Abstract

Purpose. This paper describes the radiological and clinical findings identified in a group of patients with H1N1 influenza.

Materials and methods. Between May and mid-November 2009, 3,649 patients with suspected H1N1 influenza presented to our hospital. Our study population comprised 167 (91 male, 76 female patients, age range 11 months to 82 years; mean age 29 years) out of 1,896 patients with throat swab positive for H1N1 and clinical and laboratory findings indicative of viral influenza. All 167 patients were studied by chest X-ray (CXR), and 20 patients with positive CXR and worsening clinical condition also underwent computed tomography (CT). The following findings were evaluated on both modalities: interstitial reticulation (IR), nodules (N), ground-glass opacities (GGO), consolidations (CONS), bacterial superinfection and pulmonary complications.

Results. Ninety of 167 patients had positive CXR results. Abnormalities identified on CXR, variously combined and distributed, were as follows: 53 IR, 5 N, 13 GGO, 50 CONS; the predominant combination was represented by six GGO with CONS. Of the 20 CXR-positive cases also studied by CT, 17 showed pathological findings. The abnormalities identified on CT, variously combined and distributed, were as follows: 14 IR, 2 N, 5 GGO; the predominant combination was 10 GGO with CONS. Despite the differences between the two modalities, the principle radiological findings of bacterial superinfection were tree-in-bud pattern, consolidation with air

Influenza A virus: radiological and clinical findings of patients hospitalised for pandemic H1N1 influenza

Influenza virale A: caratteristiche radiologiche e cliniche dei pazienti ospedalizzati per influenza pandemica H1N1

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Introduction

Swine-origin influenza – or swine influenza; swine flu – is an acute respiratory infection caused by the novel influenza A, subtype H1N1, which was transmitted to humans from pigs in Mexico and the United States in March and April 2009 and rapidly spread worldwide [1, 2]. H1N1 virus is a subtype of the influenza A virus that belongs to the Orthomyxoviridae family, of which numerous variants exist that cause flu pandemics among animals, such as bird flu and swine flu. Genetic analyses suggest that the emergence of the novel H1N1 strain of swine flu in humans is the direct consequence of a reassortment of the viral genomes of swine flu, bird flu and human flu in North America and Eurasia [3–6]. In June 2009, following the report of the first human-to-human transmission in two countries in one World Health Organization (WHO) region and the rapid spread of the virus, the WHO declared a level-6 pandemic alert [6, 7]. High fever, sore throat, cough, fatigue, joint pain, nausea, vomiting, and/or diarrhoea are the principal symptoms of H1N1 influenza; more complex cases present with respiratory failure [1, 6, 8]. The main abnormalities in blood chemistry are leucopenia, thrombocytopenia and elevated liver function tests [1, 6, 8]. The specific tropism of the virus for the respiratory tract has led to the use of imaging to better characterise the location, distribution and type of the primary pulmonary lesions [9]. Chest X-ray (CXR) and chest computed tomography (CT) have been the investigations of choice for identifying and quantifying, respectively, pulmonary damage in patients affected by influenza A [10–12]. The aim of this paper is to describe the radiological and clinical findings in patients hospitalised for a diagnosis of suspected H1N1 swine-origin influenza.

Conclusions. Our study describes the radiological and clinical characteristics of a large population of patients affected by H1N1 influenza. CXR and chest CT identified the site and extent of the pulmonary lesions and documented signs of bacterial superinfection and pulmonary complications.

Keywords Influenza A virus · H1N1 subtype · Computed tomography · X-ray · Pneumonia · Viral broncogramma aereo, versamento pleurico e pericardico. Dei 20 pazienti studiati con Rx e TC, 15 hanno presentato complicanze respiratorie con un quadro Rx e TC di OGG e CM diffusi e bilaterali. Sei/15 sono deceduti: 4/6 per acute respiratory distress syndrome (ARDS), 2/6 per multiple organ failure (MOF).

Conclusioni. Il nostro studio ha delineato le caratteristiche radiologiche e cliniche di un’ampia popolazione di pazienti con influenza H1N1. La Rx e la TC del torace hanno identificato sede ed estensione delle lesioni polmonari, documentando i segni di sovrainfezione batterica e le complicanze polmonari.

Parole chiave Virus dell’influenza A · Sottotipo H1N1 · Tomografia computerizzata · Rx · Polmonite virale
Materials and methods

Between May and mid-November 2009, 3,649 patients with suspected swine-origin influenza A virus infection presented to our hospital. The diagnosis of H1N1 viral influenza was confirmed in 1,896/3,649 (51.9%) cases by reverse transcriptase polymerase chain reaction (RT-PCR) for detection of viral RNA in pharyngeal swabs. Of these, 261 patients (13.7%) were hospitalised and underwent standard blood chemistry tests. Imaging investigations were performed on 167/261 (63.9%) patients owing to persistent or worsening respiratory symptoms after medical treatment for at least 3 days. This group of 167 patients made up our study population: 91 male (54.4%) and 76 female (45.5%) patients, mean age 29 years (range 11 months to 82 years), 98/167 (58.7%) <18 years, 69/167 (41.3%) >18 years, and 6/167 (3.5%) >65 years.

