CASE REPORT

A case of panitumumab containing chemotherapy causing interstitial lung disease: early recognition and treatment resulting in a good outcome

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SUMMARY

Panitumumab is a recombinant human IgG₂ monoclonal antibody which is used for the treatment of patients with metastatic colorectal cancer (mCRC) with disease progression on or following FOLFIRI (fluoropyrimidine, oxaliplatin and irinotecan) containing chemotherapy regimen. We report a case of an 83-year-old Hispanic man, non-smoker, with KRAS/NRAS wild-type mCRC of the liver who was treated with 9 cycles of FOLFOX4 (fluorouracil, leucovorin and oxaliplatin) and cetuximab. Follow-up abdominal imaging showed progression of CRC, requiring initiation of panitumumab in addition to FOLFIRI. After 2 cycles of this combination chemotherapy, he presented with acute hypoxaemic respiratory failure. Pulmonary imaging showed new onset of interstitial lung disease (ILD). He was treated with systemic corticosteroids with marked improvement of ILD. We aim to highlight the risk of severe life-threatening ILD associated with panitumumab. Early recognition of this serious adverse event helps avoid unnecessary administration of systemic antibiotics and prevent mortality.

BACKGROUND

Panitumumab is an epidermal growth factor receptor (EGFR) inhibitor which binds specifically to the epidermal growth factor receptors (EGFR, HER1 and c-ErbB-1) and competitively inhibits the binding of epidermal growth factor (EGF) and other ligands. Binding to the EGFR blocks phosphorylation and activation of intracellular tyrosine kinases, resulting in inhibition of cell survival, growth, proliferation and transformation.^{1–3} We report a case of panitumumab-induced interstitial lung

disease (ILD) which is a rare but serious adverse event with a high mortality rate and could be misdiagnosed easily, highlighting diagnostic and therapeutic modalities of this adverse event.

CASE PRESENTATION

An 83-year-old Hispanic man, non-smoker had KRAS/NRAS wild-type metastatic colorectal cancer (mCRC) to the liver. Patient was having intermittent bright red bleeding per rectum and had a colonoscopy in September 2017 which showed an infiltrative and ulcerated, partially obstructing, 12 cm mass in the recto sigmoid colon. Its pathological examination showed moderately differentiated adenocarcinoma. Abdominal CT showed multiple enhancing masses in the left and right lobes of the liver which were consistent with metastases. The largest one was located in the medial segment of the left lobe and measured about 60 mm. He was diagnosed with stage IV mCRC and he was not found a candidate for any surgery.

He was treated with 9 cycles of FOLFOX4 (fluorouracil, leucovorin and oxaliplatin) (oxaliplatin was held in the last two cycles due to peripheral neuropathy) and cetuximab. In February 2018, abdominal CT showed progression of the disease with increase in the amount and size of metastatic liver lesions, leading to initiation of panitumumab beside FOLFIRI (fluoropyrimidine, oxaliplatin and irinotecan). In May 2018, on arriving for cycle 3 of FOLFIRI and panitumumab, he was having severe shortness of breath without haemoptysis. On physical examination, he was found to be in acute respiratory distress, had diffuse bilateral crackles over his lungs, respiratory rate was 30/min and his oxygen saturation was 80% on room air.

INVESTIGATIONS

After 9 cycles of FOLFOX4 and cetuximab, abdominal CT showed increased amount and size of metastatic liver lesions. After 2 cycles of FOLFIRI and panitumumab and on admission, pulmonary CT showed new onset of bilateral diffuse ground-glass opacities (figure 1), which were not present in imaging done prior to initiation of panitumumab therapy (figure 2). Complete blood count; white blood cell ($4.1 \times 10^9/L$; reference range $4–11 \times 10^9/L$).

Haemoglobin: (101 g/L; reference range 13–17 g/dL) and platelets ($326 \times 10^9/L$.000 cells/microL; reference range 150 000–450 000 cells/microL). Absolute

Figure 1 New onset ground-glass opacities, during treatment with panitumumab.

