be managed with the help of anticoagulants, thrombolysis and endovascular treatment.⁷ In the patients with malignancy as a source of SVC syndrome radiation and chemotherapy may relieve the symptoms.⁸ Surgery could help when

medical or interventional treatments fail. Our patient also responded to above mentioned supportive measures.

HL is one of the most common forms of malignancy in young adults with an average age at diagnosis of 32 years.⁹ The two main types of HL are classical HL and lymphocyte predominant HL, classical HL is further divided into four subtypes namely nodular sclerosis, mixed cellularity, lymphocyte rich and lymphocyte depleted. Classical HL accounts for 95% of all HL.

The distinguishing epidemiologic feature of HL is its bimodal age distribution. An incidence peak occurs in young adults, followed by a plateau during the ages of 40 to 45 years, and then a subsequent gradual increase in incidence with age after 45 years.¹⁰ However there are geographical variations in age distribution, in less developed countries and in lower socioeconomic groups of developed nations, one sees an increase in childhood cases (particularly in boys) and a decrease of incidence in the young adult group.¹¹ The pattern of HL incidence is parallel to economic development.¹² HL shows a slight

Figure 4 Immunohistochemical stain showing CD15 positivity.

male predominance (male: female=1.3:1) but the nodular sclerosis type is an exception as it is more common in young females.¹⁰ Children and young adults more often have nodular sclerosis and lymphocytic predominant type whereas older population more commonly have mixed cellularity or lymphocytic depletion subtypes. On the other hand in developing countries mixed cellularity and lymphocytic depletion subtypes are common in children as well as adults. Therefore in our part of the world mixed cellularity and lymphocytic depletion are the commonly occurring subtypes as was the case with our patient whose lymphoma was found to be of mixed cellularity type. Approximately 40–50% of HL are associated with Epstein–bar virus (EBV) in neoplastic cells but the causative role has yet not been clearly established.¹³

The diagnosis of classic HL is made by identification of Reed–Sternberg cells (R–S cells) and variants (Hodgkin cells) in a characteristic cellular milieu.¹⁴ Thus, attention to the atypical cells as well as to the background non-neoplastic cells is necessary for the appropriate histologic diagnosis of HL. The R–S cell is a large cell with a polypoid nucleus or multiple nuclei. Each lobe or nucleus contains a single large inclusion-like eosinophilic nucleolus, with a diameter up to 10 μ m. The paranucleolar chromatin is clear, and the nuclear membrane is thick. Various picturesque terms like ‘owl’s eye or pennies on a platter’ are used to describe different appearances of R–S cells.¹⁴ Mononuclear variants are similar to classic R–S cells but have single nucleus and a large eosinophilic nucleolus. R–S cells generally comprise less than 1% of the cellularity in any involved tissue. There is a polymorphous cellular background which is comprised predominantly of small round lymphocytes but histiocytes, eosinophils, plasma cells, neutrophils and fibroblast are also seen. These background cells show no cellular atypia.¹⁴ The biopsy of mediastinal mass from our patient also revealed heterogenous cellular infiltrate, comprising of small lymphocytes, plasma cells and histiocytes. Mononuclear variants of R–S cells with abundant

cytoplasm and large round nucleus with a thick membrane and a huge, hyperchromatic nucleolus were also present. Based on these light microscopic findings which were further supported by immunohistochemistry, we made a diagnosis of mixed cellularity HL.

Previously the presence of at least one classic R–S cell was considered essential for a definitive diagnosis of HL but now morphologic identification of a R–S cell is no longer considered necessary because adjunct immunohistochemical studies may yield a characteristic phenotype to support a definitive diagnosis of HL.¹⁴

Formalin fixed-paraffin embedded section immunohistochemistry is most useful ancillary investigation for diagnosis of HL. The R–S cells usually test positive for CD15 and CD30 and negative for CD45/45RB. Among lineage-specific markers, CD20 stains a subset of R–S cells in approximately 25% of cases of classic HL. Results of testing for CD3 are almost always negative in R–S cells. Using only these five markers (CD15, CD30, CD45/45RB, CD20, CD3), one can resolve most (>90%) cases of classic HL.¹⁴ The major difference between classical and lymphocyte predominant HL is R–S cells are CD15+ and CD30+ in classical HL and they are CD15–, CD30– and CD20+ in lymphocyte predominant HL.⁹ Immunohistochemical staining in our patient also revealed CD 15 positivity.

Most patients of HL present with palpable lymphadenopathy that is non-tender, in most patients these lymph nodes are in the neck, supraclavicular area and axilla.¹⁵ More than half the patients will have mediastinal adenopathy at diagnosis and this is sometimes the initial manifestation.¹⁵ Despite this common occurrence of mediastinal involvement in HL SVC syndrome rarely occurs.³ One-third of the patients present with fever, night sweats and/or weight loss.¹⁵ Clinical staging is done using Ann Arbor classification.¹⁶

A number of complex prognostic factor schemes have been developed for limited Hodgkin lymphoma treated with radiotherapy alone. Massive mediastinal disease and

constitutional symptoms were consistently identified as independent predictors of relapse, whereas only older age was predictive of inferior survival.^{17 18}

An international consortium pooled patient data and identified a prognostic score for advanced Hodgkin lymphoma based on seven factors: male sex, age at least 45 years, stage IV, white cell count at least 15 000/ μ l, lymphocyte count less than 600/ μ l or <8%, haemoglobin less than 10.5 g/dl and albumin less than 4 g/dl. The presence of each factor reduced the freedom from disease progression by approximately 7%.¹⁹ The cure rates for patients with stage I and IIA are close to 90%. Even with advanced disease (stage IVA and IVB), 60–70% 5 year disease free survival is obtained.⁹