CXR was performed on all 167 patients, 20 of whom (11.9%) were also studied by CT to assess equivocal findings on CXR or discrepancies between the CXR and clinical findings. CXR was performed using the standard technique (posteroanterior projection: 10 mAs, 70 kV; lateral projection: 60 mAs, 80 kV; film-focus distance 180 cm) with the patient in standing position in 150 cases (89.9%); only 17 patients (10.1%) were imaged in a sitting or lying position and with anteroposterior projection due to an inability to maintain a standing position and/or inspiration.

CT study was performed with a 64-detector-row CT scanner immediately after the CXR in 11/20 cases and 24 h after CXR in the remaining 9/20 cases. On clinical request, 18/20 patients – 12/20 large and 6/20 poorly cooperative patients – underwent unenhanced chest and abdominal CT with the spiral technique: breath-hold volumetric scans, slice thickness 1 mm, kV 120, mA 180, pitch 1. Only 2/18 patients with suspected pulmonary embolism were subsequently imaged after intravenous administration of nonionic iiodinated contrast material with the Sure Start technique at a flow rate of 3 ml/s and dose of 100 ml. The resulting CT images were viewed with a lung window (width 1,500 HU, level –700 HU) and mediastinal window (width 350 HU, level 40 HU). The remaining 2/20 patients were studied with high-resolution CT of the chest for clinical suspicion of concurrent interstitial pulmonary disease using a standard protocol: collimation 1 mm, interval 10 mm, acquisition time 1–2 s, high-spatial-frequency reconstruction algorithm, matrix 512 × 512, 120 kV, 200 mA, FOV encompassing both lungs, window level –600 HU (range –500/–900 HU), window width 1,500 HU (range 1,100/2,000 HU), expiratory scans and patient in prone position when needed. Two radiologists independently examined and interpreted the CXR and CT images stored in the Picture Archiving and Communications System (PACS).

The primary lesions assessed at CXR and chest CT were di riferimento ai fini rispettivamente dell’individuazione e quantificazione del danno polmonare nei pazienti affetti da influenza virale A [10–12]. Scopo del nostro studio è defi ni re il quadro radiologico e clinico dei pazienti ospedalizzati per diagnosi di influenza virale H1N1 di origine suina.

Materiali e metodi

Dal mese di maggio alla metà di novembre 2009, 3,649 paziente con sospetta influenza virale A di origine suina si sono presentati presso il nostro presidio ospedaliero. La diagnosi di influenza virale H1N1 è stata confermata in 1896/3649 (51,9 %) casi con tecnica reverse transcription-polymerase chain reaction (RT-PCR), mediante ricerca dell’RNA virale nel materiale prelevato con tampone faringeo. Duecentoventicinque (13,7%) casi sono stati ospedalizzati presso la nostra struttura e sottoposti ad esami ematochimici generali. Di essi, 167/261 (63,9%) pazienti sono stati sottoposti ad indagini diagnostiche strumentali a causa del persistere e/o dell’aggravarsi della sintomatologia respiratoria dopo terapia medica da almeno 3 giorni. Questi ultimi hanno costituito la popolazione del nostro studio: 91 uomini (54,4%) e 76 donne (45,5%), di età media di 29 anni (range di età 11 mesi–82 anni), di cui 98/167 (58,7%) di età inferiore ai 18 anni, 69/167 (41,3%) di età superiore ai 18 anni, 6/167 (3,5%) di età >65 anni.

Hanno eseguito l’esame radiografico del torace 167 pazienti e, di essi, 20 (11,9%) sono stati sottoposti ad esame TC, al fine di valutare reperti dubbi o discordanti fra Rx del torace e manifestazioni cliniche. L’esame radiografico del torace è stato effettuato mediante tecnica standard (proiezione postero-anteriore [PA]: 10 mAs, 70 kV; proiezione latero-laterale [LL]: 60 mAs, 80 kV; distanza tubo-paziente 180 cm) ed in posizione ortostatica in 150 casi (89,9%); solo in 17 casi (10,1%) sono stati effettuati radiogrammi in posizione seduta o sdraiata ed in proiezione antero-posteriore (AP) per incapacità da parte dei pazienti a mantenere la posizione ortostatica e/o l’inspirio.

L’indagine TC è stata eseguita mediante apparecchiatura TC multidetettore (TCMD) a 64 file di detettori subito dopo la Rx del torace in 11/20 casi, dopo 24 ore dall’esame radiografico in 9/20 casi. Su richiesta clinica, 18/20 pazienti, di cui 12/20 di elevata taglia corporea e 6 non collaboranti, sono stati sottoposti ad esame TC torace ed addome senza somministrazione di mezzo di contrasto endovenoso mediante tecnica spirale: scansioni volumetriche in inspirio, spessore di strato di 1 mm, kV 120, mA 180, pitch 1. Solo in 2/18 pazienti, per sospetto di embolia polmonare, è stato successivamente somministrato mezzo di contrasto iodato non ionico endovenoso mediante tecnica Sure Start, velocità di flusso 3 ml/s, volume di contrasto 100 ml. Le immagini TC così acquisite sono state visualizzate mediante finestra
defined according to the Fleischner Society glossary [13] and recent publications [10, 11] describing the main radiological pulmonary manifestations of A/H1N1 influenza: interstitial reticulation (RI; linear opacities of the central and peripheral interstitium appearing as radio-opaque lines on CXR and hyperdensities on CT), nodules (N; well- or ill-defined, rounded opacities/hyperdensities, with maximum diameter of 3 cm.), ground-glass opacities (GGO; heterogeneous increase in parenchymal opacity with preservation of bronchial and vascular margins), consolidation (CONS; homogeneously increased parenchymal attenuation that obscures the margins of the bronchial and vessels walls).