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Figure 2 CT chest prior to initiation of panitumumab therapy.

lymphocyte count (400 cells/microL; reference range 1000–4 000 cells/microL) and absolute neutrophil count (2900 cells/microL; reference range 1800–8 000 cells/microL). Lactic acid (1.35 mmol/L; reference range 0.9–1.7 mmol/L). Lactic acid dehydrogenase (460 IU/L; reference range 140–271 IU/L). Brain natriuretic peptide (BNP) (90 pg/mL; reference range 0.0–100 pg/mL). Blood and sputum cultures did not show growth of any bacteria. After a course of systemic corticosteroids, a follow-up pulmonary CT (**figure 3**) showed marked improvement of ILD with resolution of diffuse ground-glass opacities. Pulmonary X-ray, 3 years before receiving any chemotherapy, did not show any evidence of ILD (**figure 4**), on admission showed diffuse interstitial opacities (**figure 5**) and 2 weeks after systemic corticosteroids showed improvement of the diffuse interstitial opacities (**figure 6**).

DIFFERENTIAL DIAGNOSIS

The patient had never smoked earlier and did not have a history of ILD (**figure 4**). We did not check serum levels of Krebs von den Lungen-6 (KL-6) and surfactant protein D (SP-D) on admission.

Pulmonary lymphangitic carcinomatosis was not ruled out by pathological confirmation but marked improvement of the patient after systemic corticosteroids made this possibility very unlikely.

As the patient improved markedly right after initiation of systemic corticosteroids on admission (day 0) and without receiving any systemic antibiotics, he did not have bronchoscopy,

Figure 3 Resolution of ground-glass opacities with steroid treatment.

Figure 4 Pulmonary X-ray 3 years before receiving any chemotherapy did not show any evidence of interstitial lung disease.

or bronchoalveolar lavage (BAL) and no work-up to exclude pneumocystis pneumonia was needed. Given the necessity of urgent initiation of systemic corticosteroids without any delay, the advanced age of the patient, absence of haemoptysis, fever

Figure 5 Pulmonary X-ray on admission showed diffuse interstitial opacities.

Figure 6 Pulmonary X-ray 2 weeks after systemic steroids showed improvement of the diffuse interstitial opacities.

and the development of symptoms right after starting panitumumab, he did not have lung biopsy to confirm the presence of ILD but based on CT findings (figure 1), we considered it as clinically diagnosed ILD.⁴

He did not have any history or symptoms suggestive of autoimmune disorders also, given the rapid onset of symptoms right after initiation of panitumumab, did not indicate necessity of laboratory exclusion of autoimmune disorders.

Acute decompensated congestive heart failure was ruled out by normal BNP 90 pg/mL (0.0–100 pg/mL), normal echocardiogram and absence of pulmonary venous congestion on X-ray and signs of volume overload. Patient was diagnosed with right-upper-extremity deep vein thrombosis 3 months prior to admission, for which he was on rivaroxaban 20 mg daily. He took it for 2 months and then stopped taking it. Although, CT pulmonary angiography showed very small chronic bilateral pulmonary embolism, there was no evidence of massive pulmonary embolism explaining the clinical picture. Absence of leucocytosis or systemic signs of sepsis like fever along with negative sputum and blood cultures ruled out possible pulmonary infection.

Several case reports of oxaliplatin-induced ILD have already been published although the abdominal CT done at the end of FOLFOX4-cetuximab course and prior to starting FOLFIRI and panitumumab did not show any diffuse ground-glass opacities (figure 7), which was seen in the same pulmonary section shown on pulmonary CT done after 2 cycles of panitumumab (figure 1). Also, cetuximab-induced ILD was excluded for the same reason.

TREATMENT

In the emergency room, supplemental oxygen was delivered through nasal cannula (6 L/min) and his oxygen saturation improved to 85%. Oxygen delivery was increased through

Figure 7 Abdominal CT done at the end of FOLFOX4 (fluorouracil, leucovorin and oxaliplatin) course and prior to starting FOLFIRI (fluoropyrimidine, oxaliplatin and irinotecan) and panitumumab without evidence of interstitial lung disease.

non-rebreather mask and his oxygen saturation improved into 96%. He was sent to our emergency room. He was admitted and received intravenous injection of methylprednisolone sodium succinate 60 mg every 6 hours, through day 4. On day 2 through day 4, the non-rebreather mask was replaced by high-flow nasal cannula (10 L/min) with oxygen saturation remaining at 94%. On day 5 through day 7, methylprednisolone sodium succinate 60 mg was changed to every 8 hours. On day 5 his oxygen saturation remained 94% on low flow-rate nasal cannula (6 L/min). He was discharged on day 8 on nasal cannula (2 L/min) and oral prednisone 40 mg daily for 1 week; then it was gradually tapered to 5 mg daily through 4 months and it was discontinued by the end of the 4th month.