Patients with localised or good prognosis are given brief course of chemotherapy followed by radiotherapy to site of node involvement. Patients with extensive disease or those with 'B' symptoms are given complete course of chemotherapy. The most popular chemotherapy regime used in HL include doxorubicin, bleomycin, vinblastine and dacarbazine (ABVD) and mechlorethamine, vincristine, procarbazine and prednisolone (MOPP).¹⁵

Learning points

- ▶ Lymphomas are a common cause of SVC syndrome in young age.
- ▶ HL may present as SVC syndrome.
- ▶ Pathological confirmation of diagnosis should be done before initiating therapy while dealing with a case of SVCS.

Competing interests None.

Patient consent Obtained.

REFERENCES

1. **Rheingold SR**, Lange BJ. Oncologic emergencies. In: Pizzo PA, Poplack DG, eds. *Principles and Practice of Pediatric Oncology*. Fourth Edition. Philadelphia, PA: Lippincott Williams and Wilkins 2002:1177–203.
2. **King RM**, Telander RL, Smithson WA, et al. Primary mediastinal tumors in children. *J Pediatr Surg* 1982;**17**:512–20.
3. **Gucalp R**, Dutcher J. Oncologic emergencies. In: Fauci AS, Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL, Loscalzo J, eds. *Harrison's Principles of Internal Medicine*. 17th Edition. New York: McGraw Hills 2008:1730.
4. **Wan JF**, Bezjak A. Superior vena cava syndrome. *Emerg Med Clin North Am* 2009;**27**:243–55.
5. **Abner A**. Approach to the patient who presents with superior vena cava obstruction. *Chest* 1993;**103**:394S–7S.
6. **DeCamp MM Jr**, Swanson SJ, Sugarbaker DJ. The mediastinum. In: Baue AE, Geha AS, Hammond GL, Laks H, Naunheim KS, eds. *Glenn's Thoracic and Cardiovascular Surgery*. Sixth Edition. Connecticut: Appleton and Lange 1996:643–64.
7. **Bauset R**. Pacemaker-induced superior vena cava syndrome: a case report and review of management strategy. *Can J Cardiol* 2002;**18**:1229–32.
8. **Warren WH**, Piccione WJ Jr, Faber LP. As originally published in 1990: Superior vena caval reconstruction using autologous pericardium. Updated in 1998. *Ann Thorac Surg* 1998;**66**:291–2; discussion 292–3.
9. **Aster JC**. Diseases of white blood cells, lymph nodes, spleen and thymus. In: Kumar V, Abbas AK, Fausto N, eds. *Pathologic Basis of Disease*. Seventh Edition. Philadelphia, PA: Elsevier 2004:686–90.
10. **MacMahon B**. Epidemiology of Hodgkin's disease. *Cancer Res* 1966;**26**:1189–201.
11. **Correa P**, O'Connor GT. Geographic pathology of lymphoreticular tumors: summary of survey from the geographic pathology committee of the International Union Against Cancer. *J Natl Cancer Inst* 1973;**50**:1609–17.
12. **Glaser SL**. Hodgkin's disease in black populations: a review of the epidemiologic literature. *Semin Oncol* 1990;**17**:643–59.
13. **Poppema S**. Immunobiology and pathophysiology of Hodgkin lymphomas. *Hematology Am Soc Hematol Educ Program* 2005;**2005**:231–8.
14. **Chang KL**, Arber DA, Weiss LM. Lymph nodes. In: Weidner N, Cote RJ, Suster S, Weiss LM, eds. *Modern Surgical Pathology*. Second Edition. Philadelphia, PA: Saunders 2009:1431–511.
15. **Longo DL**. Malignancies of Lymphoid cells. In: Fauci AS, Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL, Loscalzo J, eds. *Harrison's Principles of Internal Medicine*. 17th Edition. New York: McGraw Hills 2008:698–9.
16. **Carbone PP**, Kaplan HS, Musshoff K, et al. Report of the Committee on Hodgkin's Disease Staging Classification. *Cancer Res* 1971;**31**:1860–1.
17. **Mauch P**, Gorschtein D, Cunningham J, et al. Influence of mediastinal adenopathy on site and frequency of relapse in patients with Hodgkin's disease. *Cancer Treat Rep* 1982;**66**:809–17.
18. **Specht L**, Nordentoft AM, Cold S, et al. Tumor burden as the most important prognostic factor in early stage Hodgkin's disease. Relations to other prognostic factors and implications for choice of treatment. *Cancer* 1988;**61**:1719–27.
19. **Hasenclever D**, Diehl V. A prognostic score for advanced Hodgkin's disease. International Prognostic Factors Project on Advanced Hodgkin's Disease. *N Engl J Med* 1998;**339**:1506–14.

This pdf has been created automatically from the final edited text and images.

Copyright 2012 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.

BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Please cite this article as follows (you will need to access the article online to obtain the date of publication).

Rizvi I, Zaman S, Zaidi N, Ashraf SMK, Kumar A, Gupta A, Ahmad M. Superior vena cava syndrome caused by Hodgkin's lymphoma in an adolescent girl. *BMJ Case Reports* 2012;10.1136/bcr.01.2012.5487, Published XXX

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow

Keep up to date with all published cases by signing up for an alert (all we need is your email address) <http://casereports.bmj.com/cgi/alerts/etoc>