Images were also assessed for signs of bacterial suprainfection: consolidation with air bronchogram (area of radiolucency at CXR and low attenuation at CT, reflecting the air-filled bronchi on a background of opaque or high-attenuation consolidation), tree-in-bud pattern (branching centrilobular structures), pleural and/or pericardial effusion (fluid in the pleural/pericardial cavity), lymphadenopathy (short-axis diameter >1 cm for mediastinal nodes and >3 mm for hilar nodes). In patients with suspected bacterial suprainfection, blood and bronchoaspirate cultures were ordered to search for pathogenic microorganisms. Lastly, the images were assessed for possible pulmonary complications. Extent of pulmonary damage was defined univocally at CXR and chest CT: unilateral or bilateral; symmetrical or asymmetrical; focal, multifocal or diffuse; with predominant distribution in the upper, middle or lower lobes. On CT we also determined the predominant distribution of lesions as being central (perihilar) or peripheral (subpleural). Multiplanar reconstructions (MPR) and maximum intensity projections (MIP) were obtained through postprocessing in all patients studied with volumetric CT scans.

Results

Of the 167 patients studied, 161 (96.4%) had fever, 153 (91.6%) headache, 143 (85.6%) cough, 58 (34.7%) sore throat, 69 (41.3%) diarrhoea and 57 (34.1%) vomiting. At least one underlying condition was present in 113/167 (67.6%) patients: 76 (45.5%) had asthma, 25 (14.9%) diabetes, 13 (7.7%) chronic obstructive pulmonary disease (COPD), 23 (13.7%) immunosuppression, 65 (38.9%) heart disease, 17 (10.1%) chronic renal failure, 11 (6.5%) cognitive disorders, 5 (2.9%) neuromuscular disease, 3 (1.7%) skeletal malformations, 2 (1.1%) pregnancy, 1 (0.5%) drug abuse. All patients had abnormal blood chemistry results: 157 (94%) elevated erythrocyte sedimentation rate (ESR), 150 (89.8%) elevated C-reactive protein (CRP), 144 (86.2%) elevated lactate dehydrogenase (LDH), 83 (49.7%) elevated lactate dehydrogenase (LDH), 150 (89.8%) elevated C-reactive protein (CRP), 144 (86.2%) elevated lactate dehydrogenase (LDH), 83 (49.7%)
medi o inferiori. È stata inoltre determinata all’indagine TC
la predominante distribuzione centrale (periilare) o perife-
rica (subpleurica) delle lesioni. Ricostruzioni multiplanari
(MPR) e maximum intensity projection (MIP) sono state
eseguite nel post-processing in tutti i pazienti studiati con
scansioni TC volumetriche.

Risultati

Dei 167 pazienti studiati 161 (96,4%) presentavano febbre,
153 (91,6%) cefalea, 143 (85,6%) tosse, 58 (34,7%) farin-
godinia, 69 (41,3%) diarrea, 57 (34,1%) vomito. 113/167
(67,6%) pazienti presentavano almeno una condizione
clinica patologica pregressa: 76 (45,5%) erano affetti da
asma, 25 (14,9%) erano diabetici, 13 (7,7%) presentavano
broncopneumopatia cronica ostruttiva (BPCO), 23 (13,7%)
immunosoppressione, 65 (38,9%) cardiopatie, 17 (10,1%)
insufficienza renale cronica, 11 (6,5%) disordini cognitivi,
5 (2,9%) patologie neuro-muscolari, 3 (1,7%) malformazio-
ni scheletriche, 2 (1,1%) gravidanza, 1 (0,5%) uso di dro-
ghi. In tutti i pazienti sono state osservate alterazioni dei
parametri ematochimici: 157 pazienti (94%) mostravano
aumento della velocità di eritrosedimentazione (VES), 150
(89,8%) della proteina C reattiva (PCR), 144 (86,2%) della
lattato-deidrogenasi (LDH), 83 (49,7%) linfopenia (<1000
linfociti per mm$^3$), 30 (17,9%) leucocitosi (>10000 leuco-

Fig. 1a, b Uomo, età 55 anni. Presentazione clinica: febbre (38°C), tosse, dispnea. a Radiogramma del torace in proiezione PA: ispessimento diffuso e bilaterale dell’interstizio polmonare più evidente nel campo polmonare inferiore di destra in cui si osserva un addensamento parenchimale del tipo vetro smerigliato. b Sezione assiale di MDCT del torace: l’estensione bilaterale delle aree di GGO viene definita con una più elevata accuratezza rispetto al radiogramma del torace. Un ispessimento dell’interstizio polmonare, rappresentato da aree lineari di incremento della densità polmonare, si osserva nel contesto delle aree di OGG ed intorno ad esse.