OUTCOME AND FOLLOW-UP

The patient was admitted for 8 days only. He was discharged to skilled nursing facility for rehabilitation and went home after 2 weeks. He was weaned off supplemental nasal oxygen over 1 month and his oxygen saturation remained above 93% on room air at rest and while walking. Prednisone was gradually tapered to 5 mg daily through 4 months and it was discontinued by the end of the 4th month. The patient has been following up with the oncologist at our cancer centre.

DISCUSSION

Panitumumab is an EGFR Inhibitor, leading to inhibition of cell survival, growth, proliferation and transformation. It was approved by the US Food and Drug Administration in 2006 for the treatment of patients with EGFR-expressing, mCRC with disease progression on or following FOLFIRI containing chemotherapy regimens. Panitumumab approval is based on the result of a single, open-label, randomised, multinational study that enrolled 463 patients with EGFR-expressing (at least one membrane staining in >1% of tumour cells) mCRC.^{5 6} In these clinical studies, pulmonary fibrosis was reported in 1% (2/1467) of patients enrolled in panitumumab clinical studies. Two patients died (one with worsening underlying pulmonary fibrosis and the other with new onset of pulmonary fibrosis)

Following the initial fatality, patients with a history of interstitial pneumonitis or pulmonary fibrosis or evidence of interstitial pneumonitis or pulmonary fibrosis were excluded from clinical studies. A Japanese post-marketing survey of panitumumab revealed that panitumumab-associated ILD occurred in approximately 1.3% (39/3085) of patients and causing death in 51.3% (20/39) of these cases.⁷ No specific findings of panitumumab-induced ILD are usually observed in CT images but induction of diffuse alveolar damage is a suggested mechanism.^{8,9} Pulmonary toxicity is rarely seen with most commonly used targeted therapies.⁸ The vascular endothelial growth factor receptor (VEGFR) small-molecule tyrosine kinase inhibitors (TKIs) gefitinib and erlotinib can cause ILD through decreasing alveolar regeneration.^{10,11} BCR-ABL TKIs imatinib and dasatinib can cause pleural effusions.^{12–14} Bevacizumab is a recombinant humanised monoclonal IgG₁ antibody to VEGF that is currently approved for use in mCRC, non-small lung cancer (NSCLC), renal cell carcinoma and glioblastoma multiforma. Phase III trial of bevacizumab in NSCLC showed that bevacizumab was still associated with more haemoptysis (1.9% vs 0.2%) and five patients (1.2%) died of pulmonary haemorrhage although patients with baseline haemoptysis and squamous histology were excluded from this trial.¹⁵ Reversible non-infectious pneumonitis and diffuse alveolar haemorrhage have been described with mammalian target of rapamycin inhibitors such as everolimus and temsirolimus.^{16–20} Cetuximab is a monoclonal antibody that binds directly to EGFR, it causes severe hypersensitivity infusion reactions including bronchospasms in up to 3% of patients²¹ and bronchiolitis obliterans.²² Infusion-related bronchospasms, acute respiratory distress syndrome and interstitial pneumonitis can be seen with the anti-lymphocyte monoclonal antibodies rituximab, ofatumumab and alemtuzumab.^{23–25} Oxaliplatin is associated with ILD.²⁶

High-resolution CT (HRCT) should be considered for patients who are clinically suspected of having new onset ILD.²⁷

Indications for lung biopsy in patients with ILD include atypical clinical features (age <50 years, fever, weight loss, haemoptysis and signs of vasculitis); a progressive course; a normal, atypical, or rapidly changing chest radiograph or HRCT; unexplained extra pulmonary manifestations; or pulmonary vascular disease of unclear origin.^{28,29} Changes in the relative and absolute numbers of cells in BAL fluid have been described in a variety of ILD. Usually, these changes are non-specific, but occasionally they are sufficiently characteristic to narrow the differential diagnosis so the the 2018 official clinical practice guideline of the American Thoracic Society (ATS), European Respiratory Society (ERS), Japanese Respiratory Society (JRS), And Latin American Thoracic Society (ALAT) for patients with newly detected ILD, suggested, but did not recommend to cellular analysis of their BAL fluid.²⁷ Serological testing to exclude connective tissue disease as a potential cause of the ILD is recommended.²⁷ Okamoto *et al* found that KL-6 and SP-D levels in acute hypersensitivity pneumonitis (2710 U/mL and 338 ng/mL, median) and chronic hypersensitivity pneumonitis (1500 U/mL and 264 ng/mL, median) were significantly higher than in idiopathic pulmonary fibrosis (IPF), collagen vascular disease-associated interstitial pneumonia and sarcoidosis.³⁰ The 2018 official clinical practice guideline of the ATS, ERS, JRS and, the ALAT recommended not measuring serum matrix metalloproteinase-7, SP-D, chemokine ligand-18, or KL-6 for the purpose of distinguishing IPF from other ILDs.²⁷ To our knowledge, other than discontinuation of panitumumab, there is no specific guidelines for treatment of panitumumab-induced ILD.