lymphopenia (<1,000 lymphocytes per cubic mm), 30
(17.9%) leucocytosis (>10,000 leucocytes per cubic mm),
75 (44.9%) elevated transaminase levels – associated with
hepatomegaly in 19 (25.3%) and 5 (2.9%) thrombocyto-
penia. Elevated ESR (94%), CRP (89.8%) and LDH (86.2%)
were the most frequent blood chemistry abnormalities. On
standard CXR, 90/167 (53.8%) patients showed primary
pulmonary lesions (Figs. 1a, 2a, 3a, 4a) characterised by
different associated patterns, locations and extent (Table
1): IR was seen in 53/90 (58.8%), N in 5/90 (5.5%), GGO
in 13/90 (14.4%), CONS in 50/90 (55.5%). The predomi-
nant combination was GGO and CONS, seen in 6/90 cases
(6.6%). On CT examination, 17/20 (85%) patients showed
primary pulmonary lesions (Figs. 1b, 2b, 3b, 4b, c) charac-
terised by different associated patterns, locations and extent
(Table 2): IR was seen in 14 (82.3%), N in 2 (11.7%), GGO
in 5 (29.4%). The predominant combination was GGO with
CONS, seen in 10 (58.8%). None of the patients showed
isolated pulmonary consolidation, and none of those studied
with contrast-enhanced multidetector-row CT (MDCT)
showed direct and/or indirect signs of pulmonary embo-
lism.

On CXR, findings suggestive of bacterial suprainfection
were seen in various combinations in 14/90 patients (15.5%)
(Table 1): pleural effusion in 9/14 (64.2%), consolidation
with air bronchogram in 4 (28.5%), lymphadenopathy in 2
(14.2%), cavitation in 1 (7.1%), hydropneumothorax in 1
medi o inferiori. È stata inoltre determinata all’indagine TC
la predominante distribuzione centrale (periilare) o perife-
rica (subpleurica) delle lesioni. Ricostruzioni multiplanari
(MPR) e maximum intensity projection (MIP) sono state
eseguite nel post-processing in tutti i pazienti studiati con
scansioni TC volumetriche.
ti per mm³), 75 (44,9%) ipertransaminasemia associata in 19 pazienti ad epatomegalia (25,3%), 5 (2,9%) trombocitopenia. L’aumento della VES (94%), della PCR (89,8%) e dell’LDH (86,2%) hanno rappresentato le alterazioni ematochimiche più frequenti. All’esame radiografico standard del torace 90/167 (53,8%) pazienti presentavano lesioni elementari polmonari (Figg. 1a, 2a, 3a, 4a) caratterizzate da vari pattern di associazione, sede ed estensione (Tabella 1): 53/90 (58,8%) RI, 5/90 (5,5%) N, 13/90 (14,4%) OGG, 50/90 (55,5%) CM. Il pattern di associazione percentualmente più frequente, OGG con CM, si è osservato in 6/90 casi (6,6%). Diciassette/20 (85%) pazienti mostravano all’indagine TC lesioni elementari polmonari (Figg. 1b, 2b, 3b, 4b-c), caratterizzate da vari pattern di associazione.

**Table 1**

| Primary and associated lesions | n     |
|-------------------------------|-------|
| IR, interstitial reticulation; N, nodules; GGO, ground glass opacities; CONS, consolidations |
| **IR**                       | 53 (58.8%) |
| Bilateral, symmetrical and diffuse | 48 (90.5%) |
| Unilateral, multifocal         | 5 (9.4%)  |
| Middle and lower lung fields   | 46 (86.7%) |
| Lower lung field               | 7 (13.2%)  |
| **N**                         | 5 (5.5%)  |
| Unilateral, focal              | 3 (60%)   |
| Bilateral, multifocal and symmetrical | 2 (40%)   |
| Lower lung field               | 3 (60%)   |
| Middle and lower lung fields   | 2 (40%)   |
| **GGO**                       | 13 (14.4%) |
| Unilateral, focal              | 8 (61.5%) |
| Bilateral, symmetrical, diffuse| 5 (38.5%) |
| Middle and lower lung fields   | 6 (46.1%) |
| Lower lung field               | 4 (3%)    |
| Middle lung fields             | 2 (1.5%)  |
| Upper lung fields              | 1 (0.75%) |
| **CONS**                      | 50 (55.5%) |
| Unilateral, focal              | 33 (66%)  |
| Bilateral, symmetrical, multifocal | 7 (14%)  |
| Bilateral, symmetrical, diffuse| 7 (14%)  |
| Bilateral, asymmetrical, multifocal | 3 (6%)    |
| Lower lung fields              | 23 (46%)  |
| Middle and lower lung fields   | 19 (38%)  |
| Middle lung fields             | 6 (12%)   |
| Upper lung fields              | 2 (4%)    |
| **CONS+GGO**                  | 6 (6.6%)  |
| Symmetrical and multifocal     | 5 (83.3%) |
| Focal and unilateral           | 1 (16.7%) |
| Middle and lower lung fields   | 3 (50%)   |
| Lower lung fields              | 3 (50%)   |
| **Signs of bacterial superinfection** | 14 (15.5%) |
| Pleural effusion               | 9 (64.2%) |
| Consolidation with air bronchogram | 4 (28.5%) |
| Lymphadenopathy                | 2 (14.2%) |
| Cavitation                     | 1 (7.1%)  |
| Hydropneumothorax              | 1 (7.1%)  |

**Table 1**

| Lesioni elementari ed associate | n     |
|---------------------------------|-------|
| **RI**                          | 53 (58.8%) |
| Bilaterale, simmetrico e diffuso| 48 (90.5%) |
| Monolaterale, multifocale        | 5 (9.4%)  |
| Campi polmonari medio ed inferiore | 46 (86.7%) |
| Campo polmonare inferiore       | 7 (13.2%)  |
| **N**                           | 5 (5.5%)  |
| Monolaterali, focali            | 3 (60%)   |
| Bilaterali, multifocali e simmetrici | 2 (40%)   |
| Campo polmonare inferiore       | 3 (60%)   |
| Campi polmonari medi ed inferiori | 2 (40%)  |
| **OGG**                         | 13 (14.4%) |
| Monolaterale, focale            | 8 (61.5%) |
| Bilaterale, simmetrico, diffuso| 5 (38.5%) |
| Campi polmonari medi ed inferiori | 6 (46.1%) |
| Campo polmonare inferiore       | 4 (3%)    |
| Campi polmonari medi            | 2 (1.5%)  |
| Campi polmonari superiori       | 1 (0.75%) |
| **CM**                          | 50 (55.5%) |
| Monolaterale, focale            | 33 (66%)  |
| Bilaterale, simmetrica, multifocale | 7 (14%)  |
| Bilaterale, simmetrica, diffusa| 7 (14%)  |
| Bilaterale, asimmetrica, multifocale | 3 (6%)    |
| Campi polmonari inferiori       | 23 (46%)  |
| Campi polmonari medi ed inferiori | 19 (38%) |
| Campi polmonari medi            | 6 (12%)   |
| Campi polmonari superiori       | 2 (4%)    |
| **CM e OGG**                    | 6 (6.6%)  |
| Simmetrica e multifocale         | 5 (83.3%) |
| Focale e monolaterale            | 1 (16.7%) |
| Campi polmonari medi ed inferiori | 3 (50%)  |
| Campi polmonari inferiori       | 3 (50%)   |
| **Segni di sovrainfezione batterica** | 14 (15.5%) |
| Versamento pleurico             | 9 (64.2%) |
| CM con broncogramma aereo        | 4 (28.5%) |
| Linfonodadenopatie               | 2 (14.2%) |
| Cavitazione                     | 1 (7.1%)  |
| Idropneumotorace                | 1 (7.1%)  |

RI, reticolazione dell’interstizio; N, nodulazioni; OGG, opacità ground glass; CM, consolidamenti

On CT, signs of bacterial suprainfection were seen in various combinations in 9/17 (52.9%) patients (Table 2): tree-in-bud pattern in 9/9 (100%), consolidation with air bronchogram in 6 (66.6%), pleural effusion in 4 (44.4%) and pericardial effusion in 3 (33.3%), lymphadenopathy >1 cm in 2 (22.2%), cavitation in 1 (11.1%), and hydropneumothorax in 1 (11.1%). CT confirmed the CXR findings of bacterial superinfection in 9 cases (9/14, 64.2%) and identified as false positive five cases of suspected pleural effusion detected on CXR. In all five cases, the radiograms had been obtained in the supine position and with anteroposterior projection only in poorly cooperative patients. In addition, in 2/9 cases in which CT confirmed CXR signs of bacterial superinfection, it also revealed consolidations with air bron-
chogram, which had gone undetected on CXR. These were located in the basal and retrocardiac regions in radiograms acquired with anteroposterior projection only. Finally, in 3/9 patients in whom CT confirmed the CXR signs of bacterial suprainfection, it also identified the presence of pericardial effusion, which had been missed at CXR in all cases owing to very small size.

Blood and bronchoaspirate culture identified *Staphylococcus aureus* in 3/9 patients and a mixed bacterial flora in 6/9 cases. In 15/167 patients (8.98%), worsening clinical and radiological features required orotracheal intubation and mechanical ventilation after admission to the Intensive Care Unit. All of these patients were affected by an underlying condition: arterial hypertension complicated by placenta previa and postpartum uterine atony (1/15; 6.6%), hypertensive cardiopathy (3/15; 20%), bullous dystrophy (1/15; 6.6%), rib-cage malformations (2/15; 13.3%), obesity (4/15; 26.6%), diabetes (2/15; 13.3%), and drug abuse (1/15; 6.6%). In all cases, CXR and CT findings were characterised by bilateral and diffuse GGO with CONS (Figs. 3a, b, 4a–c). Death occurred in 6/15 (40%) patients due to acute respiratory distress syndrome (ARDS) in four cases and multiple organ failure in two.

**Discussion**

Human influenza pandemics are caused by influenza viruses from nonhuman reservoirs: among the influenza pandemics sede ed estensione (Tabella 2): 14 (82.3%) RI, 2 N (11.7%), 5 (29.4%) OGG. Il pattern di associazione percentualmente più frequente, OGG con CM, si è osservato in 10 pazienti (58.8%). Nessun paziente presentava consolidazioni polmonari isolate. Nessuno dei pazienti sottoposti a MDCT del torace con mezzo di contrasto endovena mostrava segni diretti e/o indiretti da attribuire ad embolia polmonare.