The 2011 (ATS) guidelines regarding ILD did not make specific recommendations regarding the dose, route and duration of corticosteroid therapy in acute exacerbation of IPF, but suggested to use intravenous corticosteroids up to a gram per day.³¹

Panitumumab-induced ILD is considered part of non-specific interstitial pneumonia (NSIP).³²

Experts usually recommend systemic glucocorticoids as the first line therapy for (NSIP) but the optimal dose and duration of glucocorticoid therapy is not known and most studies of patients with idiopathic NSIP consist of a small number of patients and a variety of regimens.^{33–37} The suggested starting dose for mild to moderate NSIP is prednisone 0.5 to 1 mg/kg ideal body weight per day up to a maximum of 60 mg/day for 1 month followed by 30 to 40 mg/day for an additional 2 months then tapered gradually to reach 5 to 10 mg daily or on alternate days, by the end of 6 to 9 months, with attempted cessation after 1 year of therapy.^{36,37} For patients who relapse when prednisone is tapered or discontinued, low-dose prednisone can be maintained for a longer period.^{37,38}

For patients with severe NSIP requiring hospitalisation, pulse intravenous methylprednisolone may be preferred for initial therapy. A typical regimen is 1000 mg/day for 3 days followed by oral prednisone as dosed above.^{39,40}

For patients with more severe initial disease or an inadequate response to or intolerance of glucocorticoids, therapy is usually expanded to include an additional immunosuppressive drug, such as azathioprine or mycophenolate.^{39,40}

The mechanical ventilation in patients with respiratory failure due to IPF is questionable. There are several small studies of mechanical ventilation in patients with IPF and respiratory failure, all of which show a high hospital mortality rate.^{41–45}

A systematic review of mechanical ventilation in patients with IPF and respiratory failure reports a similarly poor hospital mortality of 87% among the 135 reported cases.⁴⁶

While the most recent 2018 ATS guidelines did not comment on mechanical ventilation in ILD,²⁷ the 2011 ATS guidelines recommended that mechanical ventilation should not be used in the majority of patients with IPF, but may be a reasonable choice in a minority.³²

We conclude that panitumumab induced-ILD is associated with high mortality rate.⁴⁷ Its early recognition, discontinuation of panitumumab and initiation of systemic corticosteroids are associated with better outcomes.

Learning points

- ▶ Panitumumab induced-acute interstitial lung disease (ILD) should be suspected in patients receiving panitumumab with new onset of dyspnoea, persistent cough and or haemoptysis.
- ▶ High-resolution pulmonary CT is usually sufficient for diagnosis of panitumumab-induced ILD.
- ▶ It is imperative to have a low threshold of suspicion for diagnosis to enable early initiation of therapy
- ▶ Early recognition, discontinuation of panitumumab and initiation of systemic corticosteroids are associated with better outcomes and avoidance of high mortality rate which is very high (more than 50%).
- ▶ As survival and outcome improves, it will enable us to follow these patients in the long run, giving us more insight into the side-effect profile of panitumumab