Quattordici/90 pazienti (15,5%) presentavano reperti radiografici sospetti per sovrainfezione batterica (Tabella 1), variamente combinati tra di loro: 9/14 (64,2%) segni di versamento pleurico, 4 (28,5%) consolidamenti con broncogramma aereo, 2 (14,2%) linfonodi, 1 (7,1%) cavitazione, 1 (7,1%) idropneumotorace. Nove/17 (52,9%) casi mostravano segni di sovrainfezione batterica, variamente combinati, all’indagine TC (Tabella 2): 9/9 (100%) albero in fiore, 6 (66,6%) consolidamenti con broncogramma aereo, 4 (44,4%) versamento pleurico e 3 (33,3%) pericardico, 2 (22,2%) linfonodi >1 cm, 1 (11,1%) cavitazione, 1 (11,1%) idropneumotorace. L’indagine TC ha confermato in 9 casi i segni di sovrainfezione batterica identificati alla Rx del torace (9/14, 64,2%) ed ha indicato come falsi positivi 5 casi di sospetto versamento pleurico rilevati alla Rx del torace. In tutti i 5 casi i radiogrammi erano stati acquisiti in posizione supina e nella sola proiezione AP, in pazienti scarsamente collaboranti. Inoltre, in due dei 9 casi in cui la TC ha confermato i segni radiografici di sovra infezione batterica, essa ha individuato consolidamenti con broncogramma aereo misconosciuti alla Rx del torace. Essi erano disposti in sede basale e retro cardiaca in radiogrammi acquisiti nella
of the twentieth century, that of 1918 was cause by a virus of avian origin [14] and the other two, in 1957 and 1968, were caused by new strains resulting from the combination of avian and human viruses through a reassortment process [15, 16]. Viral influenza A is a pandemic caused by a novel influenza virus A/H1N1, which spread worldwide from Mexico in March 2009. The infection is due to pig-to-human transmission of a viral pathogen produced by the triple genetic reassortment of human, swine and avian viral strains in North America and Eurasia; human-to-human transmission occurs through respiratory droplets or contact with infected surfaces [9, 14, 16].

According to the WHO, from the beginning of the pandemic to 15 November 2009, >78,000 cases of influenza A H1N1 were notified in Europe and 190,765 in the Americas, with a death toll of at least 350 and 4,806, respectively [17]. From 19 October, when Influenet monitoring began in Italy [18], to 8 November, there were an estimated 1,521,000 cases of influenza A/H1N1 in Italy sola proiezione AP. Infine, in 3 dei 9 pazienti in cui la TC ha confermato i reperti radiografici di sovrainfezione batterica, essa ha anche rilevato la presenza di versamento pericardico. In tutti i 3 casi esso era stato misconosciuto alla Rx del torace a causa della sua modestissima entità.

All'emocoltura e nel broncoaspirato, in 3/9 pazienti è stato identificato il batterio Staphylococcus aureus, in 6/9 casi una flora batterica mista. Quindici/167 pazienti (8,98%) hanno necessitato di intubazione oro-tracheale e ventilazione assistita, previo ricovero in Unità di Terapia Intensiva, per il peggioramento delle condizioni clinico-radiologiche.

Tutti presentavano condizioni patologiche concomitanti rappresentate da ipertensione arteriosa complicata da placenta previa ed atonía uterina post-partum (1/15; 6,6%), cardiopatia ipertensiva (3/15; 20%), enfisema (3/15; 20%), distrofìa bollosa (1/15; 6,6%), malformazioni scheletriche della gabbia toracica (2/15; 13,3%), obesità (4/15; 26,6%), diabete (2/15; 13,3%), uso di droghe (1/15; 6,6%). Il quadro radiografico e TC si caratterizzava in tutti i casi per la pre-
senza di OGG con CM a distribuzione bilaterale e diffusa (Figg. 3, 4). Sei/15 (40%) pazienti morirono per l’insorgere in 4 casi di acute respiratory distress syndrome (ARDS), in 2 di multi-organ failure (MOF).

Discussione

Le pandemie influenzali umane derivano da virus influenzali provenienti da reservoir non umani: delle tre pandemie influenzali del ventesimo secolo, quella del 1918 è stata causata da un virus influenzale di origine aviaria [14] e le altre due, nel 1957 e nel 1968, sono state provocate da nuove linee virali risultanti dalla combinazione di virus aviari e umani attraverso un processo di riassortimento [15, 16].

L’influenza virale A rappresenta un’epidemia su scala mondiale causata da un nuovo virus influenzale A/H1N1 che si è diffuso nel marzo 2009 dal Messico in tutto il mondo. L’infezione è dovuta alla trasmissione, da parte di alcuni allevamenti suini all’uomo, di un patogeno virale prodotto dal triplo riassortimento genetico delle tipologie virali umana, suina ed aviaria nel Nord America e nei paesi Eurasiatici: il contagio interuomo si realizzerbbe mediante la trasmissione di goccioline di saliva o il contatto delle mani con superfici infette [9, 14, 16].

Secondo l’OMS, dall’inizio della pandemia al 15 novembre 2009, oltre 78000 casi di influenza A H1N1 sono stati notificati in Europa e 190765 nelle Americhe, con un numero di decessi rispettivamente di almeno 350 e 4806 [17]. Dal 19 ottobre, giorno di avvio della sorveglianza Influenet in Italia [18], all’8 novembre, sono stimati 1521 mila i casi di influenza A H1N1 nel nostro paese, con un numero di decessi pari a 53 secondo l’European Centre for Disease Prevention and Control (ECDC) [19].

In Italia le Regioni dove si è registrata la più ampia diffusione del virus sono state le Marche con un incidenza del 2,9% seguite da Emilia Romagna (1,8%), Latium (1,7%), Abruzzo (1,6%) e Campania (1,6%). As of 15 November 2009, when the infection reached its peak, and 53 deaths according to the ECDC (European Centre for Disease Prevention and Control (ECDC) [19]. The Italian regions that recorded the highest incidence of the virus were: Marche (2.9%), followed by Emilia Romagna (1.8%), Latium (1.7%), Abruzzo (1.6%) and Campania (1.6%). As of 15 November 2009, when the infection reached its peak,
the number of influenza A victims had risen to 53, 23 of whom were in Campania, seven in Emilia Romagna, and five in Lombardy. All but three were affected by severe underlying conditions. The most affected age groups were children and teenagers from birth to 14 years of age (incidence 3.6%), and, to a lesser extent, individuals aged 15–64 years (0.7%) and >65 years (0.1%) [19]. A recent paper [8] confirmed that the H1N1 virus is typically transmitted among children and young adults, affecting individuals <18 years in 45% of cases and those >65 years in 5% of cases only. Although in our personal experience the epidemiological impact of H1N1 influenza has been substantially milder than expected, our study population showed a prevalent involvement of the younger age groups [8, 19]: 68.7% <18 years of age, 3.5% >65 years. It has been suggested that older individuals have cross-reactive neutralising antibodies to the H1N1 virus [20]. The higher incidence among individuals <18 years of age may, instead, be related – espe-

Fig. 4a-c A 24-year-old man with moderately fatty liver, alteration of liver function indices, and drug abuse. Clinical findings: fever (38°C), jaundice, acute respiratory failure. a Chest X-ray, anteroposterior projection: diffuse consolidations of both the lungs. b,c Emergency chest MDCT, axial images: massive lobar CONS of both lungs with consequent severe reduction of pulmonary function.

Fig. 4a-c Uomo di 24 anni, affetto da steatosi epatica moderata, alterazione degli indici di funzionalità epatica, abuso di droghe. Presentazione clinica: febbre (38°C), ittero, insufficienza respiratoria. a Radiogramma del torace in proiezione AP: esteso consolidamento di ambedue gli ambiti polmonari. b,c Sezioni assiali di MDCT del torace eseguita in regime di urgenza: estesi consolidamenti panlobari interessano diffusamente ambedue i polmoni con severa riduzione della funzionalità polmonare.
cially as regards children – to mechanisms of immunodeficiency and/or immunological immaturity [21, 22].

The most important reported [8] clinical manifestations of H1N1 virus influenza are: fever (95%), cough (88%), headache (34%), sore throat (31%), vomiting (29%) and diarrhoea (25%). In agreement with these data, the clinical signs of influenza A identified in our study population were fever (96.4%), cough (85.6%), angina (41.3%), vomiting (34.1%) and diarrhoea (41.3%). In addition, similar to previous reports [8], we found elevated liver function tests (44.9%), leucocytes (17.9%) and thrombocytopenia (2.9%). The main underlying conditions were asthmatic bronchitis (45.5%), which was more frequent than reported in the literature [8], heart disease (38.9%) and diabetes (14.9%).

To date, few studies addressing chest imaging in patients affected by influenza A/H1N1 have been published [10–12], and the presentation of H1N1 virus pneumonia on both CXR and chest CT seems to reflect the general features of viral pneumonia [23]. One study [11] reported on the main CXR and chest CT findings in seven patients affected by influenza A/H1N1: bilateral GGO, more frequently associated with focal or multifocal areas of consolidation. At CT, the GGO and the areas of consolidation had a predominant peribronchovascular and subpleural distribution. Agarwal et al. [10] conducted a larger study involving 222 patients affected by influenza A/H1N1 seen between May and July 2009. Of the 66 (30%) patients studied with CXR, 28 (42%) had consolidations (50%), more frequently distributed in the lower lobes. Of the 15/66 (22.7%) patients who underwent CT, 9/15 (60%) had GGO combined with consolidation, with diffuse or lobar extension in 70% of cases. Thromboembolic complications occurred in 8% of cases, and 8% of the patients died.

In agreement with the literature [10, 11], the main primary pulmonary lesions we identified on CXR (53%) (Table 1) were consolidations (55.5%), with prevalent bilateral, symmetrical, diffuse/multifocal extension (14%/14%) and predominant basal distribution (46%) (Figs. 2a, 3a), and GGO (14.4%) (Fig. 1a). The latter had, however, prevalent unilateral and focal extension (61.5%) and predominant distribution in the middle–basal region (46.1%). In our series, we had fewer cases (6.6%) of consolidation combined with GGO, which showed diffuse, symmetrical and multifocal extension (83.3%) and predominant middle–basal distribution (50%) (Fig. 4a). At CXR we found a typically high proportion of patients with interstitial reticulation (58.8%) (Fig. 1a), which showed bilateral, symmetrical and diffuse extension (90.6%) and predominant basal distribution (86.8%). It is likely that the alarmism regarding influenza infection prompted many patients to seek early medical attention, thus allowing detection of interstitial reticulation, an early finding in viral disease. Only 5% of patients had (45.5%), with valori percentuali più alti rispetto ai dati della letteratura [8], cardiopatie (38,9%) e diabete (14,9%).