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REFERENCES

- Hynes NE, Lane HA. ERBB receptors and cancer: the complexity of targeted inhibitors. *Nat Rev Cancer* 2005;5:341–54.
- Keating GM. Panitumumab: a review of its use in metastatic colorectal cancer. *Drugs* 2010;70:1059–78.
- Yang XD, Jia XC, Corvalan JR, et al. Development of ABX-EGF, a fully human anti-EGF receptor monoclonal antibody, for cancer therapy. *Crit Rev Oncol Hematol* 2001;38:17–23.
- Raghu G, Mageto YN, Lockhart D, et al. The accuracy of the clinical diagnosis of new-onset idiopathic pulmonary fibrosis and other interstitial lung disease: a prospective study. *Chest* 1999;116:1168–74.
- Van Cutsem E, Peeters M, Siena S, et al. Open-label phase III trial of panitumumab plus best supportive care compared with best supportive care alone in patients with chemotherapy-refractory metastatic colorectal cancer. *J Clin Oncol* 2007;25:1658–64.
- Giusti RM, Shastri KA, Cohen MH, et al. FDA drug approval summary: panitumumab (Vectibix). *Oncologist* 2007;12:577–83.
- Osawa M, Kudoh S, Sakai F, et al. Clinical features and risk factors of panitumumab-induced interstitial lung disease: a postmarketing all-case surveillance study. *Int J Clin Oncol* 2015;20:1063–71.
- Camus P, Kudoh S, Ebina M. Interstitial lung disease associated with drug therapy. *Br J Cancer* 2004;91(Suppl 2):S18–23.
- Barber NA, Ganti AK. Pulmonary toxicities from targeted therapies: a review. *Target Oncol* 2011;6:235–43.
- Dimopoulou I, Bamias A, Lyberopoulos P, et al. Pulmonary toxicity from novel antineoplastic agents. *Ann Oncol* 2006;17:372–9.
- Danson S, Blackhall F, Hulse P, et al. Interstitial lung disease in lung cancer: separating disease progression from treatment effects. *Drug Saf* 2005;28:103–13.
- Quintas-Cardama A, Kantarjian H, O'Brien S, et al. Pleural effusion in patients with chronic myelogenous leukemia treated with dasatinib after imatinib failure. *J Clin Oncol* 2007;25:3908–14.
- Kantarjian H, Pasquini R, Hamerschlak N, et al. Dasatinib or high-dose imatinib for chronic-phase chronic myeloid leukemia after failure of first-line imatinib: a randomized phase 2 trial. *Blood* 2007;109:5143–50.
- Stephens J, et al. The burden of managing pleural effusions in patients with chronic myelogenous leukemia post-imatinib failure: a literature-based economic analysis. *Int J Gen Med* 2010;3:31–6.
- Johnson DH, Fehrenbacher L, Novotny WF, et al. Randomized phase ii trial comparing bevacizumab plus carboplatin and paclitaxel with carboplatin and paclitaxel alone in previously untreated locally advanced or metastatic non-small-cell lung cancer. *Journal of Clinical Oncology* 2004;22:2184–91.
- Vandewiele B, Vandecasteele SJ, Vanwalleghem L, et al. Diffuse alveolar hemorrhage induced by everolimus. *Chest* 2010;137:456–9.
- Hudes G, Carducci M, Tomczak P, et al. Temsirolimus, interferon alfa, or both for advanced renal-cell carcinoma. *N Engl J Med Overseas Ed* 2007;356:2271–81.
- Bellmunt J, Szczylik C, Feigold J, et al. Temsirolimus safety profile and management of toxic effects in patients with advanced renal cell carcinoma and poor prognostic features. *Ann Oncol* 2008;19:1387–92.
- Maroto JP, Dutcher JP, et al. Drug-related pneumonitis in patients with advanced renal cell carcinoma treated with temsirolimus. *J Clin Oncol* 2011;29:1750–6.
- Duran I, Siu LL, Oza AM, et al. Characterisation of the lung toxicity of the cell cycle inhibitor temsirolimus. *Eur J Cancer* 2006;42:1875–80.
- Lenz HJ. Management and preparedness for infusion and hypersensitivity reactions. *Oncologist* 2007;12:601–9.
- Chua W, Peters M, Loneragan R, et al. Cetuximab-associated pulmonary toxicity. *Clin Colorectal Cancer* 2009;8:118–20.
- Stephens J, Carpiuc KT, Botteman M, et al. The burden of managing pleural effusions in patients with chronic myelogenous leukemia post-imatinib failure: a literature-based economic analysis. *Int J Gen Med* 2010;3:31–6.
- Coiffier B, Lepretre S, Pedersen LM, et al. Safety and efficacy of ofatumumab, a fully human monoclonal anti-CD20 antibody, in patients with relapsed or refractory B-cell chronic lymphocytic leukemia: a phase 1-2 study. *Blood* 2008;111:1094–100.