Allo stato attuale sono stati realizzati pochi studi di imaging del torace nei pazienti affetti da influenza virale A/H1N1 [10–12]. La presentazione della polmonite virale H1N1, sia alla radiografia del torace che alla TC sembra rispecchiare le caratteristiche generali delle polmoniti virali [23]. Alcuni autori [11] hanno descritto le principali alterazioni radiografiche e TC in 7 pazienti affetti da influenza A/H1N1: opacità ground-glass bilaterali, più di frequente associate ad aree di consolidamento a distribuzione multifocale, talora anche focali. All’indagine TC le opacità ground-glass e le aree di consolidamento presentavano una predominante distribuzione peribroncovascolare e subpleurica. Agarwal et al. [10] hanno effettuato uno studio più esteso su 222 pazienti affetti da influenza A/H1N1 da maggio a luglio 2009. Dei 66 (30%) pazienti che avevano effettuato Rx del torace, 28/66 (42%) presentavano consolidamenti (50%), maggiormente distribuiti ai lobi inferiori; dei 15/66 (22.7%) pazienti sottoposti ad esame TC, 9/15 (60%) presentavano l’associazione di ground glass e consolidamenti, ad estensione diffusa ed a sede lobare inferiore nel 70% dei pazienti. Complicanze tromboemboliche venivano descritte dagli stessi autori nel 8% dei casi e, nella stessa percentuale, venivano registrati da essi i decessi.

In accordo con i dati della letteratura [10, 11], le principali lesioni elementari da noi individuate alla Rx del torace (53%) (Tabella 1) sono state CM (55,5%), ad estensione prevalentemente bilaterale, simmetrica, diffusa/multifocale (14%/14%) ed a distribuzione predominante basale (46%) (Figg. 2a, 3a) ma anche OGG (14,4%) (Fig. 1a). Queste ultime presentavano, tuttavia, un’estensione prevalentemente monolaterale e focale (61,5%) e distribuzione più evidente in sede medio–basale (46,1%). Meno rappresentativa (6,6%) è stata, nella nostra casistica, l’associazione di CM e OGG che mostravano estensione diffusa, simmetrica e multifocale (83,3%) e predominante distribuzione medio–basale (50%) (Fig. 4a). Alla Rx del torace abbiamo registrato, caratteristicamente, un’elevata percentuale di pazienti con RI (58,8%) (Fig. 1a) che mostravano estensione bilaterale, simmetrica e diffusa (90,6%) e predominante distribuzione basale (86,8%). È verosimile che l’allarmismo per il contagio influenzale abbia indotto numerosi pazienti a recarsi prontamente all’attenzione medica, rendendo precoce l’osservazione radiografica delle RI, reperto iniziale di danno in corso di malattia virale. Solo il 5% dei pazienti presentava nodulazioni, nel 60% dei casi ad estensione monolaterale e focale e distribuzione basale.

Dei 20/167 (11,9%) pazienti sottoposti ad esame TC abbiamo individuato in 17/20 (85%) pazienti reperti patologici. In accordo con i dati della letteratura [10, 11] le lesioni elementari evidenziate in TC (Tabella 2) sono state OGG associate a CM (58,8%), ambedue ad estensione bilaterale,
nODULES, which showed unilateral and focal extension and basal distribution in 60% of cases.

Of 20/167 (11.9%) patients studied with CT, 17/20 (85%) showed pathological abnormalities. In agreement with the literature [10, 11] the primary lesions identified on CT (Table 2) were GGO combined with consolidation (58.8%), both with bilateral extension and a tendency to asymmetrical and multifocal (80%) (Fig. 2b), rather than diffuse and symmetrical distribution (Fig. 4b,c) (20%). The distribution of GGO combined with consolidation was predominant in the lower lobes (60%) and subpleural regions and was associated in 60% of cases with similar peribronchovascular lesions. Additionally, there were no cases of isolated consolidation without GGO, probably owing to the relatively early observation of the primary pulmonary lesions: in the initial phase of infection, GGOs – earlier lesions in which bronchial and vessel margins are still discernible – manifest alongside consolidations compared with the later phases of disease (not necessarily evolving to ARDS) in which they increase in attenuation and coalesce into consolidations. On CT we also identified 82.3% cases of interstitial reticulation, with prevalent bilateral, diffuse and symmetrical extension (78.6%) and predominant middle–basal distribution (Fig. 1b). These findings appear to corroborate the CXR results and reflect, similarly to CXR, the same early observation of the radiographic findings. Only two cases showed parenchymal nodules, which were focal and unilateral and distributed in the lower lobe; these nodules had already been identified at CXR and were referable to an underlying infectious disease. At variance with previous reports [10], in the contrast-enhanced examinations requested for suspected pulmonary embolism, we found no thromboembolic phenomena involving the pulmonary arteries or their branches.

Recent literature [24–26] has extensively described the principal pulmonary abnormalities seen in bacterial infections: consolidations with air bronchogram, tree-in-bud pattern, cavitation, pleural and/or pericardial effusion and lymphadenopathy. In agreement with these data [24–26], although differently identified by the two imaging modalities (Tables 1 and 2), the most common signs of bacterial suprainfection in our series were tree-in-bud pattern, consolidation with air bronchogram and pleural and pericardial effusion. Blood and bronchoaspirate culture revealed *S. aureus* in 3/9 cases (33.3%) and mixed bacterial flora in 6/9 cases (66.7%). Of the 15/167 patients (8.98%) who received mechanical ventilation due to worsening clinical and radiological features, all had an underlying condition, and in particular, COPD (33.3%). Six of these 15 patients died (40%): four (66.6%) due to ARDS. In agreement with the literature [27], the radiographic and CT findings in these 15 patients were characterised by diffuse and bilateral GGO and consolidation (Figs. 3, 4).
Conclusions

Our study allowed us to determine the main clinical features of a large population of patients admitted to an infectious disease referral centre with a diagnosis of H1N1 virus influenza, thus allowing correct diagnostic, prognostic and therapeutic management.

Conflict of interest None

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