- Sachdeva A, Matuschak GM. Diffuse alveolar hemorrhage following alemtuzumab. *Chest* 2008;133:1476–8.
- Shimura T, Fuse N, Yoshino T, et al. Clinical features of interstitial lung disease induced by standard chemotherapy (FOLFOX or FOLFIRI) for colorectal cancer. *Ann Oncol* 2010;21:2005–10.
- Raghu G, Remy-Jardin M, Myers JL, et al. Diagnosis of idiopathic pulmonary fibrosis. An Official ATS/ERS/JRS/ALAT Clinical practice guideline. *Am J Respir Crit Care Med* 2018;198:e44–68.
- Poletti V, Chilosi M, Olivieri D. Diagnostic invasive procedures in diffuse infiltrative lung diseases. *Respiration* 2004;71:107–19.
- Halkos ME, Gal AA, Kerendi F, et al. Role of thoracic surgeons in the diagnosis of idiopathic interstitial lung disease. *Ann Thorac Surg* 2005;79:2172–9.
- Okamoto T, Fujii M, Furusawa H, et al. The usefulness of KL-6 and SP-D for the diagnosis and management of chronic hypersensitivity pneumonitis. *Respir Med* 2015;109:1576–81.
- Raghu G, Collard HR, Egan JJ, et al. An official ATS/ERS/JRS/ALAT statement: idiopathic pulmonary fibrosis: evidence-based guidelines for diagnosis and management. *Am J Respir Crit Care Med* 2011;183:788–824.
- Travis WD, Costabel U, Hansell DM, et al. An official American Thoracic Society/European Respiratory Society statement: update of the international multidisciplinary classification of the idiopathic interstitial pneumonias. *Am J Respir Crit Care Med* 2013;188:733–48.
- Nagai S, Kitaichi M, Itoh H, et al. Idiopathic nonspecific interstitial pneumonia/fibrosis: comparison with idiopathic pulmonary fibrosis and BOOP. *Eur Respir J* 1998;12:1010–9.
- Daniil ZD, Gilchrist FC, Nicholson AG, et al. A histologic pattern of nonspecific interstitial pneumonia is associated with a better prognosis than usual interstitial pneumonia in patients with cryptogenic fibrosing alveolitis. *Am J Respir Crit Care Med* 1999;160:899–905.
- Fujita J, Yamadori I, Suemitsu I, et al. Clinical features of non-specific interstitial pneumonia. *Respir Med* 1999;93:113–8.
- Travis WD, Matsui K, Moss J, et al. Idiopathic nonspecific interstitial pneumonia: prognostic significance of cellular and fibrosing patterns: survival comparison with usual interstitial pneumonia and desquamative interstitial pneumonia. *Am J Surg Pathol* 2000;24:19–33.
- Park IN, Jegal Y, Kim DS, et al. Clinical course and lung function change of idiopathic nonspecific interstitial pneumonia. *Eur Respir J* 2009;33:68–76.
- Belloli EA, Beckford R, Hadley R, et al. Idiopathic non-specific interstitial pneumonia. *Respirology* 2016;21:259–68.
- Kondoh Y, Taniguchi H, Yokoi T, et al. Cyclophosphamide and low-dose prednisolone in idiopathic pulmonary fibrosis and fibrosing nonspecific interstitial pneumonia. *Eur Respir J* 2005;25:528–33.
- Nanki N, Fujita J, Yamaji Y, et al. Nonspecific interstitial pneumonia/fibrosis completely recovered by adding cyclophosphamide to corticosteroids. *Intern Med* 2002;41:528–33.
- Kim DS, Park JH, Park BK, et al. Acute exacerbation of idiopathic pulmonary fibrosis: frequency and clinical features. *Eur Respir J* 2006;27:143–50.
- Blivet S, Philit F, Sab JM, et al. Outcome of patients with idiopathic pulmonary fibrosis admitted to the ICU for respiratory failure. *Chest* 2001;120:209–12.
- Stern JB, Mal H, Groussard O, et al. Prognosis of patients with advanced idiopathic pulmonary fibrosis requiring mechanical ventilation for acute respiratory failure. *Chest* 2001;120:213–9.
- Al-Hameed FM, Sharma S. Outcome of patients admitted to the intensive care unit for acute exacerbation of idiopathic pulmonary fibrosis. *Can Respir J* 2004;11:117–22.
- Rangappa P, Moran JL. Outcomes of patients admitted to the intensive care unit with idiopathic pulmonary fibrosis. *Crit Care Resusc* 2009;11:102–9.
- Mallick S. Outcome of patients with idiopathic pulmonary fibrosis (IPF) ventilated in intensive care unit. *Respir Med* 2008;102:1355–9.
- Al-Asadi O, Almusarhed M, Rizvi SAJ, et al. Fatal interstitial lung disease caused by Panitumumab-containing chemotherapy regimen. *Ecancermedicalscience* 2018;12:841.

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